THE EFFECTS OF RECIPROCAL IMITATION TRAINING

ON BEHAVIOUR AND BRAIN ACTIVITY IN

CHILDREN WITH AUTISM

By

SUPRIYA MALIK

A thesis submitted to

The University of Birmingham

for the degree of

DOCTOR OF PHILOSOPHY

School of Psychology

University of Birmingham

March 2016.

UNIVERSITY OF BIRMINGHAM

University of Birmingham Research Archive

e-theses repository

ABSTRACT

The work presented in this thesis comprises the execution and evaluation of a pilot quasi-Randomised Controlled Trial of Reciprocal Imitation Training (RIT) in an attempt to replicate previously reported effects of RIT on imitation skills in children with autism and an evaluation of the effect of RIT on brain functioning. Children with autism were randomised into two groups, Treatment and Wait-List Control, and were assessed before and after intervention. Behavioural measures of spontaneous and elicited imitation were used to assess change in imitation. Event-Related Potentials (ERP) and Electroencephalography (EEG) techniques were used to index changes in human action processing as well as global social and non-social processing. An increase in spontaneous, social imitation skills was evident in the Treatment group compared with the Wait-List Control group. Also, ERP measures assessing auditory human action processing reflected differences in processing at outcome between the Treatment and Wait-List Control group. However, no effect of RIT was observed on global social or non-social neural processing. Together, these findings make contributions towards evaluating the efficacy of RIT as an early intervention program for children with autism with evidence of an impact on social imitation skills at the behavioural and neural level.

To,

The World's Best Parents & Greatest Clinicians,

Ma & Papa

ACKNOWLEDGMENTS

A popular African saying states, "It takes a village to raise a child." I would like to extend this and say it takes a village to complete a PhD! I have many people who I need to acknowledge here for their contributions, efforts and support through the entire PhD.

First and the biggest thank you goes to all the families and children who participated in this research. I want to thank all the parents for continuously supporting and believing in this work and all the wonderful children who made each day of this PhD so joyful. I am forever indebted.

Next, I would like to thank Dr Joe McCleery, my first supervisor, for trusting me with this wonderful project and giving me an opportunity of a lifetime. I am grateful for your guidance, invaluable inputs, training on EEG research and experimental rigour, and support and encouragement till the very end. Next, I would like to acknowledge the contributions of my second supervisor, Prof Chris Oliver. Your guidance, amazing feedback and gentle nudge every time pushed me to take a bigger step. I am grateful to the two of you for turning a clinician into a researcher. I would also like to acknowledge the contributions of my third supervisor, Dr Jo Moss, for her timely feedback and constant encouragement during the writing of this PhD.

I would like to acknowledge the contributions of my colleague and dear friend Dr Chrysi Stefanidou, in training and supporting me during ERP assessments and analysis. You also graciously agreed to be a blind assessor for all the ADOS-G assessments. Sissy, you can now finally come out of the dark! I am also thankful for your encouraging words, the endless crazy conversations and all the love.

giving me the life I have and for encouraging me to pursue my dreams (and for being a great editor!). Papa, you will always be my hero, no day goes by when I don't miss you and wish you were here… I strive to make you both proud each day.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ABBREVIATIONS

ABA	Applied Behaviour Analysis
ADOS-G	Autism Diagnostic Observation Schedule-Generic
ASD	Autism Spectrum Disorders
CA	Chronological Age
CTMs	Comprehensive Treatment Models
DIR	Developmental, Individual-differences & Relationship-based Intervention
dlPFC	Dorsolateral Prefrontal Cortex
EEG	Electroencephalography
EIBI	Early Intensive Behavioural Intervention
ERPs	Event-Related Potentials
ESDM	Early Start Denver Model
FFA	Fusiform Face Area
fMRI	functional Magnetic Resonance Imaging
fNIRS	functional Near-Infrared Spectroscopy
IFG	Inferior Frontal Gyrus
IPL	Inferior Parietal Lobule
JAML	Joint Attention Mediated Learning
JASPER	Joint Attention, Symbolic Play and Emotion Regulation
MNS	Mirror Neuron System
MPFC	Medial Prefrontal Cortex
MSEL	Mullen Scales of Early Learning
NDBI	Naturalistic Developmental Behavioural Interventions

NHS	National Health Service, UK
NVMA	Non-Verbal Mental Age
OFC	Orbitofrontal Cortex
PACT	Pre-school Autism Communication Trial
PEERS	Program for the Education and Enrichment of Relational Skills
PRT	Pivotal Response Training
PSD	Power Spectral Density
Q-CHAT	Quantitative Checklist for Autism in Toddlers
RAMM	Rapid Auditory Mismatch Paradigm
RCT	Randomised Controlled Trial
RDI	Relationship Development Intervention
RIT	Reciprocal Imitation Training
SCERTS	Social Communication, Emotional Regulation and Transactional Support
SCQ	Social Communication Questionnaire
SIA	Structured Imitation Assessment
STS	Superior Temporal Sulcus
T1	Time 1
T2	Time 2
TD	Typically Developing
TPJ	Temporal-parietal Junction
UIA	Unstructured Imitation Assessment
VA	Verbal Age
VABS	Vineland Adaptive Behavior Scales

CHAPTER 1

LITERATURE REVIEW

INTRODUCTION

Autism Spectrum Disorder is a neurodevelopmental disorder characterised by social-communication difficulties and repetitive stereotyped behaviours (DSM-V; American Psychiatric Association, 2013). Since first described by Leo Kanner in 1943, understanding of autism has grown significantly leading to substantive changes in both diagnosis and treatment (Blumberg et al., 2013). The term Autism Spectrum Disorder (ASD) is used as an umbrella term encompassing the previously recognised diagnosis of Pervasive Developmental Disorders, Autistic disorder, Aspergers' Syndrome, Childhood Disintegrative Disorder and Pervasive Developmental Disorder – Not Otherwise Specified (American Psychiatric Association, 2013; the terms autism and autism spectrum disorder (ASD) will be used interchangeably in the text henceforth). Autism interventions have become a prominent strand of autism research with the growing recognition of the highly debilitating effects of the disorder. As autism is primarily a social and communication disorder (American Psychiatric Association, 2013) interventions have mainly focused on the development of social and communication skills. This thesis focuses on Reciprocal Imitation Training (RIT) a social-communication intervention that has been demonstrated to show effectiveness in improving social functioning, particularly social imitation.

The first section of the following review focuses on Autism Spectrum Disorders and imitation deficits observed in autism. Autism interventions are discussed subsequently focusing on RIT as an emerging effective early intervention. The second part of the review focuses on methods of neuroscience as novel techniques for understanding the disorder and evaluating interventions. In this section, social processing in autism and interventions that

have used neuroscientific methods as outcome measures are reviewed. Finally, the rationale and aims of the thesis and an outline of the subsequent chapters is described.

1.1. AUTISM SPECTRUM DISORDER

Descriptions of autism spectrum disorder (ASD) date back to the sixteenth century when a French physician, Itard, described a boy with symptoms of autism (Frith, 1991; Wing, 1997). Autism spectrum disorder, as understood today, was first described comprehensively by Leo Kanner in 1943 with detailed descriptions of deficits in social and communication skills, repetitive behaviours, the desire for sameness and 'special interests'. Since these early descriptions, changes in the definition of autism ensued, the spectrum of autism-related difficulties has been recognised and interventions and treatment practices have changed considerably (Volkmar & McPartland, 2014).

The current prevalence rates for autism vary between 1 in 68 to 1 in 160 in the general population (Blumberg et al., 2013; Centre for Disease Control and Prevention, 2014; Elsabbagah et al., 2012). Diagnosis is five times more likely in boys than girls (Centre for Disease Control and Prevention, 2014) and although age of diagnosis varies, evidence suggests that the earliest signs of autism emerge between 12 and 18 months (Zwaigenbaum, Bryson, & Garon, 2013).

There is substantial variability in the symptomatology observed across individuals and it is now considered that symptoms fall on a continuum (American Psychiatric Association, 2013). Furthermore, autism is often accompanied by co-morbid disorders, with sensory processing difficulties and intellectual disability being the most common. Approximately 80% prevalence of sensory difficulties (Ben-Sasson et al., 2009) and 31% prevalence of intellectual disability are estimated in children with autism (Centre for Disease Control and Prevention,

2014). Attention deficits (Hanson et al., 2013), anxiety disorders (Van Steensel, Bogel, & Perrin, 2011) and depression (Stewart, Barnard, Pearson, Hasan, & O'Brien, 2006) are also co-morbid disorders diagnosed in adolescence and adulthood (Simonoff et al., 2008).

Many theories of the aetiology of autism have attempted to explain the disorder and in the process have also informed intervention practices. Various neurobiological theories focusing on brain mechanisms have been proposed. Gliga and colleagues (2014) and Leekam (2016) have comprehensively classified the theories belonging to four overarching strands: 1) the 'social brain' hypotheses, including social orienting and social motivation theories of autism, 2) domain-general theories, including the executive function and weak central coherence accounts of non-social symptoms in autism, 3) domain-specific theories, primarily including the theory of mind hypothesis and the mentalizing accounts, and 4) the theory of brain-wide neural impairments, including the connectivity accounts (see Gliga, Jones, Bedford, Charman, & Johnson, 2014; Leekam, 2016 for a review). The work presented in this thesis is based largely on the 'social brain' hypotheses and therefore this is the focus of the review.

1.1.1. 'Social Brain' Hypothesis

This hypothesis is based on the premise that there is a network of brain structures associated with processing of social information and perception and it is the dysfunctions seen in this network that lead to symptoms observed in autism (Pelphrey, Shultz, Hudac, & Vander Wyk, 2011).

1.1.1.1. *Social Motivation Theory*

According to this account, core impairments in autism lie in social motivation in infancy, and are responsible for secondary impairments (Dawson, 2008; Dawson, Webb, & McPartland, 2005; Dawson, Webb, Wijsman, et al., 2005). The social motivation theory is based on the premise that motivation deficits have an effect on social cognition and therefore, the behavioural deficits in autism are the result of a lack of social interest (Chevallier, Kohls, Troiani, Brodkin, & Schultz, 2012). Deficits in manifestations of social motivation - social orienting and attention, social rewards, and social maintaining have been found in both the behavioural and neuropsychological literature, providing support for this hypothesis (Chevallier et al., 2012; Dawson, 2008). Additionally, intervention research has shown that an increase in social orienting behaviours, social attention and social synchrony results in better prognosis in early childhood development for children at-risk as well as those diagnosed with autism (Sullivan, Stone, & Dawson, 2014). However, evidence regarding the direction of postulated causal direction, that is, whether social motivation is impaired due to early social cognitive impairments or whether social cognitive deficits are a result of lack of social motivation, is mixed. Some early studies of infants at-risk for autism have found intact social processing while others have found increased social attention. Therefore, although most of the literature in children and adults supports this theory, little conclusive evidence is available from infant research (Gliga et al., 2014). Also, this theory fails to account for all aspects of autism, such as the non-social difficulties, and does not answer questions around the impact of social motivation on learning non-social skills. Furthermore, it does not address the wide range of individual profiles seen in autism or the impact of age on social motivation (Chevallier et al., 2012). Finally, co-morbidities or strengths often associated with the disorder are not accounted for within this framework (Chevallier et al., 2012).

One early childhood skill that is strongly related to social motivation is imitation. Social motivation is argued to drive typically developing children to imitate partners (see Over & Carpenter, 2013) and imitation skill deficits are observed in autism early in life. According to the social motivation theory, lack of social motivation early in life accounts for imitation deficits observed in autism (Van Etten & Carver, 2015).

1.1.2. Imitation Skills

Impairments in imitation in children with autism have been observed as early as 12 months (Rogers, Young, Cook, Giolzetti, & Ozonoff, 2008; Wallace & Rogers, 2010; Young et al., 2011) and are associated with later social-communicative development (Bloom, Hood, & Lightbown, 1974; Byrne & Russon, 1998; Charman et al., 2000; Charman et al., 1997; Rogers & Williams, 2006; Williams, Whiten, & Singh, 2004). There is also evidence of imitation-related impairments in brain responses and mechanisms (Bernier, Dawson, Webb, & Murias, 2007; Oberman et al., 2005; Williams et al., 2004; Vivanti & Hamilton, 2014). Importantly, imitation has been a focus of intervention and a backdrop for future skill development.

1.1.2.1.   Imitation in Typical Development

It has been suggested that newborns as old as only 24-hours can imitate an adult's facial movements successfully (e.g. Meltzoff & Moore, 1983). However, a study by Heimann (1998) highlighted that there was no significant relationship between neonatal imitation and imitation at 12 months, and instead imitation skills at 3 months were correlated to imitation at 12 months (Rogers, 2006). It is believed that neonatal imitation may involve sub-cortical mechanisms in the brain while imitation at 12 months may be controlled by more cortical,

complex mechanisms (Meltzoff & Decety, 2003). The developmental sequence of imitation has yet to be determined with longitudinal studies but reviews suggest that oral-facial movement imitation may develop first followed by object and then goal-directed imitation (Sevlever & Gillis, 2010). A major criticism of neonatal imitation studies relates to the authenticity of imitative responses by the infants, that is, the responses are proposed to be examples of mimicry rather than true imitation (Rogers, 2006). It therefore becomes important to distinguish the various kinds of copying behaviour seen in infants and children.

1.1.2.1.1. Definition of Imitation

Facets of imitation have been described as: stimulus enhancement, emulation, true or insightful imitation, and mimicry or automatic imitation (Sevlever & Gillis, 2010; Vivanti & Hamilton, 2014; Want & Harris, 2002). Stimulus enhancement is any action that directs attention to an object which was previously not attended to, thereby increasing the probability of the observer performing the action (Sevlever & Gillis, 2010; Vivanti & Hamilton, 2014). Emulation involves reproduction of the goals of an action but not the means used to achieve the goals (Heyes, 2001; Vivanti & Hamilton, 2014). True or insightful imitation may be defined as replication of the action along with the understanding of the goals or intention (Heyes, 2001; Uzgiris, 1999; Want & Harris, 2002). Mimicry, on the other hand, is a duplication of the action performed without any understanding of the goal or intention of the action where the observer automatically and unintentionally matches body movements (Vivanti & Hamilton, 2014). For example, seeing a smiling face one may match the facial expression.

Each of these facets of imitation involves observation of a partner performing an act. Therefore, apart from learning the action or object use, there is a social aspect involved in

imitation, with the interaction itself being rewarding (Want & Harris, 2002). Thus, imitation can serve both a learning function (skill development) and a social purpose (engage in social and emotional interactions; Ingersoll, 2008a; Over & Carpenter, 2013). For the purpose of the thesis, imitation is considered in the context of social imitation, where imitative behaviours are embedded in social interaction and the primary purpose of imitation is assumed to be social engagement with a partner.

Another way to examine imitation is based on the task at hand. Object imitation refers to imitation of an action on an object, whereas action or gestural imitation involves imitation of bodily movements, including gestures (Sevlever & Gillis, 2010). Furthermore, imitation may be goal-directed, that is, an action-on-object or meaningful gesture has a clear 'goal', or non-goal directed, where the imitation serves no clear purpose (Bekkering, Wohlschlager, & Gattis, 2000; Vanvuchelen, Roeyers, & De Weerdt, 2011a). Additionally imitation tasks can be single or sequential, immediate or deferred and spontaneous or elicited (Sevlever & Gillis, 2010). The focus of the studies described in this thesis is on spontaneous and elicited imitation of object and gestural or action imitation involving both single and sequential imitation.

1.1.2.1.2. *Social Nature of Imitation*

Imitation does not develop in isolation as it primarily involves observation of a partner's actions and then mapping those actions. Reciprocal interactions involving an interest in the partner and turn taking are key components of imitation (Ingersoll, 2008a; Nadel, Guerini, Peze, & Rivet, 1999; Over & Carpenter, 2013). Child-caregiver interactions by the end of first year focus on imitative play with objects (Uzgiris, 1999) while imitative play in mother-child interactions forms a stable backdrop of interaction throughout early childhood.

Additionally, in the comparative psychology literature the terms imitation and 'social learning' have been used interchangeably (Want & Harris; 2002; Nielsen, Subiaul, Galef, Zentall, & Whiten, 2012). Studies involving peer interactions in toddlers also demonstrate that imitation forms a major part of the peer-interaction as well as basis for both verbal and non-verbal communication between partners (Nadel -Brulfert & Baudonniere, 1982; Eckerman & Didow, 1996). Eckerman and Didow (1996) analysed the use of speech in peer interactions from 16 to 32 months of age. They found that speech vocalisations increased as imitative interactions increased, and imitative vocalisations were also higher during these instances. Thus, this kind of social imitation is important for development of later language (Bloom, Hood, & Lightbown, 1974; Masur, 2006; Charman, 2006). Implications of the importance of imitation in theory of mind development have also been described (Charman et al., 2000; Gopnik & Meltzoff, 1994). Understanding of partner goals and intentions are the building blocks for theory of mind skills and it is in imitative play that children learn intentions and goals (Uzgiris, 1999; Over & Carpenter, 2013). Therefore, the social nature of imitation seems to be closely linked with the development of later, more complex social-communication skills, and disruption in early social imitation may have a significant impact on later development (Rogers & Pennington, 1991; Rogers & Williams, 2006; Williams, Whiten, Suddendorf, & Perrett, 2001).

1.1.2.2. *Imitation Impairments in Autism: The Social Deficit*

Imitation has been argued to be a core deficit in ASD that is strongly associated with later developing social-communication skills (Rogers & Pennington, 1991; Vanvuchelen, Roeyers, Weerdt; 2011a; Vivanti & Hamilton, 2014). In a study by Stone, Ousley and Littleford (1997) the longitudinal association between object and gesture imitation in children

with autism with play skills and expressive language was analysed. The findings suggested that along with a significant improvement in imitation skills from 2 to 3 years, type of imitation was associated with different social-communication skills (Stone et al., 1997). Object imitation was significantly associated with later play skills, while gesture imitation was correlated with expressive language (Stone et al., 1997). McDuffie and colleagues (2005) also demonstrated the association between expressive language and gesture imitation in children with autism where they found that 'commenting' behaviours such as declarative pointing and gesture imitation in children between 2 to 3 years were the only two covariates associated with expressive language 6 months after (McDuffie, Yoder & Stone, 2005). Conversely, Rogers and colleagues (2003) did not find correlations between imitation and later language or play skills in children with autism, although they did report a significant relationship between imitation and initiation of joint attention (Rogers, Hepburn, Stackhouse, & Wehner, 2003). They further reported a highly significant relationship between developmental age and imitative ability, thereby supporting the hypothesis that the relationship between imitation and social communication skills may be mediated by developmental age. A study by Carpenter, Pennington and Rogers (2002) also supports the association between imitation and joint attention in autism where they found that object imitation preceded the development of joint attention. Ingersoll and Schreibman (2006) examined the association between imitation and joint attention and found that teaching object imitation to children with autism increased joint attention skills. In another longitudinal study, Young et al. (2011) followed up four groups of children between 12, 18, 24 and 36 months: infant siblings of children with autism who at 36 months received a diagnosis of autism, infant siblings of children with autism who showed general developmental delay at 36 months, infant siblings of children with autism who developed typically (high-risk) and infant

siblings of typically developing children (low-risk). The study found that an imitation delay in young children later diagnosed with autism was observed at 12 months and this delay was significantly associated with expressive language and social engagement (Young et al., 2011). Thus imitation impairments appear fairly early in life in autism.

Studies that have described in detail the specific nature of imitation impairments in autism demonstrate that impairments can be observed in various aspects of imitation. In one of the first experimentally controlled studies, DeMyer et al. (1972) found that children with autism demonstrated difficulties on bodily imitation tasks to a greater degree than object imitation. Subsequently, studies have demonstrated impairments in object, facial, motor and gesture imitation in individuals with autism of varying ages (for reviews see Edwards, 2014; Williams et al., 2004). However, some studies have not shown an imitation deficit in autism (e.g. Bird, Leighton, Press, & Heyes, 2007; Carpenter, Pennington, & Rogers, 2001; Hamilton, Brindley, & Frith, 2007). At the same time, some researchers have shown that imitation deficits in autism go beyond the difficulties to copy actions to problems associated with more subtle aspects of imitation.

Hobson and Lee (1999) demonstrated the difference in the imitation 'style' of adolescents with autism compared to adolescents with developmental delay. They found that although adolescents with autism demonstrated some imitation, the primary difference was in their inability to imitate the 'harsh' vs. 'gentle' style of the action (Hobson & Lee 1999). The social context also seems to affect imitation abilities in children with autism. In a study by Stone et al. (2004) it was found that children with autism imitated significantly more in structured-elicited and spontaneous instrumental conditions as compared to naturalistic social conditions (Ingersoll, 2008a). Ingersoll (2008b) also found that the context in which imitation is measured is highly important, with children with autism performing worse in a naturalistic

imitation task as compared to structured task. Furthermore, she found that children with autism used much less joint attention during imitation than typically developing children. In another study, McDuffie et al. (2007) assessed motor imitation skills in two to three year old children with autism in three different contexts: elicited, interactive play and observational learning. Attention following was found to be associated with elicited imitation and imitation through observational learning, while social reciprocity was associated with imitation in interactive play (McDuffie et al., 2007). Another aspect of imitation, overimitation, seems to be atypical in children with autism. Overimitation is seen in typical children when children imitate even those actions of their partners that are irrelevant to the goal of the task for the purpose of social interaction (Van Etten & Carver, 2015). Marsh, Pearson, Ropar and Hamilton (2013) found that children with autism, matched on verbal and chronological age to a group of typical children, showed less overimitation as compared to the typically developing group demonstrating that the typically developing children understood overimitation as social interaction with a partner while children with ASD were focused only on the goal of the task. In summary, imitation deficits in autism appear early in life, are particularly related to the social function of imitation and evidence suggests that this skill is fundamental to successful development of later social communication skills.

1.2.   AUTISM INTERVENTIONS

Research on early brain development in autism has suggested that early interactions with the environment can influence neural responses and brain development, thus having a potentially significant impact on later development (Sullivan et al., 2014). Therefore, early

intervention[1] for children with autism could have a beneficial impact on social interaction and future brain development (Dawson, 2008; Gliga et al., 2014; Sullivan et al., 2014; Wallace & Rogers, 2010).

1.2.1. Early Interventions based on Theoretical Models

Early interventions may be based on various theoretical models. A large number of early intervention practices are based on the behavioural model, which highlights reinforcement, prompting, and related processes as key drivers of behavioural change. A number of studies using various experimental designs have evaluated early intensive behavioural interventions (EIBI) with a considerably large evidence-base for these practices (see for reviews Howlin, Magiati, & Charman, 2009; Reichow, Barton, Boyd, & Hume, 2012; Tonge, Bull, Brereton, & Wilson, 2014). However, only one randomised trial has been conducted to date and other trials have used treatment-as-usual groups, making evaluation of EIBI in contrast to other available interventions difficult (Howlin et al., 2009; Reichow et al., 2012). A significant criticism of this approach is that teaching methods are not child friendly, with children working in highly structured settings, primarily listening and following commands (Gresham & MacMillian, 1998; Ingersoll, 2008a; Schreibman et al., 2015).

A second model early intervention practices are based on is the developmental model. This model stresses the importance of early building blocks as crucial for later development. Wagner and colleagues (2014) have identified the key features of developmental approaches as: following the sequence of typical development, using principles of developmental science,

---

[1] The terms intervention, therapy and treatment are used interchangeably in the thesis. There is debate on 'treatment' being an appropriate term in psychological therapies, however, in the present context treatment is defined as any therapy intended to reduce symptoms of a disorder and improve quality of life of the individual.

and being child-centred, relationship based and play based (Wagner, Wallace, & Rogers, 2014). Adult responsiveness is the most important facilitative strategy used, based on the premise that interactions with significant others is critical to social development (Dawson, 2008; Rogers & Dawson, 2010; Wagner et al., 2014). Therefore, social and communication competence is achieved via the reciprocal interaction with the others. Studies of effectiveness of these approaches (in their pure forms) have shown considerable variability depending on the severity of symptoms, age, experimental design of the study, and sample size (Dawson & Bruner, 2011; Foxx, 1996; Lord et al., 2005; Ospina et al., 2008).

Due to the limitations of these intervention programs, recently, researchers have amalgamated the two approaches, resulting in an upsurge of early interventions using both behavioural and naturalistic techniques and approaches (Schreibman et al., 2015).

1.2.1.1.   *Naturalistic Developmental Behavioural Interventions in Autism*

There is growing recognition that both operant and respondent learning in early childhood influence attainment of developmental milestones (Wagner et al., 2014). Thus, the two processes of developmental growth and operant learning cannot be easily separated. In an attempt to bridge the gap between the two approaches and tap the strengths of each, a set of early intervention programs have been developed which combine empirically-driven practices from the learning and developmental models into a new approach called Naturalistic Developmental Behavioural Interventions (NDBI; Schreibman et al., 2015). A few such interventions, with research supporting their effectiveness, include Pivotal Response Training (PRT; Koegel, O'Dell, & Koegel, 1987; Schreibman & Koegel, 2005), Incidental Teaching (Hart & Riseley, 1975; McGee, Morrier & Daly, 1999), Milieu teaching (Alpert & Kaiser, 1992), Early Start Denver Model (ESDM, Rogers & Dawson, 2010), Joint Attention,

Symbolic Play and Engagement Regulation (JASPER; Kasari, Freeman, & Paparella, 2006), Reciprocal Imitation Training (RIT, Ingersoll 2008a) and Early Achievements (Landa, Holman, O'Neill, & Stuart, 2011). They are based on theories of social motivation (Dawson et al., 2005; Dawson, 2008) and interpersonal development in autism (Rogers & Pennington, 1991) and the primary target behaviours are early key deficits such as social imitation skills (Ingersoll, 2008a; Rogers & Dawson, 2010), social synchrony (Landa et al., 2011) and joint attention (Kasari, Paparella, Freeman, & Jahromi, 2008; Kasari et al., 2010).

There is an emerging body of research support for these interventions (Dawson et al., 2010; Landa et al., 2011; Kasari et al., 2006, 2008, 2010, 2014). Also, follow-up studies of these interventions have shown that children are able to successfully maintain gains in social and communication skills (Estes et al., 2015; Kasari, Gulsrud, Freeman, Paparella, & Hellemann, 2012). Therefore, studies of NDBIs have been able to show that by closing the gap between developmental and behavioural approaches, more robust and promising results can be achieved. However, trials comparing the NDBIs to other established interventions such as the EIBI would be necessary to draw firm conclusions regarding their effectiveness over and above the behavioural or developmental models.

The models discussed above can either be comprehensive, aiming to have a broader impact on core ASD deficits, while others may be focused, targeting a single skill (Odom et al., 2010a, b).

Reciprocal Imitation Training (RIT) is one such focused intervention with emerging evidence, which combines both behavioural and developmental methods, and has been shown

to have a significant positive impact on social and communication skills of children with autism (Wong et al., 2013).

1.2.2. Reciprocal Imitation Training (RIT)

The review of the literature in section 1.1.2 outlines the link between imitation and other social skills in both autism and typical development and highlights social imitation as a key skill interlinked with the development of other social abilities. Previous intervention research has demonstrated that children with autism do learn to imitate (Lovaas, Freitas, Nelson, & Whalen, 1967; Metz, 1965), but studies evaluating the context of imitation suggest that imitation skills seem to be more impaired in naturalistic social settings (see section 1.1.2.2.). Therefore, teaching imitation skills to children with autism in a social context may have an impact on the development of later social communication skills, and hence be a key skill to target for early intervention for young children with autism.

Reciprocal Imitation Training or RIT is a naturalistic developmental behavioural intervention that focuses on increasing social imitation skills and gesture use in young children with autism (Ingersoll, 2008a,b; 2010b; 2012). Previous early intervention programs, usually based on behavioural methods, have primarily taught imitative skills in an isolated manner and focused on its learning function i.e. its importance in acquiring new skills, rather than on its social function i.e. its importance to the ability to engage socially and emotionally (Ingersoll, 2008a). RIT was developed to address the social function of imitative behaviour in young children with autism. RIT combines key components from both the behavioural and developmental approaches - prompting, pacing of the prompt, praise, linguistic mapping, contingent imitation, high adult responsiveness, environmental manipulation, following the child's lead, and modelling.

RIT is a brief intervention lasting only 12 weeks with a clear focus on targeting social imitation skills. It is a manualised intervention and has a well-defined fidelity protocol. Even though intensive therapist training in required, being based on highly intuitive practices such as following the child, commenting on what the child is doing etc., it is easily transferrable to parents and naïve therapists. Additionally, being a short-term intervention it can be easily embedded into child programs and allows greater flexibility for individualisation.

Research has demonstrated RIT to be an effective approach in increasing spontaneous object and gesture imitation in young children with autism (Ingersoll, 2010b; Ingersoll & Schreibman, 2006). In a single-subject, multiple baseline design study, RIT was effective in teaching young children with autism object and bodily imitation with increases in language, joint attention and play evident (Ingersoll & Schreibman, 2006). Another study using multiple baseline design showed that RIT was effective in teaching descriptive gesture imitation in a small sample of children with autism (Ingersoll, Lewis, & Kroman, 2007). To assess impact of gesture imitation training on language use, a multiple baseline design study with four children found that three out of the four children improved in language use with addition of gesture imitation training (Ingersoll & Lalonde, 2010). In the only pilot randomised controlled trial involving 21 children with autism, RIT was compared with treatment-as-usual (Ingersoll, 2010b). Children in the treatment group demonstrated significant improvement in both elicited and spontaneous imitation as well as object and gesture imitation (Ingersoll, 2010b). Improvements in joint attention, play and language were also observed post intervention (Ingersoll, 2012). In all the studies mentioned above, naïve, undergraduate therapists were trained for treatment delivery. RIT has been adapted for parent-implementation (Ingersoll & Gergans, 2007; Wainer & Ingersoll, 2013a, 2015) and implementation by siblings (Walton & Ingersoll, 2012). All three studies assessing parent implementation of RIT used multiple

baseline designs, with two studies using a telehealth model of intervention training. In the study by Ingersoll and Gergans (2007) both parent and child behaviour were assessed, and it was found that mothers were able to successfully learn the techniques involved in RIT, and also generalise to their home environment. Further, increase in spontaneous object and gesture imitation was observed in the children (Ingersoll & Gergans, 2007). Wainer and Ingersoll (2013a) compared delivery of RIT between undergraduate therapists and mothers of children with autism, when RIT was taught using an online programme. All therapists and mothers were trained using a manual and online short quizzes and interactive learning tasks (Wainer & Ingersoll, 2013a). Findings showed that both undergraduate therapists and mothers were able to learn RIT techniques (based on fidelity of implementation measures) and children in both groups gained on imitation skills (Wainer & Ingersoll, 2013a). Additionally, another study of parent implementation comparing internet-training model of RIT and parent coaching model found that parents were successfully able to deliver RIT to their children for 10 weeks and children showed an increase in spontaneous imitation from baseline to follow-up (Wainer & Ingersoll, 2013b). Translating RIT to sibling implementation, six sibling dyads were assessed (Walton & Ingersoll, 2012). Four out of six siblings correctly implemented all the key techniques employed in RIT (linguistic mapping, contingent imitation, modelling, prompting and praise) while two children showed variable results (Walton & Ingersoll, 2012). All children with autism showed an increase in imitation skills and joint engagement post-sibling training (Walton & Ingersoll, 2013). Further, RIT has been evaluated with adolescents with intellectual disability, again using a multiple baseline design (Ingersoll, Walton, Carlsen, & Hamlin, 2013). Adolescents with autism demonstrated an increase in both object and gesture imitation and a decrease in self-stimulatory behaviour after RIT (Ingersoll et al., 2013).

RIT has also been compared with other interventions. In a study looking at the use of video modelling and RIT for targeting imitation skills in children with autism, both treatments had similar effects on imitation (Cardon & Wilcox, 2011). Another study comparing the effect of RIT, Milieu teaching and Responsive Interaction on language skills in children with autism showed that children who underwent RIT and Milieu teaching showed significantly greater changes in language skills compared to children who underwent Responsive Interaction; while all three interventions led to increase in social engagement (Ingersoll, Meyer, Bonter, & Jelinek, 2012). Thus, overall, there is consistent evidence of RIT influencing imitation skills in children with autism.

To summarise:

- Social imitation impairments are observable in children with autism and impact later social communication development. RIT is an intervention that targets this primary impairment.

- RIT is a short-term intervention with a 12-weeks programme. Having a short time frame makes it easy to deliver.

- It has a clear focus, a manual and well-defined training protocols including fidelity measures.

- RIT uses simple techniques and is easy to learn. Previous RIT research has used undergraduate students as therapists as well as adapted it for implementation by parents and siblings, all suggesting that it is easily transferrable.

- RIT has a growing evidence-base with studies suggesting its effectiveness in teaching spontaneous object and gesture imitation skills.

- A few studies have also shown that RIT has an impact on broader social skills such as play, joint attention and language. Thus, research suggests that brief,

focused intervention may have a wider impact on social communication development.

All these strengths make RIT a compelling intervention to evaluate for children with autism. The available results suggest that RIT is an effective intervention for social-communicative behaviours in children with autism. However, all studies, except one, have used single-subject multiple baseline designs. Also, one of the major criticisms towards establishing evidence-base for RIT has been that all studies, except one, have come from a single research group and replication of RIT in other lab-settings is required (Wong et al., 2013; Wong et al., 2015). The present study aimed to fill this gap in the RIT literature.

1.2.3. Response to Treatment

As discussed in the above sections, various studies have demonstrated success of early intervention in influencing social-communication skills in children with autism. However, systematic reviews have shown that response to intervention can vary considerably (Howlin et al., 2009; Vivanti, Prior, Williams, & Dissanayake, 2014; Warren et al., 2011). It has been suggested that factors associated with intervention or ingredients of an intervention can impact outcome. There are different aspects of an intervention program that can influence response: dose or number of hours in intervention, the method or techniques used to teach, content or focus of the intervention, and timing or developmental age of the child (Kasari, Freeman, Paparella, Wong, Kwon, & Gursrud, 2005).

Individual child characteristics can also impact outcome such that factors such as IQ, autism symptom severity, chronological age, language, imitation and play skills at pre-treatment have been suggested as predictors of response to treatment (Howlin et al., 2009;

Vivanti et al., 2014). These individual characteristics are important to identify as there is growing agreement in the field that not all children benefit from a single intervention and therefore recommendations for treatment need to be child specific (Camarata, 2014; Howlin et al., 2009; Vivanti et al., 2014; Warren et al., 2011). However research systematically evaluating "responders" and "non-responders" to treatment is limited (Camarata, 2014) and recommendations include efficacy trials to incorporate analysis of predictors of outcomes (Warren et al., 2011; for a detailed discussion see Vivanti et al., 2014).

Previous pilot randomised controlled trial of RIT evaluated association between verbal and non-verbal mental age, spontaneous play acts, and response and initiation of joint attention at pre-treatment to outcome on imitation measures (Ingersoll, 2010b). Number of spontaneous play acts was the only pre-treatment child characteristic associated with increase in spontaneous imitation (Ingersoll, 2010b). Chronological age and autism symptom severity was not evaluated. Harris and Handleman (2000) have previously found that chronological age and IQ at pre-treatment were predictive of outcome such that younger age and higher IQ was associated with better school placement four to six years after EIBI. In a much larger study Perry et al. (2011) also found younger age to be a predictor of better outcomes post-EIBI but also autism symptom severity to be associated with outcome. Sallows and Graupner (2005) found that children with low scores on the communication and social interaction domain of the Autism Diagnostic Interview (ADI, Lord, Rutter, & LeCouteur, 1994) were associated with greater gains in IQ after EIBI suggesting that children with greater social difficulties had poorer outcomes (Sallows & Graupner, 2005). Furthermore, restricted/repetitive behaviours have been previously shown to be associated with later social and play skills (Watt, Wetherby, Barber, & Morgan, 2008) and therefore possible that severity of autism symptoms may be a moderator in impacting play and subsequently imitation skills

in RIT. Thus, along with verbal and non-verbal mental age, chronological age and autism severity may be other child characteristics predicting outcome after RIT and the present study aimed to evaluate these child characteristics.

1.3.   INTERIM SUMMARY

Social imitation is an important early milestone that aids future social-communication development and is a deficit in children with autism. Therefore, intervention practices focusing on social imitation could beneficially influence future development. Early intervention practices have seen considerable growth and Naturalistic Developmental Behavioural Interventions hold promise as effective treatments. Reciprocal Imitation Training is one such intervention program that focuses on developing social imitation skills and has an emerging evidence base. Due to the strengths associated with RIT as a focused intervention but gaps in replication of treatment effects in the literature, it warrants further evaluation of the treatment. Research on factors associated with response to treatment is limited and previous RIT research has shown that child characteristics before treatment can influence outcome post treatment.

1.4.   NEUROLOGICAL   APPROACHES   TO   INVESTIGATING   SOCIAL DIFFICULTIES IN AUTISM

Autism has been discussed primarily from behavioural and developmental perspectives to delineate approaches to understanding the social imitation impairments in children with autism. However, neurophysiological and neuroimaging techniques have also generated research implicating the role of various brain mechanisms in the social deficits observed in autism.

Understanding social difficulties observed in autism from a biological, brain-based perspective is imperative. From the day a child is born the environment directly influences brain development and the steady progress in brain development helps the infant acquire new skills and more complex behaviours. Thus, there is a mutual, interactive inter-relationship between brain and behaviour development that governs growth and progress. In autism, difficulties in social and communication skills have been identified at a behavioural level as early as 12 months (Zwaigenbaum et al., 2013; see also section 1.1.2). Neurological research demonstrates differences in brain activity as early as 6 months (Gliga et al., 2014). Thus, neurological markers may help identify autism earlier and hence contribute to prevention and thus the long-term negative impact autism can have on an individual's life. Therefore, as more sophisticated models of social-communication interventions develop, incorporating measures of neural activity in research studies will help to further understanding of neural markers for autism and modify treatments to have better brain-based outcomes.

Various neurological techniques have been used in autism research. Imaging techniques such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have identified brain regions and circuits implicated in atypical social behaviours while neurophysiological techniques using electroencephalography (EEG) and event-related potentials (ERP) have enhanced understanding of the temporal sequence of social and non-social processing in various parts of the brain. Specifically, ERPs reflect changes in brain activity associated with a stimulus while continuous EEG activity can be measured for power spectral density (PSD), which reflects consistency of synchronous firing of large number of neurons. The following sections highlight studies using both techniques to understand how social processes, such as human action, imitation and social stimuli, are processed in people

with autism, and the use of novel tools such as EEG to evaluate impact of interventions on neural processes[2].

1.4.1. The 'Social Brain' Hypotheses: Neural Processing of Social versus Non-Social stimuli in ASD

Studies have shown the involvement of a network of brain regions in processing social information and perception labelled the 'social brain' (Adolphs, 2009; Grossmann & Johnson, 2007). First proposed by Brothers (1990), the social brain was said to comprise the orbitofrontal cortex (OFC), amygdala and superior temporal gyrus (Adolphs, 2009). Other regions have since been identified in social processing such as the fusiform face area (FFA) during facial perception (Pelphrey et al., 2003); the motor cortex, inferior frontal gyrus (IFG) and inferior parietal lobe (IPL) in human action execution and observation (Rizzolatti, Fogassi, & Gallese, 2001), temporal-parietal junction (TPJ) during mentalizing tasks (Lombardo, Chakrabarti, Bullmore et al., 2011), medial prefrontal cortex (MPFC) in theory of mind (Amodio & Frith, 2006) and the superior temporal sulcus (STS) in a variety of social perception tasks (Pelphrey et al., 2011; Hari, Henriksson, Malinen, & Parkkonen, 2015).

Atypical processing of social stimuli in autism has been suggested based on evidence derived from various neurological techniques, such as fMRI (see Di Martino et al., 2009 for a review) and EEG/ERP (see Jeste & Nelson, 2009 for a review). fMRI studies have shown atypical activation of the amygdala (Baron-Cohen et al., 2000; Baron-Cohen et al., 1999), OFC (McPartland & Jeste, 2015; Sabbagh, 2004), TPJ (Lombardo et al., 2011; Pantelis, Byrge, Tyszka, Adolphs, & Kennedy, 2015), STS (Saitovitch et al., 2012; Zilbovicius et al.,

---

[2] This review focuses on social processes evaluated through various neurological techniques. A review and justification of use of EEG and ERP as novel techniques for measuring change through intervention is presented in Chapter 4.

2013), all regions of social cognition, among others. EEG/ERP studies have also evidenced atypical activity in people with autism. EEG activity is measured in various frequency bands and abnormal activity has been suggested for all bands, delta (1-3Hz), theta (4-7Hz), alpha (8-12 Hz), beta (13-30Hz) and gamma (above 30Hz; Coben, Clarke, Hudspeth, & Barry, 2008; Dawson, Klinger, Panagiotides, Lewy, & Castelloe, 1995; Orekhova et al., 2007; Tierney, Gabard-Durnam, Vogel-Farley, Tager-Flusberg, & Nelson, 2012).

Neurological research has shown disruption in processing across different sensory modalities in individuals with autism. In the visual domain, differences have been found in the perception of biological motion. Biological motion may be defined as characteristic human and animal body movements (Koldewyn, Whitney, & Rivera, 2011). ERP and magnetoencephalography (MEG) studies have shown the role of right hemispheric activity of the occipitotemporal and parietal regions in both infants (Hirai & Hiraki, 2005; Reid, Hoehl, & Striano, 2006) and adults (Hirai, Fukushima, & Hiraki, 2003; Jokisch, Daum, Suchan, & Troje, 2005; Krakowski et al., 2011; Pavlova, Lutzenberger, Sokolov, & Birbaumer, 2004) where source analysis has shown the origins of this activity to be located on the right posterior STS (Jokisch et al., 2005; Krakowski et al., 2011). Neuroimaging studies using point-light displays of whole-body movement have found differences in activation in areas involved with biological motion perception between typically developing individuals and individuals with autism (Herrington et al., 2007; Kaiser et al., 2010; Koldewyn et al., 2011). ERP studies have also found lateralisation differences as well as latency differences in autism compared to typical children (Hirai et al., 2014; Kröger et al., 2013). Moreover, in typically developing children studies have shown specificity of response to biological motion compared to scrambled motion, and differential temporal responses between scrambled and biological

motion (Hirai et al., 2014). Conversely, in autism differential processing between scrambled and biological motion has not been found (Hirai et al., 2014).

Face processing studies show decreased activity in the right FFA in individuals with ASD (Schultz, 2005). Extensive ERP studies in face processing found atypical responses to familiar versus unfamiliar faces (as seen in the P400 response; Dawson et al., 2002) and impaired early processing of upright versus inverted faces (N170 component; McPartland, Dawson, Webb, Panagiotides, & Carver, 2004). Furthermore, evidence for face processing atypicalities are evidenced across ages from infants at-risk for autism (McCleery, Akshoomoff, Dobkins, & Carver, 2009), and children (Webb, Dawson, Bernier, & Panagiotides, 2006) to adults (Webb et al., 2012). Additionally, as for biological motion processing, face processing studies also show specific deviation in processing faces compared to objects in people with autism. Dawson et al. (2002) found that when shown familiar and unfamiliar faces and objects, children with autism evidenced preserved differential processing of familiar and unfamiliar objects (P400 response) but did not show differential processing of familiar and unfamiliar faces, while typically developing children showed a clear differential response. Additionally, children with autism show larger amplitude responses to objects compared to typically developing children and showed slower ERP responses to faces (Webb et al., 2006).

Differential processing in autism has also been reported for auditory stimuli. Gervais et al. (2004) found that individuals with autism did not show activation of the STS as observed for the typically developing control group during vocal sound processing but did show preserved activation patterns during non-vocal sounds. In an EEG study, Jochaut and colleagues found that individuals with autism have atypical gamma and theta oscillations in response to speech (Jochaut et al., 2015). In an ERP study of differential processing between

speech and non-speech (tones) sounds, orienting deficits (measured by the P3a response) were found for speech sounds and no such deficits were observed in the non-speech sounds compared with typically developing children (Čeponienė et al., 2003). These differences in processing have also been observed early in life in children at-risk for autism. Lloyd-Fox et al. (2013) used functional near-infrared spectroscopy (fNIRS) to look at neural responses to auditory social and non-social stimuli (human vocalisation of coughing, crying, laughing or environmental sounds) and visual-social stimuli (adult playing peek-a-boo or incy wincy spider) in 4 to 6 months infants at-risk for autism (siblings of children with autism) and low-risk controls (no immediate family history of autism). It was found that infants at-risk for autism showed a diminished response to visual-social stimuli in the STS as compared to low-risk children. For auditory responses, the infants at-risk showed an absence of response to human vocalisations in the mid-posterior STS while low-risk children showed significant specialisation (Lloyd-Fox et al., 2013). No group differences were observed for environmental sounds (Lloyd-Fox et al., 2013). In combination, these studies highlight the a social deficit across domains and ages in autism at a neural level.

1.4.2. Imitation at a Neural Level: Studies of Human Action Processing in ASD

Imitation studies at a neural level have focused primarily on human action processing. Imitation typically involves observation of an action undertaken by a partner and executing the action observed. EEG studies have shown mu rhythm activity (8-13Hz), measured from the central electrodes over the sensorimotor cortex, is associated with human action processing (Braadbaart, Williams, & Waiter, 2013; Oberman et al., 2005; Oberman, Ramachandran, & Pineda, 2008; Pineda, 2005). Specifically, reduced power in mu rhythm activity (mu suppression) over the sensorimotor cortex was associated with action observation

and execution (Muthukumaraswamy, Johnson, & McNair, 2004). In a study by Saby, Meltzoff, and Marshall (2013) infants as young as 14 months showed mu rhythm desynchronisation over sensorimotor cortex for both hand and foot motion observation. Most studies of action processing though, have considered visual action processing. A few studies published regarding auditory processing and visual-auditory integration in human action observation have implicated various brain regions including the STS, inferior parietal lobule and inferior frontal gyrus in auditory action processing showing separate systems for action sounds and non-action, environmental sounds (Galati et al., 2008; Giusti, Bozzacchi, Pizzamiglio, & Di Russo, 2010; Pizzamiglio et al., 2005).

Studies of children with autism suggest atypical activity in different parts of the brain as well as atypical mu rhythm activity during imitation and action/gesture observation. Nishitani, Avikainen, and Hari (2004) examined responses to oro-facial gestures using MEG in adults with Asperger syndrome and found delayed activation in the inferior frontal lobe and weaker activation in the frontal lobe and primary motor cortex. In an fMRI study, Williams et al. (2006) found weaker activation of parietal lobe, TPJ and amygdala during imitation and action observation conditions. Similar results were found using transcranial magnetic simulation (TMS) for hand gestures, with a negative correlation between ventral premotor cortex and IFG and social impairments in adults with autism (Enticott et al., 2012). Support for atypical action processing in autism also comes from EEG and ERP studies. Oberman et al. (2005) found that both, individuals with ASD and age-matched typical controls, showed mu suppression in EEG activity during action execution (i.e. imitation). However, individuals with ASD did not show mu suppression during action observation while typical individuals did. Similarly, Bernier and colleagues (2007) reported a significant correlation between mu suppression and imitation skills (Bernier et al., 2007). Martineau, Cochin, Magne, and

Barthelemy (2008) examined theta and alpha activity in children with autism and typical controls while watching videos of human action, non-human action, no movement sequence and blank screen. EEG desynchronisation was evident for theta activity (3-5.5Hz) in fronto-temporal and central regions in the left hemisphere for the typical children during human action observation while no desynchronisation was seen in children with autism. Furthermore, an association with familiarity of individual performing action and mu suppression while observing hand actions was seen in children with autism (Oberman et al., 2008). A recent EEG study by Bernier et al. (2013) found that even though there were no differences in mu suppression between a group of children with autism and age-matched typical children, there was a subset of children across the two groups who showed minimal mu suppression and this was associated with poor imitation skills. The authors concluded that imitation skills modulated mu suppression irrespective of diagnosis (Bernier et al., 2013).

There have been no studies conducted using mu suppression and auditory processing of human action stimuli in children with autism, although a recent auditory human action ERP study by Stefanidou (2014) showed that high functioning children with autism demonstrated decreased processing of human action sounds recorded over the frontal and parietal regions. On the other hand, some studies have not found dysfunctions in mu suppression in autism or atypical brain activity during action processing (Bernier, Aaronson, & McPartland, 2013; Fan, Decety, Yang, Liu, & Cheng, 2010; Raymaekers, Wiersema, & Roeyers, 2009; Ruysschaert, Warreyn, Wiersema, Oostra, & Roeyers, 2014; see also Hamilton, 2013 for a review).

Many of the studies of human action processing reported above have implicated the Mirror Neuron System (MNS) in action processing. The MNS, discovered in the macaque monkeys, is considered to be a part of the social brain network (Adolphs, 2009; Frith & Frith, 2010). It is thought to include a specific set of neurons that fire both when an action is

executed and observed, and because of the mirroring properties have importance for processes such as imitation and empathy (Rizzolatti et al., 2001; Iacoboni, 2009). In typically developing individuals, the MNS is said to comprise of the STS, IFG, areas of the parietal cortex, sensorimotor, and premotor cortex (Iacoboni, 2005, 2009). The role of MNS in imitation has been asserted (Iacoboni, 2005, 2009; Molenberghs, Cunnington, & Mattingley, 2009; Rizzolatti & Fabbri-Destro, 2010; Rizzolatti et al., 2001). Furthermore, other social behaviours like action understanding, language, empathy and goal-directed behaviour/intentionality have also been suggested to involve the MNS (for reviews see Molenberghs, Cunnington, & Mattingley, 2012, and Cook, Bird, Catmur, Press, & Heyes, 2014).

Some researchers have extended the MNS theory to autism and have suggested that imitation deficits are observed due to a broken mirror system (Williams et al., 2000). However, many have challenged the theory of mirror neuron deficits as the core driver of imitation difficulties in autism. Some have even queried the existence of the mirror neurons in humans. MNS was originally studied in macaque monkeys and, at present, has not been systematically validated in humans (for detailed discussion see Hickok, 2009). Another major problem in this theory is that a bulk of evidence comes from EEG studies suggesting an association of mu rhythm and MNS functioning. A recent study using a sequential EEG-fMRI design has shown that mu suppression, as seen in EEG activity during action observation, was not linked exclusively to the mirror neuron network but also with other regions of the brain (Braadbaart et al., 2013). It is then difficult to interpret most EEG findings of mu suppression as being associated with MNS activity due to the lack of specificity of mu rhythms to MNS and most EEG studies not using source localization analysis. Also, there is scarcity of

research evaluating the MNS as the cause of the range of imitation difficulties observed in autism (Vivanti & Hamilton, 2014).

Some other researchers have suggested the importance of social experience as a core moderator of the MNS system (Hamilton, 2013; Heyes, 2010, 2013). According to Heyes (2010, 2013), sensorimotor experiences in early infancy shape the integration of motor and sensory neurons by coding similar experiences, which then strengthen the MNS network.

Hamilton (2013) proposed a 'social top-down response modulation' (STORM) model suggesting that past social experiences modulate the visual and motor representations of actions in the brain and then an imitation response is not automatic but rather controlled by social cues and demands. This is supported by findings of atypical action observation and auditory processing of actions where neural mechanisms associated with action execution (upon instruction) are preserved but those associated with action observation, driven by social motivation and social reciprocity, show atypical neural responses. Both these models align with the social theories of autism, especially social motivation theory, (Dawson, 2008; Chevallier et al., 2012) suggesting the importance of early experiences in shaping neural systems and thus supporting the importance of early intervention in autism (see also section 1.2. above).

In summary, although there is no conclusive evidence of mirror neuron functioning, studies using various neurological techniques suggest atypical human action processing in autism.

1.4.3. Integrating Neurological Techniques in Study of Interventions

An important aspect of intervention is to influence biological mechanisms. As the number of studies showing neural dysfunctions in social processing in autism is increasing, there is growing interest in what happens to these dysfunctions post behavioural treatment

(Dawson, 2008). For example, in a study of Pivotal Response Training (PRT), two children with autism aged 5 years underwent training for 4 months (Voos et al., 2013). Both children received the manualised package but individual goals were set based on presenting difficulties. fMRI scans were conducted both pre- and post-intervention while children watched a biological motion task. Both children showed increase in activation of various regions, for Child 1 fusiform gyrus and dlPFC while for Child 2 pSTS, ventrolateral prefrontal cortex and fusiform gyrus (Voos et al., 2013). However, with such a small number of participants and no controls, it is impossible to ascertain the effects of PRT. It is possible that the focus on specific skills may have resulted in greater activation rather than the generic intervention package. Also, the two children showed activation of different regions. A second study of the Early Start Denver Model (ESDM) utilized ERP and EEG power spectral density. EEG data were collected at post-treatment only on a face recognition task from 29 children with autism who were randomised to the ESDM or community intervention group (Dawson et al., 2012). Children in the ESDM group were given intensive intervention over a period of two years and trained on face recognition of colour photographs of four familiar adults (Dawson et al., 2012). Results showed that children in the ESDM group had a faster response to faces as compared to objects while the community intervention group had a faster response to objects than faces (Dawson et al., 2012). Alpha and theta band activity was evaluated for difference of EEG activity for faces and objects. The difference scores showed alpha suppression and greater theta activity for faces compared to objects for the ESDM group with the reverse pattern in the community group (Dawson et al., 2012). No pre-treatment EEG assessments were conducted and EEG/ERPs were used as outcome measures. Without a baseline for brain activity one cannot be sure of whether the effects were due to intervention or the groups differed pre-treatment and therefore, it is difficult to draw conclusions about any

effects from this study. Additionally, the ESDM group was trained on facial recognition. A separate face processing training study has shown that when trained specifically on face recognition, adults with autism showed a greater face inversion effect otherwise known to be atypical in autism (Faja et al., 2012). It is difficult to deduce whether the effects observed in the ESDM study were a result of the special face recognition training the children received or ESDM intervention.

A third study of social-communication intervention in adolescents examined EEG asymmetry in adolescents in response to Program for the Education and Enrichment of Relational Skills (PEERS) intervention (Van Hecke et al., 2013). Adolescents were randomised to a treatment or wait-list group where the treatment group was given 14 weeks of group sessions. Continuous EEG was recorded in an eyes-open condition both at pre- and post-intervention. A change from right to left hemispheric activity in the gamma band was seen in the PEERS group while no change in hemispheric activity was observed in the wait-list group (Van Hecke et al., 2013). All studies mentioned above included participants with an IQ in the typical range. Research suggests that responsiveness to intervention is likely to be different based on intellectual functioning in children with autism. Brain activity patterns have also been observed to depend on verbal abilities and IQ in children with autism (Webb et al., 2015). Therefore, neurological research on how children with autism with lower abilities respond to intervention is limited.

Overall, the results of these intervention studies are unclear whether autism treatment may be modulating brain activity. Including neurological measures in intervention studies could generate valuable information regarding the neural signatures a treatment may affect at the same time enhancing identification of biomarkers associated with behavioural changes

observed in treatment. This, in turn could lead to better understanding of the disorder and refinement of intervention practices.

1.5. CONCLUSION

Autism is a developmental disorder with life-long effects. To date, no single theory has been able to address all the bio-psycho-social deficits along with explaining the strengths and preserved skills often observed. Owing to the widespread social difficulties in autism, many researchers are interested in understanding the link between behavioural-social impairments and the social brain network. The social motivation hypothesis postulates that early social motivation deficits down regulate later social difficulties in autism (Chevallier et al., 2012). Early imitation skill impairments have been linked closely to social motivation deficits.

Early imitation skills have been shown to be impaired in children with autism and studies have differentiated deficits in imitation based on function. Research indicates a social deficit in imitation in which imitation impairments occur primarily in reciprocal, interactive settings and early imitation skills have been associated with development of more complex social communication skills. Neurological research also points towards a particular deficit in social processing. Thus, it has been suggested that intervention practices for children with autism might usefully focus on imitation development in order to influence later social development. Also, as biological mechanisms associated with social processing have been implicated in autism, it is important to understand how early intervention may influence neural processing. Evidence from naturalistic developmental behavioural interventions is promising and indicates more stable child gains though gaps in literature remain.

Reciprocal Imitation Training (RIT) is a focused intervention program that addresses social imitation deficits and aims to increase social reciprocity, social imitation and engagement in children with autism. Research shows significant gains in gesture and object

imitation and other social skills (Ingersoll, 2010b, 2012). Although there is some evidence for efficacy of RIT, independent replication is required and RIT is not currently recognised as an evidence-based treatment (Wong et al., 2015; Figure 1.1). Finally, with evidence that the methods of neuroscience can help understand the biological underpinnings of behaviour in autism and the efficacy for treatments, research evaluating RIT would be strengthened by the inclusion of neurological assessment.

The main aim of the work described in this thesis was to conduct a pilot Randomised Controlled Trial to examine the effects of RIT in young children with autism at the behavioural and neural level. The aims of the thesis were to:

1. Attempt possible replication of the previous effects of RIT on social imitation skills by examining the effects on spontaneous and elicited imitation.

2. Explore the association of different child characteristics with changes in imitation post-RIT.

3. Investigate neurological correlates of behaviour changes in imitation by using ERP methodology to examine auditory human action processing in children who underwent RIT compared to controls.

4. Investigate correlation between ERP responses and changes in imitation skills post-RIT.

5. Examine, neural correlates of global social and non-social processing differences using an EEG measure in children with autism and typical children.

6. Examine differences in global social and non-social processing in children who underwent RIT compared to controls.

7. Examine association between global social and non-social processing reflected in EEG activity and changes in imitation skills after RIT.

Thus, the studies were designed to extend the evidence-base for efficacy of RIT as a social-communication intervention that targets both the behavioural and brain development of children with autism.

1.6.   OVERVIEW OF THE SUBSEQUENT CHAPTERS

This thesis investigates effects of an early intervention program, Reciprocal Imitation Training, in children with autism using a rigorous experimental design and novel methodologies. The subsequent chapters are focused on design of the study and the aims outlined above. All chapters may include some overlap in studies reviewed due to the specific focus of the thesis on imitation, RIT and neural techniques for evaluating autism interventions. Also, in the introduction of each chapter aims are refined and specific aims and hypotheses are defined based on focus of the study discussed.

Due to the increasing recognition of the importance of Randomised Controlled Trials (RCT) as an experimental design, Chapter 2 describes RCTs along with recognised strengths and limitations. The chapter highlights the stringent criteria of RCTs adhered to by the present study and various ethical considerations

Chapter 3 describes the first aspect of the pilot RCT, which focuses on the effect of RIT on imitation skills in children with autism. This study is a replication trial to address the issue of independent replicability of the positive results observed through RIT in previous studies.

Chapter 4 describes the use of a neurophysiological measure, event-related potentials (ERP) to understand the impact of RIT on auditory processing of human action and non-human action sounds. This chapter reviews the advantages of using EEG and ERP techniques in evaluating autism interventions and addresses questions about the impact of an imitation intervention on neural mechanisms impaired in human action/imitation processing.

Chapter 5 investigates the use of another neurological measure, electroencephalography (EEG) to understand the impact of RIT on continuous EEG activity in children with autism while watching social and non-social stimuli. The chapter involves a review of EEG studies focusing on theta and alpha band frequencies and atypical processing observed in autism in these two bands. The first study is an investigation of differences in EEG activity during social and non-social processing in children with autism and typically developing children, and the second study examines the effect of RIT on global social and non-social processing in children with autism using EEG as a measure of change. This chapter addresses the questions regarding dysfunctions observed in social brain activity and the impact of RIT on general social processing.

Finally, Chapter 6 concludes with findings from the thesis and implications and suggestions for future research.

CHAPTER 2

STUDY DESIGN: RANDOMISED CONTROLLED TRIALS

2.1. INTRODUCTION

Randomised controlled trials (RCT) are considered the "gold standard" for establishing evidence-based practice in all spheres of healthcare (Concato, Shah, & Horwitz, 2000). Typically, an RCT involves individuals being randomly assigned to one of two or more groups in order to examine causality of relationship (Stolberg, Norman, & Trop, 2004). RCTs have detailed, strict design features that make this form of experimental design a robust method for determining a causal relationship and assessing effects of treatment.

All RCTs have two important characteristics: a control condition and random assignment of participants (Sibbald & Roland, 1998; Nock, Janis, & Wedig, 2008). The comparison control condition helps researchers to draw conclusions about whether the outcome is an effect of treatment and not due to extraneous variables. Similarly, random assignment reduces possible differences between the treatment and control group(s) that might affect results, thereby minimising confounding factors. Hence, any significant differences between the groups at outcome can be more confidently attributed to the intervention. Additionally, in order to control for experimenter/therapist bias, blinding procedures can be used so that examiners are unaware of the group/condition assignments of participants (West & Spring, 2007). Through these mechanisms researchers can minimise confounding factors. Furthermore, RCTs can exercise strict control over exposures to treatment and aim to reduce the role of chance factors. These experimental designs are, therefore, considered optimal to detect statistically small to moderate treatment effects, which is often a challenge in other observational and experimental designs.

Despite their strengths, RCTs can have serious limitations. Most often, studies using placebo-based control groups involve designs in which some individuals are randomised to a

treatment group receiving the new, potentially effective treatment while others, randomised to a control group, receive a placebo (Nock et al., 2008). However, in psychosocial intervention studies placebos are not always feasible, even though placebo-therapies have been used in a few psychosocial trials (e.g. Hofmann & Smits, 2008). The control group, then, comprises of either a treatment-as-usual (TAU) group, that is, all treatments readily used in the community or a specific treatment against which to evaluate comparative effectiveness. In some cases, a No Treatment group is used, in which control participants receive no other treatment. To address the ethical issue of not providing intervention, a *Wait-List Control group* design can be employed in which a group of individuals serve as a control group for a specific period of time and, then receive treatment (Nock et al., 2008). In this approach, no one is denied treatment, however, attrition rates may be higher, as people who are not receiving the given treatment may find clinical help or support elsewhere and drop out of the study (West & Spring, 2007). Furthermore, Wait-List and TAU control studies can result in somewhat heterogeneous clinical exposures in the comparison group, as many of the participants often receive a mix of different treatments while others may receive no treatment at all. Finally, wait-list control designs in which the waiting period is long may result in worsening of symptoms over time (West & Spring, 2007). Therefore, when designing an RCT it is essential to consider the nature of the control group as well as how participants and clinical exposures are monitored. Other critical questions associated with RCTs relate to costs and feasibility (West & Spring, 2007). Randomised trials are typically expensive and involve a large consortium of individuals, including both research participants and clinical/research experts. This often makes RCTs less feasible when compared with other experimental designs (West & Spring, 2007). Lastly, it may not be feasible to conduct a robust RCT for some

interventions or settings; for example, when examining treatments for serious medical conditions involving high and short-term rates of mortality (Stolberg et al., 2004).

It is clear that carefully and properly designing the RCT is an important first step. The study design for the present RCT is described below.

2.2. THE PRESENT STUDY

The current quasi-randomised controlled trial was designed to evaluate Reciprocal Imitation Training (RIT; see section 1.2.3) as a treatment programme for developing social imitation skills in young children with autism spectrum disorders. Previous research, including a pilot-RCT, has suggested that children with autism who undergo RIT make gains in spontaneous imitation skills as compared with children with autism who did not receive RIT (Ingersoll, 2010b). In order for a treatment program to be recognised as evidence-based, independent replication of results is crucial along with replication by researchers other than the treatment developers (Carroll & Rounsaville, 2008). Replicability of results helps to ascertain effectiveness of treatment in different sample populations, reducing population bias and therefore increasing the reliability and generalisability of treatment effects for different individuals with a particular condition (Carroll & Rounsaville, 2008). Therefore, the broad aim was to conduct a pilot-RCT to attempt possible replication of behavioural findings and explore neurological correlates of behavioural treatment in children with autism spectrum disorders, thereby adding to the body of evidence for RIT as an effective focused treatment program for children with autism.

2.1.1. Study Design

The quasi-RCT was designed using a Wait-List Control design (Figure 2.1), wherein participants were randomised using stratified randomisation procedures into a Treatment or

Wait-List Control group. All children were then tested at two time points: initial assessment (T1) prior to any intervention and post-intervention assessment (T2) twelve to fourteen weeks following the initial assessment.

The length of waiting time was matched to the length of time in treatment, 12 to 14 weeks. The waiting time between diagnosis and receiving access to support services in the community is approximately 10 months (Keenan, Dillenburger, Doherty, Byrne, & Gallagher, 2010; Renty & Roeyers, 2006), thus waiting time in this study was seen to be comparable, reasonable and appropriate. Furthermore, the time of the second round of post-intervention assessment (T2) was matched across participants in order to decrease threats to internal validity (see Appendix F). Lastly, both groups were monitored for other treatment services that they may be enrolled in through the use of an Intervention Record Form (Appendix D) with families asked to complete Part A and B if the child was in the Treatment group and Part B only if the child was in Wait-List Control group.

Figure 2.1: Study design of the present quasi- RCT

Recruitment
website, word of mouth, parent support groups

Telephone Call

Eligibility Screening
sensory impairment, seizure disorder, genetic syndrome, etc.

1 to 2 Lab Visits

Intake Assessments (T1)
ADOS, MSEL, VABS, SCQ, Dev History

2 to 3 Lab Visits

Experimental Change Measures (T1)
Behaviour: Structured Imitation Assessment (SIA), Unstructured Imitation Assessment (UIA)
Electrophysiology: EEG Social vs Non-Social Videos, ERP Human vs Non-Human Sounds

Stratified Randomisation
MSEL-EL/CA, Coin-flip

12 to 14 Weeks

Treatment Group
20 Sessions of RIT

Wait-List Control Group
Treatment-as-Usual

2 to 3 Lab Visits

Experimental Change Measures (T2)
Behaviour: SIA, UIA
Electrophysiology: EEG Social vs Non-Social Videos, ERP Human vs Non-Human Sounds

12 to 14 Weeks

Training
20 Sessions of RIT

2 to 3 Lab Visits

Experimental Change Measures (T3)
Behaviour: SIA, UIA

A-priori inclusion and exclusion criteria were employed to maintain a homogenous sample and reduce the impact of pre-treatment participant characteristics on results. Inclusion criteria were as follows: (1) chronological age of two to six years, (2) formal clinical diagnosis of ASD or in the process of being formally assessed for a diagnosis of ASD from a licensed NHS clinician, (3) difficulties in spontaneous imitation skills as measured by The Unstructured Imitation Assessment (McDuffie et al., 2007). Exclusion criteria for the study were as follows: (1) having a primary sensory impairment (e.g. blindness, hearing loss), (2) known presence of a seizure disorder, (3) major birth complications[3], (4) extreme prematurity at birth (3+weeks), and (5) known presence of a neurogenetic disorder (e.g. Down Syndrome, fragile X Syndrome). There were also exclusion criteria set for after T1 assessments that included: (6) not meeting the ASD criteria on Autism Diagnostic Observation Schedule – Generic (ADOS-G; Lord et al., 2000) or (7) having a developmental age below 15 months on the Mullen Scales of Early Learning (MSEL; Mullen, 1995). Children were not excluded on the basis of gender, intellectual ability, challenging behaviours, or autism symptom severity, in order to have a sample heterogeneous enough to produce generalisable conclusions to the larger ASD population.

Stratified randomisation was used whereby participants were first matched on chronological and expressive language age (as assessed by the expressive language scale of the MSEL) before being randomised to one of the two experimental conditions. As previous research indicates a strong association between imitation and expressive language, expressive language was chosen as a matching criterion (Charman et al., 2000; Ingersoll & Meyer, 2011). Furthermore, expressive language is considered a more stringent matching criterion

---

[3] Major birth complications were assessed using the first section of the Early Developmental History questionnaire (Golding, 2009), which asks questions around pregnancy and birth of the child. If any complication was reported by parent, it was then dealt with on a case-by-case basis to decide if the complication reported is known to have an effect on development in any way. Only two parents reported major birth complications and these are discussed in Chapter 3.

than non-verbal mental age and has been used previously in many studies of autism (Ingersoll, 2010b; Ingersoll & Lalonde, 2010). Therefore, participants were matched within $\pm$ 9 months on chronological age and $\pm$ 6 months on expressive language age. Six months of expressive language was decided as criterion based on norms used for standardised tools that suggest changes in scores on the Mullen Scales of Early Learning after 6 months of re-administration (Mullen, 1995). Nine months on chronological age was used as criteria based on previous research. Using a coin-flip method, each child was randomly assigned to one of the two groups: Treatment or Wait-List Control group. If there was a child already in the study who matched the incoming child on chronological age and expressive language age, the incoming participant was assigned to the contrast group, that is, if a child in the Treatment group matched on chronological and expressive language age with the incoming child, the incoming child was assigned to the control group.

The Treatment group received 20 sessions of RIT immediately after the first set of assessments (maximum period between last day of assessment and beginning of intervention was controlled to 14 days), over a period of 12 weeks for a duration of one hour, twice or three times every week; while the Wait-List Control group continued to receive community intervention as usual. After a period of 12 weeks, participants in both groups were invited back for a second set of assessments (T2). Following the T2 assessments, the Wait-List Control group received 20 sessions of RIT.

Data from the two groups were analysed for initial differences at T1 using two-tailed independent samples t-tests. Treatment effects were then examined by statistical tests examining the effects of Group (Treatment, Wait-List) and Time (T1, T2) using experimental change measures.

An independent postgraduate research assistant, who was blinded to the group assignment of participants, administered all primary behavioural outcome measures at T1 and T2. Further, the outcome measures were scored by a set of undergraduate student research assistants who were also blinded to group assignment and timing of assessment of the participants. This double-blinding procedure minimised examiner biases while administering and scoring assessments.

The Wait-List Control group received 20 sessions of RIT after T2 assessment. Nine out of twelve participants received RIT training after T2 assessments while three participants dropped out (attrition rate 25%). However, timing control could not be maintained in this group. Three out of the nine participants began RIT three months after T2 assessments while two participants began RIT five months after T2 assessments. As time of assessment and intervention differed by three months, and because of the developmental age of the children in the present sample, T2 assessments were not considered a valid representation of imitation skills immediately before beginning RIT. Although the Wait-List Control group was reassessed on the behavioural change measures after RIT (T3), due to the time lag between T2 assessment and the beginning of RIT for most participants, the Wait-List Control group data was not considered fit for any analysis post T2.

2.3.   ETHICAL CONSIDERATIONS

The present study was approved by the Ethical Review Committee at the University of Birmingham (Appendix A). Various ethical considerations were addressed while designing and conducting the research. Internal Review Board approved informed consents were taken from parents/caregivers (Appendix B). Data protection was ensured using strict protocols developed in the Cerebra Centre for Neurodevelopmental Disorders at School of Psychology, University of Birmingham. Potential risks to children were minimised by ensuring good lab

conditions, regular safety checks, and by using child-friendly materials and techniques. Parents/caregivers were made aware that they could withdraw from the study at any time and this would have no adverse repercussions for the family or child. For a detailed description of all ethical considerations see Appendix A.

CHAPTER 3

PILOT QUASI-RANDOMISED CONTROLLED TRIAL

OF THE EFFECTS OF RECIPROCAL IMITATION TRAINING

ON IMITATION SKILLS IN CHILDREN WITH AUTISM

3.1. INTRODUCTION

Butterworth (1999) defined imitation as "when one individual voluntarily reproduces behaviour as observed in another who acts as the model for the form of a behaviour" (p.65). Like most skills in infancy, imitation has a dyadic component, developing during interactions with caregivers. Observational studies of early mother-child interaction have found that a greater number of imitative acts by the mother are significantly associated with greater imitative behaviour in their infants (Masur, 2006). As discussed in Chapter 1 section 1.1.2.1, the very social-communicative nature of imitation has been proposed to form the basis for critical aspects of language development (Bates & Dick, 2002; Carpenter, Nagell, Tomasello, Butterworth, & Moore, 1998), pretend play (Nielsen & Dissanayake, 2004), learning tool-use (Nagell, Olguin, & Tomasello, 1993; Want & Harris, 2002), and acquiring ways of the culture (Butterworth, 1999; Uzgiris, 1999; Over & Carpenter, 2013). Therefore, imitation seems to be an extremely important skill which helps to thread together child social development and learning from infancy to early childhood (See section 1.1.2.1 for a review).

Research on children with autism suggests a particular impairment in imitation skills (Williams et al., 2004). Impairments have been found in various forms of imitation, including action-on-object (Charman et al., 1997; Williams et al., 2004), deferred imitation (Rogers et al., 2008), gesture imitation (Ingersoll & Meyer, 2011; Smith & Bryson, 2007), and social aspects of imitation (Ingersoll, 2008a; McDuffie et al., 2007, see also section 1.1.2.2). Deficits specific to the social nature of imitation have been repeatedly found in this population (Ingersoll, 2008a,b; see section 1.1.2.2). Dawson and Adams (1984) found that children with autism showing lesser social behaviours (i.e., looking, gesturing, smiling, vocalising, and touching the experimenter) also showed lesser spontaneous imitation. This

discrepancy in spontaneity of imitation versus prompted or elicited imitation highlights the dichotomy of imitation skills in children with autism where the skill per se may be preserved or delayed but the social/contextual nature of exhibiting the skill may commonly be where the impairments lie. This early social, spontaneous imitation deficit also provides support for the social motivation theory of autism (Van Etten & Carver, 2015). Recent studies examining visual attention during action observation for imitation in children with autism further support this notion of underlying social motivation deficits (Gonsiorowski, Williamson, & Robins, 2015; Ingersoll, Schreibman, & Tran, 2003).

In light of the perceived importance of imitation in development and the imitation impairments that have been associated with children with autism, a number of intervention programmes have focused on teaching imitation skills. Specifically, spontaneous, social use of imitation has been targeted previously with some success in this population (Dawson & Adams, 1984; Hwang & Hughes, 2000; Klinger & Dawson, 1992). Ingersoll (2008a, 2010b, 2012) developed a focused intervention program, Reciprocal Imitation Training (RIT), which teaches children with autism spontaneous social imitation in a naturalistic play based setting (see section 1.2.3). There is growing body of research supporting RIT as an evidence-based practice for this population (Ingersoll, 2010b, 2012; Ingersoll & Gergans, 2007; Ingersoll, Lewis, & Kroman, 2007; Ingersoll & Schreibman, 2006). Furthermore, studies have suggested that RIT also has collateral effects on language, play, and joint attention skills (Ingersoll, 2012; Ingersoll & Lalonde, 2010; Ingersoll & Schreibman, 2006). Owing to this promising dataset of positive effects in experimental studies, RIT has been recognised as an "emerging evidence-based early intervention" for children with autism (Wong et al., 2015). As mentioned in Chapter 1 section 1.2.3, a limitation in RIT research that has been

consistently found is lack of external replication studies (Wong et al., 2013; Wong et al., 2015).

An important factor affecting treatment outcome that has gained recognition is individual child characteristics (see Chapter 1 section 1.2.4). A previous RCT of RIT evaluated pre-treatment verbal and non-verbal mental age, spontaneous play and joint-attention as predictors of outcome and found only spontaneous play to be correlated with change through RIT (Ingersoll, 2010b). However as noted in Chapter 1 section 1.2.4, chronological age, IQ and autism symptomatology have been shown to predict treatment outcome and may be important child characteristics influencing outcome of RIT.

Thus, the aim of the present study was to conduct a pilot randomised controlled trial designed to replicate the previously observed behavioural effects of RIT in an external laboratory. Specifically, the study aimed to replicate the previous effects of RIT on social imitation skills by examining effects on spontaneous and elicited imitation. It was hypothesised that children with autism receiving RIT will show significantly greater gains in spontaneous imitation (as measured by the Unstructured Imitation Assessment) compared with a Wait-List Control group. Secondly, it was hypothesised that children with autism receiving RIT will show significantly greater gains in elicited imitation (measured by the Structured Imitation Assessment) compared with a control group. The second aim was to explore association of child characteristics of chronological age, autism symptoms, and verbal and non-verbal mental age, with changes in imitation post-RIT.

3.2. METHODS

3.2.1. Participants

Thirty-six children with an Autism Spectrum Disorder (ASD), or suspected ASD, aged between two and six years were recruited for participation from the Greater Birmingham region via various service agencies including parent support groups, NGOs such as Autism West Midlands and Cerebra, along with advertisements in social media (e.g., Facebook), and by word of mouth. Flyers were also distributed in the local community, and parents who expressed interested were telephoned to explain the study in detail and obtain initial agreement to participate. A brief phone interview was conducted to determine if the child met the initial criteria for participation. Exclusion criteria[4] for participation in the study included: (1) having a primary sensory impairment (e.g. blindness, hearing loss), (2) known presence of a seizure disorder, (3) major birth complications, (4) extreme prematurity at birth (3+weeks), and (5) known presence of a neurogenetic disorder (e.g. Down Syndrome, fragile X Syndrome). There were also exclusion criteria for post-initial assessments that included (6) not meeting criteria for an ASD on the Autism Diagnostic Observation Schedule – Generic (ADOS-G; Lord et al., 2000); (7) having a developmental age below 15 months on the Mullen Scales of Early Learning (MSEL; Mullen, 1995); or (8) reaching ceiling performance on the Unstructured Imitation Assessment (UIA; McDuffie et al., 2007).

Six children were excluded from participation following the initial assessment, based upon these criteria: mental age of below 15 months ($n = 1$), did not meet the ASD criteria on the ADOS-G ($n = 2$), reached ceiling on the UIA ($n = 1$), diagnosis of seizure disorder ($n = 1$) and diagnosis of genetic disorder ($n = 1$). Out of the total sample recruited, six children

---

[4] These criteria are defined in Chapter 2, however for the purpose of completeness of the chapter have been mentioned again.

dropped out of the study. Five children dropped out either after or during the first round of pre-assessments. Reasons given included time commitment required ($n = 2$) and distance between the participants' home and the research laboratory ($n = 2$). Contact could not be made with one family and therefore the reason for dropout remains unknown. One child dropped out during the intervention stage of the study due to a diagnosis of hearing loss.

A total of twenty-four children were included in the final sample. Twenty two children had received a clinical diagnosis of Autism Spectrum Disorder from a licenced NHS clinician, and two children underwent clinical assessments via the NHS and were being monitored for six months, though they all met the criteria for an Autism Spectrum Disorder on the ADOS-G (Lord et al., 2000) as administered by a research reliable administrator. Participant characteristics are described in Table 3.1. Independent samples t-tests and chi-square tests were conducted to analyse the two groups for differences on age, gender, ethnicity, hours of outside intervention, non-verbal mental age, verbal mental age, autism severity and imitation abilities at T1. No significant differences were found between groups (Table 3.1).

Table 3.1: Participant characteristics by group.

	Group *M (SD)*		χ^2 / t	*df*	*p*-value (two-tailed)
	Treatment (*n*=12)	**Wait-List Control (*n*=12)**			
Gender (% male)	58.3%	83.3%	1.82	1	0.18
Ethnicity (% minority status)	92%	66.7%	2.27	1	0.13
Chronological Age (in months)	46.1 (15.4)	44.1 (15.8)	0.27	22	0.79
Nonverbal Mental Age	25.5 (10.8)	22.7 (8.2)	0.71	22	0.49
Verbal Mental Age	15.7 (8.4)	16.5 (12.8)	-0.18	22	0.86
ADOS total score	14.17 (3.6)	14.67 (4.1)	-0.32	22	0.76
SCQ	21.9 (7.6)	22.8 (4.8)	-0.34	21	0.74
Q-CHAT	54.8 (7.8)	50.1 (11.8)	0.83	11	0.43
Adaptive Behaviour Standard Score (VABS)	67.1	65.3	0.36	19	0.73
Hours of outside intervention per week	4.33 (7.9)	8.5 (12)	-1.0	22	0.32
Elicited Imitation (T1, SIA)	8.6 (12.2)	9.9 (13.7)	-0.79	22	0.80
Spontaneous Imitation (T1, UIA)	4.58 (5.5)	6.75 (7.7)	-0.25	22	0.44

3.2.2. Design and Procedure[5]

The present study was designed as a quasi-Randomised Controlled Trial (see Chapter 2 for details). Briefly, after receiving consent for participation participants were assessed (T1) on a battery of developmental and behavioural measures assessing the child's cognitive, language, and imitation skills. Based on the matching criteria of chronological and expressive language age children were randomised to two groups – Treatment group or Wait-List Control group. Children in the Treatment group received RIT for 20 sessions for 12-14 weeks, 2-3 hours per week, while children in the Wait-List Control group received treatment as usual. Children in both groups were then re-assessed after 12-14 weeks (T2) on imitation measures, to determine whether group differences in performance were associated with the intervention. Following the second round of assessments, the control group received 20 sessions of RIT for a period of 12-14 weeks.

3.2.3. Measures

All participants underwent series of assessments that can each be categorised into one of the following: background history questionnaires, descriptive behavioural measures, and primary outcome measures.

3.2.3.1. Background History Measures

Parents were asked to complete a packet of questionnaires in order to provide detailed information regarding their child's development as well as familial history.

---

[5] The study design has been discussed in Chapter 2 in detail. A brief summary is provided here for the purpose of completeness of the chapter.

The Early Developmental History Questionnaire (Golding, 2009) is a non-standardised clinical support tool aimed at collecting early development information. The questionnaire targets six broad domains: pregnancy, birth and first months, language development, social development, self-help skills and motor development, play and use of imagination, and other behaviours. Each domain focuses on development from birth up to 36 months of age. This questionnaire was given to parents before the T1 assessments in order to collect information regarding birth and development during the first year of life. This was primarily conducted to assess exclusion criteria of prematurity at birth and major birth complications[6].

Family History Questionnaires were completed before the T1 assessment and included four questionnaires: mother, father, sibling, and participant history (see Appendix C). Each questionnaire included questions regarding the individual's development, schooling details, details of any major health complications, along with details of any family history of a mental health and/or developmental disorder. These questionnaires were developed with the purpose of informal data collection of clinical research information for a study of infant and child siblings of individuals with autism at the University of California, San Diego.

3.2.3.2. Autism Screening Measures

Two Level 1 autism screening measures were used: Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003) for children 4 years and above, and the Quantitative Checklist for Autism in Toddlers (QCHAT; Allison et al., 2008) for children 18 to 24 months. Both screening questionnaires assess the presence of social and communication skills and any restricted, repetitive behaviours or interests. A score of 15 on the SCQ and 50

---

[6] Two parents reported birth trauma but upon enquiry one parent reported that they considered forceps delivery as birth trauma even though there was no trauma to the child due to forceps use. The other parent reported that due to twin birth the child had lack of oxygen and initial difficulties in breathing though the child recovered within five minutes of birth. They were kept under observation but no serious medical complications were noted.

on the QCHAT are the recommended cut-off criteria for Autism Spectrum Disorders symptomatology.

In the study, screening measures were administered based on the age of the participant. However, the SCQ has been found to have high sensitivity (93%) for children from 2 years to 6 years of age (Allen, Silove, Williams, & Hutchins, 2007). Thus, it was administered to all children over 2 years. All parents completed the screening questionnaires and all children in the final sample scored high on both the SCQ and the QCHAT (Table 3.1).

3.2.3.3. Descriptive Measures

3.2.3.3.1. Mullen Scales of Early Learning

Mullen Scales of Early Learning (MSEL; Mullen, 1995) is a standardised developmental assessment battery for children from birth to 68 months of age with five subdomains: Gross Motor, Fine Motor, Visual Reception, Receptive Language and Expressive Language. Each scale comprises of interactive tasks. Some tasks involve parental input and assistance. Items are presented in a hierarchical order of difficulty with basal criterion of passing three consecutive items and ceiling criterion of three consecutive zeros. Raw performance scores are converted to T-scale scores for each subscale. Raw scores for the four cognitive subscales (visual reception, fine motor, receptive and expressive language) can be summed and converted to an Early Learning Composite Standard Score that offers a measure of overall cognitive functioning.

For the purposes of this study, the four subscales: fine motor, visual reception, receptive and expressive language were administered, as cognitive and language functioning were of primary interest. However, T-scale scores could not be obtained for all children due to severity of intellectual disability. Therefore, only age equivalent data for all children and all

domains was computed. The MSEL is a stable measure of verbal and non-verbal abilities in ASD and has high convergent validity with other measures of cognitive assessment such as the DAS (Bishop, Guthrie, Coffing, & Lord, 2011). It was, therefore, used to calculate Verbal and Non-Verbal Mental Age, respectively. Mean age equivalents for fine motor and visual reception scales were calculated to obtain a Non-Verbal Mental Age (NVMA) and mean of age equivalents for receptive and expressive language were used to obtain a Verbal Mental Age (VMA) for each child (see participant characteristics Table 3.1).

3.2.3.3.2. *Autism Diagnostic Observation Schedule – Generic*

The Autism Diagnostic Observation Schedule – Generic (ADOS-G; Lord et al., 2000), is a semi-structured play-based observational, standardised assessment that measures symptoms associated with Autism Spectrum Disorder. Four different modules have been developed and one module is given per participant and is chosen based on verbal ability and chronological age of the individual. Each module assesses the individual on four primary domains of reciprocal social interaction, language and communication, stereotyped behaviours and restricted interests, and play/imagination.

An administrator trained to research reliability, blind to group assignment of the participants, administered the ADOS at both intake and follow-up assessment. All children, except two, received Module 1 during the intake assessment process, as verbal ability of participants comprised of single words. Two children received Module 2, as they had developed phrase speech. All children in the final sample ($n = 24$) met the criteria for ASD based upon their performance on the ADOS.

3.2.3.3.3. *Vineland Adaptive Behavior Scales – Second Edition*

The Vineland Adaptive Behavior Scales (VABS-2; Sparrow, Balla, & Cicchetti, 2005) is a semi-structured parent interview that assesses communication, daily living skills, social, and motor skills in individuals aged from birth to 90 years. The VABS is a standardised assessment tool that provides age equivalents and standard scores for each of eleven subscales, as well as overall adaptive functioning.

The VABS was conducted either face-to-face or on the phone with a parent. Of the final sample of 24 participants, parents of 21 children completed the VABS. The first three children were enrolled in the study during the proof-of-concept stage where VABS was not included in the assessment battery. The Adaptive Behavior Standard Scores for children in the Treatment group were comparable to those of children in the Wait-List Control group (Table 3.1)

3.2.3.4. Primary Outcome Measures

3.2.3.4.1. *Unstructured Imitation Assessment*

The Unstructured Imitation Assessment (UIA) is an adaption of an assessment developed by McDuffie and colleagues (McDuffie et al., 2007); and has been used in research on the effects of RIT previously (e.g. Ingersoll, 2010b). The UIA is a play-based assessment of spontaneous object and bodily-gesture imitation in an unstructured setting. The UIA is conducted in a socially interactive manner, whereby the examiner engages in free-play with the child in a room full of two sets of several developmentally appropriate toys. The examiner then alternates imitating the non-verbal behaviour of the child and modelling actions for the child to imitate. While modelling actions to the child, the examiner verbally describes each action. No explicit prompts, instructions, or praise are provided for the child imitating the

examiner's actions. There are two scales derived from the UIA: object and gesture imitation scales (Appendix E). Each scale is composed of ten models with each model presented to the child three times irrespective of presence or absence of an imitative response. The child's responses are scored on a scale of 0-2, where '0' reflects either no response or an incorrect response, '1' for partial correct imitation, and '2' for complete correct imitation. The highest score on each scale is 20 and the total score on the UIA ranges from 0-40.

The UIA was the primary outcome measure to evaluate the effect of RIT on spontaneous imitation skills of children with autism in the context of an unstructured play setting. The UIA was administered to participants at both T1 and T2 by an examiner who was blinded experimentally to the group assignment of the participants. Three blinded independent observers analysed all UIA videos. In order to calculate inter-rater reliability, an interclass correlation coefficient (ICC) analysis was employed as scoring used a Likert scale and weighted Kappa can be used only for two observers while this study had three observers (Hallgren, 2012). Norman and Streiner (2008) have demonstrated that weighted kappa with quadratic weights for ordinal scales gives identical values to single measures ICC and therefore the two can be used interchangeably (Hallgren, 2012). Inter-rater reliability was assessed for 25% of the videos using a two-way, mixed consistency single-measures ICC and was found to be .99. This indicates excellent agreement between the independent coders and minimum measurement of error.

3.2.3.4.2. Structured Imitation Assessment

The Structured Imitation Assessment (SIA) was adapted from the Pre-school Imitation and Praxis Scale (PIPS), described in Vanvuchelen et al. (2011b), for the purpose of this study. The SIA was chosen over other measures of structured imitation because the PIPS,

from which the SIA has been adapted, is one of the only measures of imitation that has been standardised on both typical and autism populations (Vanvuchelen et al., 2011b). The drawback of the PIPS is that it has been standardised only on a Dutch population and English translations of the measure were unavailable. Therefore, an adapted version of the PIPS, based on the descriptions provided in Vanvuchelen et al. (2011b), was used.

The SIA is a structured assessment measuring elicited or prompted imitation in children with autism. This 30-item assessment measures four different aspects of imitation: single bodily imitation, sequential bodily imitation, goal-directed procedural imitation, and non-goal directed procedural imitation (for definitions see Chapter 1, Section 1.1.2.1.1). Simultaneously, it measures three different kinds of imitation: action-on-object, gestural and facial imitation. Scoring ranges from 0-4 where some items were scored on a three-point Likert scale (0-2), others from 0-3, and a few on a five-point scale from 0-4 (Appendix E). According to the guidelines, three practice tasks are administered at the beginning of the assessment. The aim of these practice tasks is to help the child understand the nature of the assessment and what is expected. Each practice task is administered three times, and every time the child does not respond or gives an incorrect response the examiner physically and verbally prompts the child to complete the task. Test items are administered only once, with no verbal or physical prompt provided to the child upon no response. The examiner presents the task, gives a brief instruction, "You do it", and waits for five seconds for child to respond. No reinforcement is given for imitation.

The SIA was administered by an experimentally blinded examiner at T1 and T2. Three blinded independent observers analysed all of the SIA videos. For the UIA, a two-way, mixed consistency single-measures ICC was deemed appropriate to index inter-rater reliability on

25% of the videos. ICC was found to be .89. This indicates excellent agreement (Cicchetti, 1994) between independent coders and minimum measurement of error.

3.2.4. Intervention

Reciprocal Imitation Training (RIT), as described in Chapter 1, Section 1.2.3, is a play-based naturalistic behavioural developmental intervention for children with autism. RIT has three primary goals: increasing social reciprocity and intrinsic motivation, teaching spontaneous object and gesture imitation, and generalisation of imitation in natural settings (Ingersoll, 2008a).

All children received 20 sessions of RIT across 12 to 14 weeks. At the beginning of the study families were asked to visit three times a week for one hour per visit. However, four families initially recruited reported the number of visits to be too high and therefore an option of two or three visits a week was provided. In cases when families missed sessions, the time period between two sessions was controlled to maximum of 14 days. Also, catch-up sessions were held if the child had missed sessions for 14 days, with up to four sessions in a week being held to ensure all children completed RIT within the maximum time frame of 14 weeks. Intervention has been described here based on descriptions in Ingersoll (2008b & 2010b).

Intervention was implemented in a large therapy room, usually a different room from that in which assessments were conducted (three children received treatment in the same room where assessments were administered). The therapy room had a small table, two chairs, one wall composed of a large one-way mirror, and two movable cameras fixed to opposing corners. All sessions were recorded and while recording parents had the option to watch the session from the observation room or wait in a waiting room. Each child interacted with either two or three therapists independently every session. Each therapist selected five pairs of toys

to play with the child for a period of 20 minutes. After every 20 minutes the child interacted with a different therapist using a different set of toys. The toys were chosen based upon the particular child's play skills and interests, and each toy had an identical pair that allowed the child and the therapist to imitate each other's actions as closely as possible.

In each session, the therapist engaged primarily in contingent imitation to begin with, imitating all verbal and nonverbal behaviour of the child, including actions, vocalisations, and body movements during the play (Ingersoll, 2008b). The therapist also used linguistic mapping, defined as describing the child's actions using simple language around his/her attention focus as well as expanding on the verbal utterances made by the child (Ingersoll, 2008b). All of these techniques were designed to increase social reciprocity and responsiveness (Ingersoll, 2008b; 2010b). Imitation was targeted once the child began to attend to the adult and, therefore, the first two sessions for all children primarily involved increasing social responsiveness. Social reinforcement in the form of praise was also used in order to increase responsiveness. All children were praised for eye contact and vocalisations/language along with imitation acts.

In order to teach imitation skills, the therapist modelled an action, either object based or gesture based, three times in succession using a clear verbal marker accompanying the model, e.g. "throw ball" (Ingersoll, 2010b). If the child imitated the modelled action independently, then he or she was praised for the imitation. If the child did not imitate the action spontaneously within 10 seconds of the third modelled trial, the child was physically prompted to imitate the action and then praised for the imitation (Ingersoll, 2008b; 2010b). The therapist then returned to imitating the child and using linguistic mapping.

Actions were modelled at an average pace of one action every one to two minutes. Praise was contingent upon spontaneous or prompted imitation, while at the same time

precision in imitation was not crucial and even directed attempts were praised such that accuracy of the imitated behaviour in response to a model was not of importance (Ingersoll, 2010b). Furthermore, to increase social imitation in play, multiple actions were modelled throughout the session based on child's interest rather than teaching specific actions (Ingersoll, 2010b). Actions were also varied for the same toy such that no specific action was repeatedly associated with a specific toy (Ingersoll, 2010b). Verbal markers remained the same during the three repeated presentations but were varied across models to ensure that imitation was not contingent upon language used (Ingersoll, 2010b). Furthermore, to increase spontaneity no instructions were given after a model (such as "you do this"), questions were avoided (e.g. 'can you roll the ball') and verbal markers accompanying the models were often descriptors of the action or sounds that increased the child's attention to the action being performed (e.g. 'vroom! vroom!' while moving the car back and forth). Lastly, as the child interacted with different therapists through the one hour session and across sessions, it was made sure that imitation did not become person specific. Use of varied models across toys and therapists along with variations in language used through different sessions ensured that imitation was not contingent upon any of these factors and therefore generalised across therapists and play contexts.

The primary behavioural goals of intervention were teaching two kinds of imitation: object and gesture. In order to teach object imitation the therapist modelled an action using an object (e.g. 'roll the ball'). Actions were modelled around the child's attention focus and the objects the child was engaged with. Object imitation models included sensorimotor (e.g. rubbing a textured block), functional (e.g. rolling the ball) and symbolic (e.g. feeding a dinosaur using a pretend spoon) play schemes and varied between children based on their developmental level and play skills (Ingersoll, 2008b; 2010b). Gesture imitation models

included modelling a gesture around the child's play (e.g. 'oh no!' with hands on face) and these ranged from conventional gestures (e.g. wave to say 'hi') to affective (e.g. rubbing eyes to show 'crying') and descriptive (e.g. hands up and wide open to show 'big ball') gestures (Ingersoll, 2008b). All children received both object and gesture imitation training, although the complexity of the model depended on the child's current developmental level. For seven children object imitation was taught for the first ten sessions solely and gesture imitation was then slowly introduced. For five children both object and gesture imitations were targeted together.

3.2.4.1.Therapist Training and Fidelity of Implementation

All treatment sessions were delivered by the author as the lead therapist along with other trained therapists including graduate level students, clinical psychology trainees and undergraduate students. A total of 17 students were trained over the three years on RIT. Each participant was assigned three therapists who worked with the child throughout the duration of the 20 sessions. Therapist retention was a challenge as most therapists were undergraduate volunteer students. Further, although all therapists were kept blind to treatment allocation, the author was the lead therapist for every child receiving training. Thus, therapist bias could not be controlled for completely and results may be influenced by the author's role in implementation of RIT.

The author trained all therapists and is a trained RIT trainer. Training included completing the online training developed by Dr Brooke Ingersoll and her team at the School of Psychology, Michigan State University, Michigan, USA. All therapists-in-training then completed three live practice sessions, two 10 minutes sessions and one 20 minutes session, in which they were scored for correct implementation of RIT. Fidelity of implementation

refs to ensuring that therapists are carrying out the intervention the way it was conceptualised and manualised (Wainer & Ingersoll, 2013b). The RIT Fidelity Form (Ingersoll & Lalonde, 2010) was used to score correct use of the six elements of RIT: contingent imitation, linguistic mapping, modelling, prompting, praise, pacing. The form uses a 1 to 5 Likert scale, with higher scores indicating greater correct implementation. Scores were averaged across these six elements to give a single fidelity composite score for each session. Composite scores of four or above were considered adequate fidelity. All therapists-in-training were scored for fidelity by a blind RIT trainer at the Michigan State University and each therapist achieved 80% correct implementation in all three-practice sessions. Therapists were assigned children only when fidelity was achieved in the three practice sessions.

3.3.   RESULTS

Mean scores of the behavioural change measures were analysed for normality using Shapiro-Wilk Test. Scores on all measures violated the assumption of normality (>0.05). Visual inspection of histograms revealed that data were positively skewed. In order to correct for skew, log transformation was used however, as the data had many zero values transformations were unsuccessful. Therefore, only non-parametric statistics were conducted. Additionally, standard deviations were found to be larger than the means on many subscales and therefore median and range scores have been reported in tables.

3.3.1. Primary Analyses

Change scores for each scale and subscale of each measure were obtained by subtracting T1 assessment scores from T2 assessment scores. Mann-Whitney U tests were then conducted on the change scores to identify treatment effects.

3.3.1.1. Spontaneous Imitation

In order to identify changes in spontaneous imitation as a result of intervention, mean total scores (object + gesture imitation domain scores) obtained on the UIA were compared across groups and time (Table 3.2). Results indicated that children assigned to the Treatment group made significantly more gains in spontaneous imitation than did children assigned to the Wait-List Control group ($U = 28$, $p = 0.01$; Figure 3.1).

In order to examine whether RIT had equivalent effects on object and gesture imitation, effects were further analysed separately for change scores on the object and gesture imitation subscales of the UIA (Table 3.2). The results indicated that children assigned to the Treatment group changed significantly more in object imitation from T1 to T2 compared with the Wait-List Control group ($U = 18.5$, $p <0.01$; Figure 3.1). However, no differences were observed in change scores of gesture imitation between the groups ($U = 56$, $p = 0.33$; Figure 3.1).

Table 3.2: Median and range scores of participants at T1 and T2 on the UIA.

Scale	Treatment (*n* = 12)		Wait-List Control (*n* = 12)	
	T1	**T2**	**T1**	**T2**
Spontaneous Imitation Total	3.0 (0-20)	7.5 (0-33)	4.5 (0-22)	1.5 (0-31)
Object Imitation	3.0 (0-14)	7.0 (0-17)	4.0 (0-16)	1.5 (0-18)
Gesture Imitation	0.0 (0-6)	1.0 (0-16)	0.0 (0-10)	0.0 (0-13)

Figure 3.1: Spontaneous, object and gesture imitation in children with autism in the Treatment (n=12) and Wait-List Control (n=12) group at T1 and T2. Error bars represent standard error.[7]

---

[7] All error bars represent standard error in the thesis. Also, * signifies $p<0.05$ & ** signifies $p<0.01$ throughout the thesis.

3.3.1.2. Elicited Imitation

Total scores were obtained from the SIA by summing together the four subscale scores: single bodily imitation (SBI), sequential bodily imitation (SQB), goal-directed procedural imitation (GDP), and non-goal directed procedural imitation (NGDP; Table 3.3). Change scores were analysed for change in elicited imitation from T1 to T2 to ascertain effect of RIT on the Treatment group. No significant group differences were observed between the Treatment and Wait-List Control groups on SIA total change scores ($U = 51$, $p = 0.22$; Figure 3.2). Non-parametric analyses on change scores for each subscale also showed no significant difference between groups from T1 to T2, SBI ($U = 41.5$, $p = 0.07$), GDP ($U = 47.5$, $p = 0.15$) SBQ ($U = 45$, $p = 0.10$), and NGDP ($U = 55$, $p = 0.26$; Figure 3.3).

Table 3.3: Median and range scores for participants at T1 and T2 on the SIA.

Scale	Treatment ($n = 12$)		Wait-List Control ($n = 12$)	
	T1	T2	T1	T2
Elicited Imitation Total	3.5 (0-44)	10.0 (0-44)	4.0 (0-34)	3.5 (0-49)
Single Bodily Imitation	0.0 (0-23)	5.5 (0-28)	1.0 (0-25)	0.0 (0-27)
Sequential Bodily Imitation	0.0 (0-4)	1.0 (0-6)	0.5 (0-3)	0.0 (0-3)
Goal Directed Procedural Imitation	1.5 (0-11)	2.0 (0-11)	1.5 (0-8)	1.0 (0-11)
Non-goal Directed Procedural Imitation	1.0 (0-6)	0.0 (0-3)	0.0 (0-6)	0.0 (0-8)
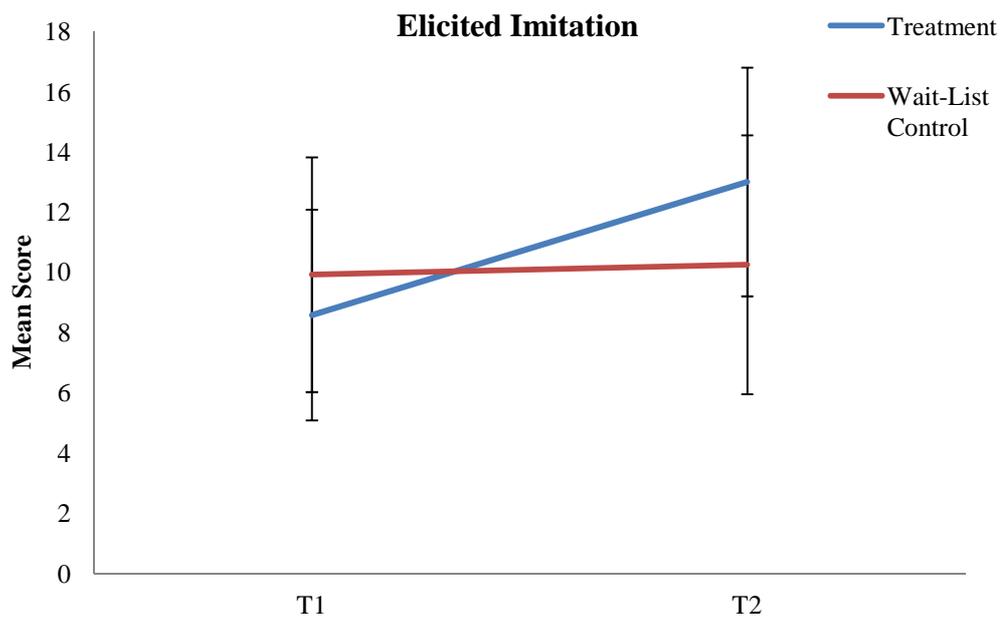
Figure 3.2: Elicited Imitation in children in the Treatment and Wait-List Control group.

Error bars represent standard error.
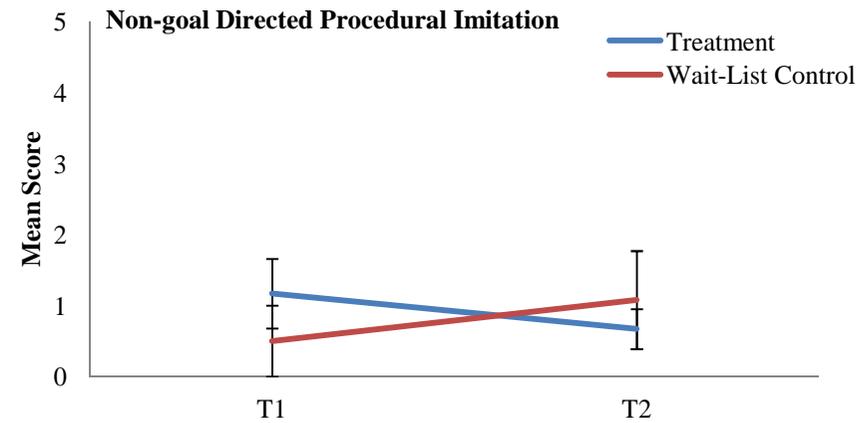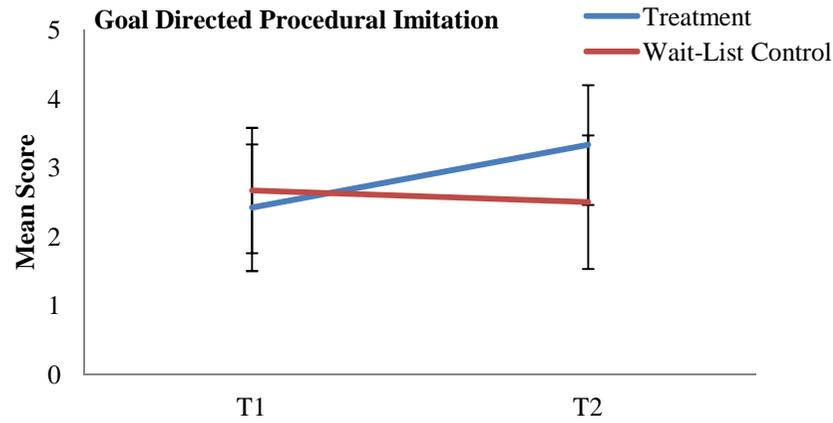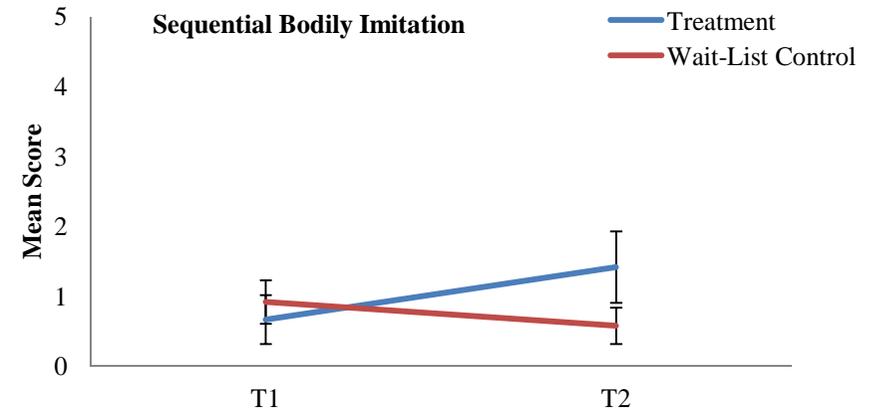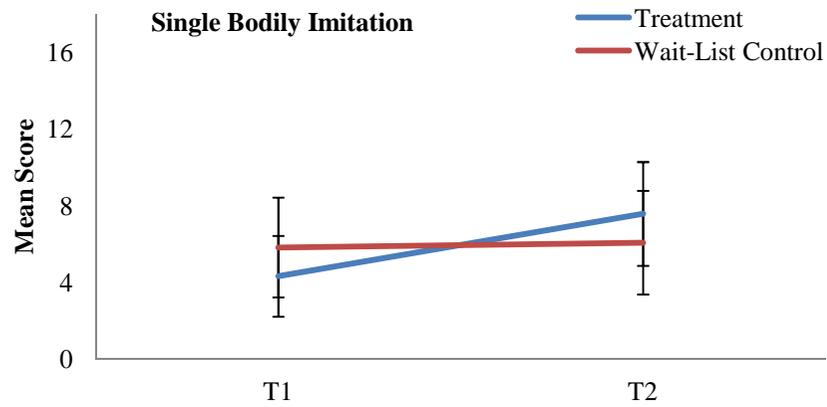
Figure 3.3: Imitation scores on the four subscales of Structured Imitation Assessment for the Treatment and Wait-List Control groups. Error bars represent standard error.

3.3.2. Secondary Analyses

Child Characteristics: In order to answer the second aim of the study, exploratory analyses were carried out to examine whether child characteristics before treatment predicted intervention effects. As significant intervention effects were only observed in spontaneous imitation scores, only UIA change scores were used for these analyses. Nonparametric two-tailed correlations using Spearman's rho were carried out between spontaneous imitation measure (UIA) change scores: total, object imitation and gesture imitation change scores, and chronological age, NVMA and VMA as measured by the MSEL and all ADOS domains (Table 3.4).

Total spontaneous imitation change scores were observed to be negatively correlated with reciprocal social interaction ($r_s = - 0.67$, $p < 0.01$), and stereotyped behaviours and restricted interests ($r_s = - 0.61$, $p = 0.01$) as indexed by the ADOS.

ADOS domain of reciprocal social interaction was negatively correlated with object imitation ($r_s = - 0.61$, $p = 0.03$), while stereotyped behaviours and restricted interests domain was negatively correlated with gesture imitation gains ($r_s = - 0.66$, $p = 0.02$).

Spearman's rho correlations were also calculated for the Wait-List Control group in order to ascertain that variables related to change were specifically associated with treatment and not other factors such as time (Table 3.5). None of the child characteristics of age, NVMA, VMA or ADOS domain and total scores were associated with change in imitation scores over time in the Wait-List Control group.

Table 3.4: Correlations between pre-treatment child characteristics and change in spontaneous imitation scores for Treatment group (n=12)

	Spontaneous Imitation	Object Imitation	Gesture Imitation
Chronological Age	- 0.51	- 0.50	- 0.04
Non-verbal mental age	0.37	0.24	0.34
Verbal mental age	0.04	- 0.04	0.09
Social interaction	- 0.67[*]	- 0.61[*]	- 0.51
Communication	0.03	0.07	0.16
Stereotyped Behaviours and Restricted Interests	- 0.61[*]	- 0.55	- 0.66[*]
Play	- 0.26	- 0.18	- 0.21
ADOS Total Score	- 0.38	- 0.36	- 0.15

*Correlation is significant at 0.05 level (2-tailed).

Table 3.5: Correlations between pre-treatment child characteristics and change in spontaneous imitation scores for Wait-List Control group (n=12)

	Spontaneous Imitation	Object Imitation	Gesture Imitation
Chronological Age	0.47	0.20	0.26
Non-verbal mental age	0.15	-0.26	0.16
Verbal mental age	0.24	- 0.16	0.17
Social interaction	- 0.21	0.10	- 0.24
Communication	0.10	0.25	0.02
Stereotyped Behaviours and Restricted Interests	- 0.04	- 0.26	- 0.09
Play	- 0.04	0.38	- 0.04
ADOS Total Scores	- 0.11	0.16	-0.16

3.3.3. Patterns of Individual Change

In order to explore individual patterns of change, the Reliable Change Index (RCI) was calculated. The RCI is a statistic that helps to understand if an individual participant's score has changed reliably, more than that can be explained by errors of measurement (Iverson, 2011). The RCI was calculated on both the Treatment and the Wait-List Control group separately (using the Leeds Reliable Change Indicator: Simple Excel[(tm)] Applications; Morley & Dowzer, 2014) in order to tease out patterns that may be specifically associated with RIT. Further, the RCI was calculated on both measures of change, that is, UIA and SIA to understand individual patterns of change on the two different kinds of imitation skills.

On the measure of Spontaneous Imitation, it was found that four children demonstrated reliable change on total UIA scores in the Treatment group, while one child showed reliable change on the total scores in the Wait-List Control group. Also, no child in the Treatment group deteriorated however one child in the Wait-List Control group showed significant deterioration from T1 to T2 (Figure 3.4). Similarly on the Object Imitation subscale, four children in the Treatment group showed reliable change while none of the participants in the Wait-List Control group showed change. Instead one child in the Wait-List group was found to deteriorate on object imitation from T1 to T2 (Figure 3.5). Lastly, on Gesture Imitation subscale, four children in the Treatment group and one child in the Wait-List Control group demonstrated reliable change from T1 to T2 (Figure 3.6).

Closer inspection of individual data showed that in the Treatment group, two children changed reliably on all three UIA scores while two children showed a significant change in spontaneous and gesture imitation only. Another two children showed a change only on object imitation scale. Looking carefully at child profiles, it was found that the four children, who changed on both the Spontaneous and Gesture Imitation scales, were the only four children in

the sample who did not show any repetitive hand or body mannerisms or self-stimulatory behaviours. This finding overlaps the significant negative correlation observed between stereotyped, restricted and repetitive behaviours on the ADOS and spontaneous imitation change scores suggesting that <u>children who have fewer mannerisms and self-stimulatory behaviours may be more likely to benefit from RIT.</u> Visual inspection of participants' profiles, who changed on Object Imitation in the Treatment group, did not show any clear patterns. Visual inspection of Wait-List Control group data did not show any clear patterns of child profiles that may be associated with the reliable change or deterioration on imitation skills.
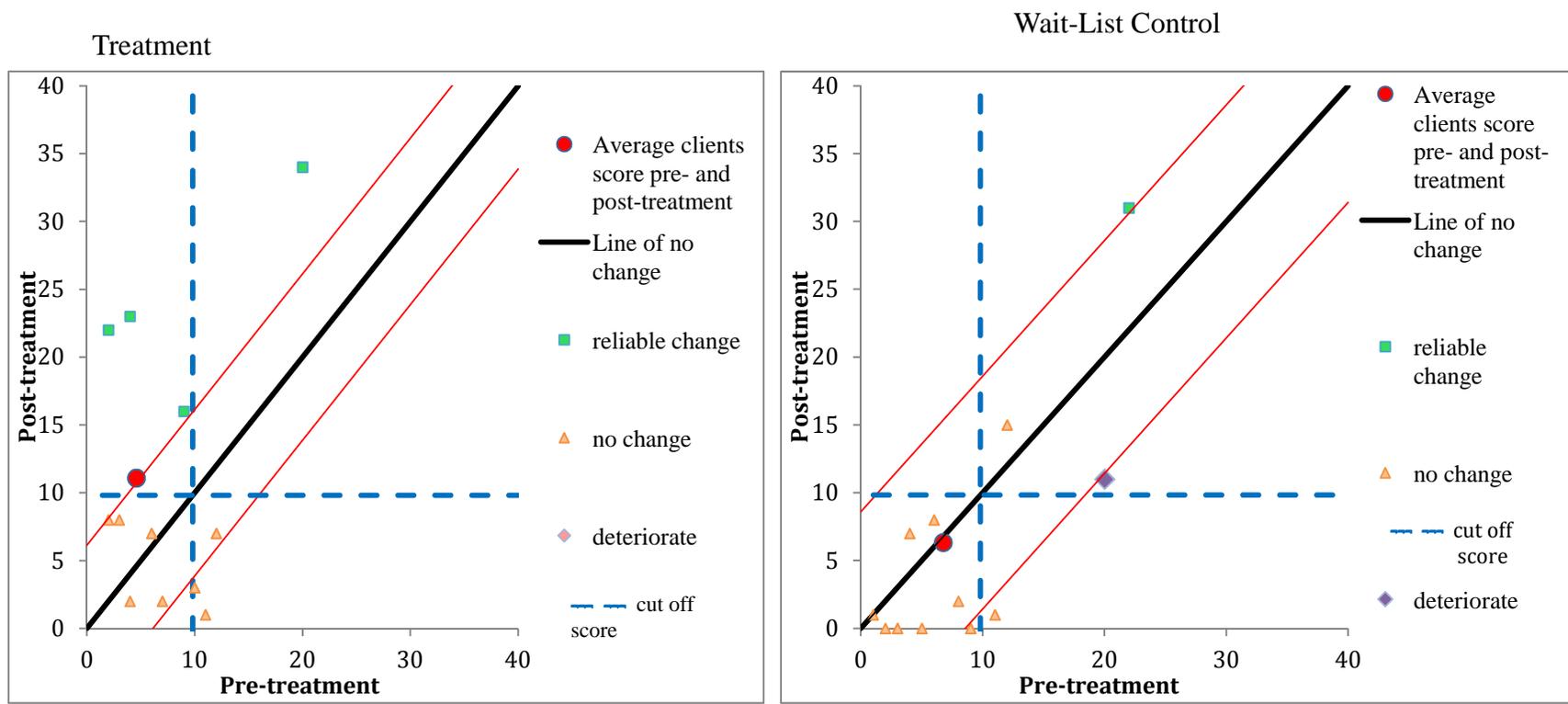
Figure 3.4: The Reliable Change Index for the Treatment and Wait-List Control Groups for Spontaneous Imitation Total Scores measured on the Unstructured Imitation Assessment.
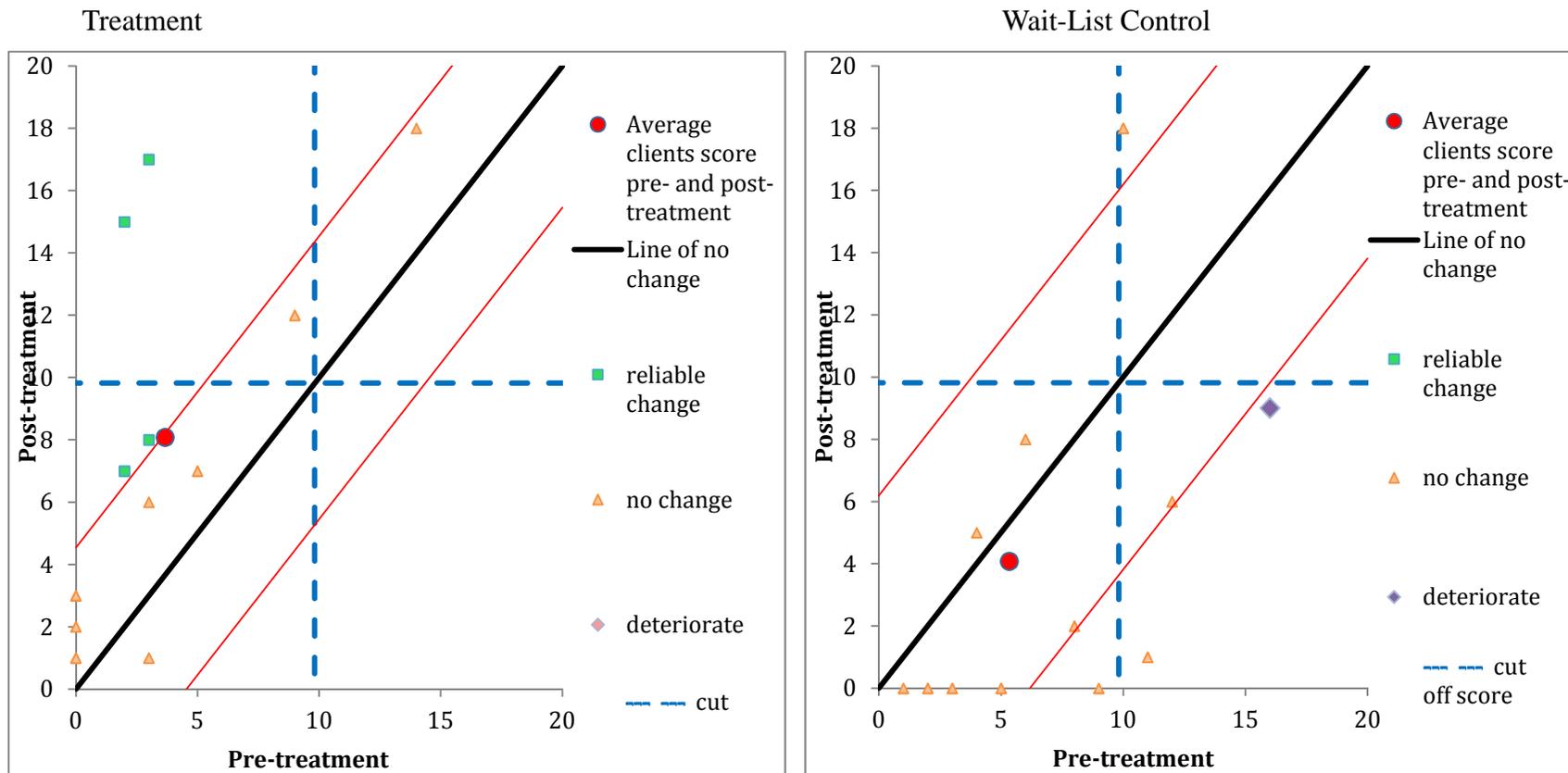
Figure 3.5: The Reliable Change Index for the Treatment and Wait-List Control Groups for Object Imitation Scores measured on the Unstructured Imitation Assessment.
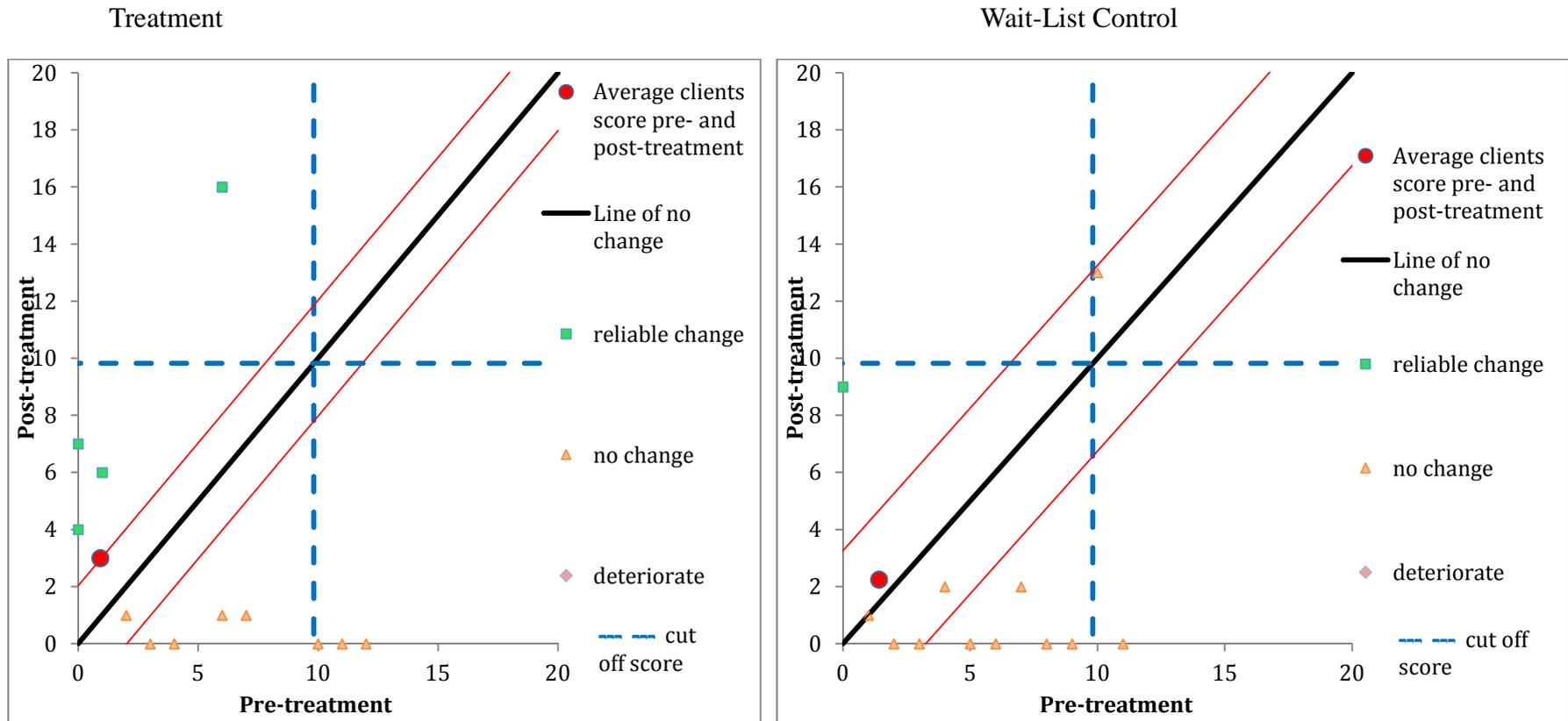
Figure 3.6: The Reliable Change Index for the Treatment and Wait-List Control Groups for Gesture Imitation Scores measured on the Unstructured Imitation Assessment.

Evaluating individual profiles on the Structured Imitation scores, it was found that one child in the Treatment group improved on total SIA scores (Figure 3.7) as well as subscale scores of single bodily imitation, sequential imitation and goal-directed procedural imitation. This child also improved on all UIA scores suggesting that RIT significantly impacted imitation development for this particular participant, and there was something individually different about this child. Therapist notes suggest that this particular participant had very good social reciprocity from the beginning of treatment, while for all other participants that was a treatment goal. However, social reciprocity was not systematically assessed or analysed for in the study to confirm this claim.

In the treatment group, one other child changed on single bodily imitation scale (Figure 3.8) and sequential bodily imitation; two other children improved on sequential bodily imitation only while one child deteriorated on this scale (Figure 3.9), and three children deteriorated from T1 to T2 on the non-goal directed procedural imitation scale (Figure 3.11). On the other hand, in the Wait-List Control group, no child changed significantly on total elicited imitation scores (Figure 3.7) or single bodily imitations (Figure 3.8); one child deteriorated on sequential bodily imitation (Figure 3.9) while one child improved on goal-directed procedural imitation subscale (Figure 3.10), and three other children improved on non-goal directed procedural imitation subscale (Figure 3.11). Closer inspection of data did not reveal any patterns in child profiles that would be associated with reliable gains or deterioration in elicited imitation skills in the two groups.

Treatment
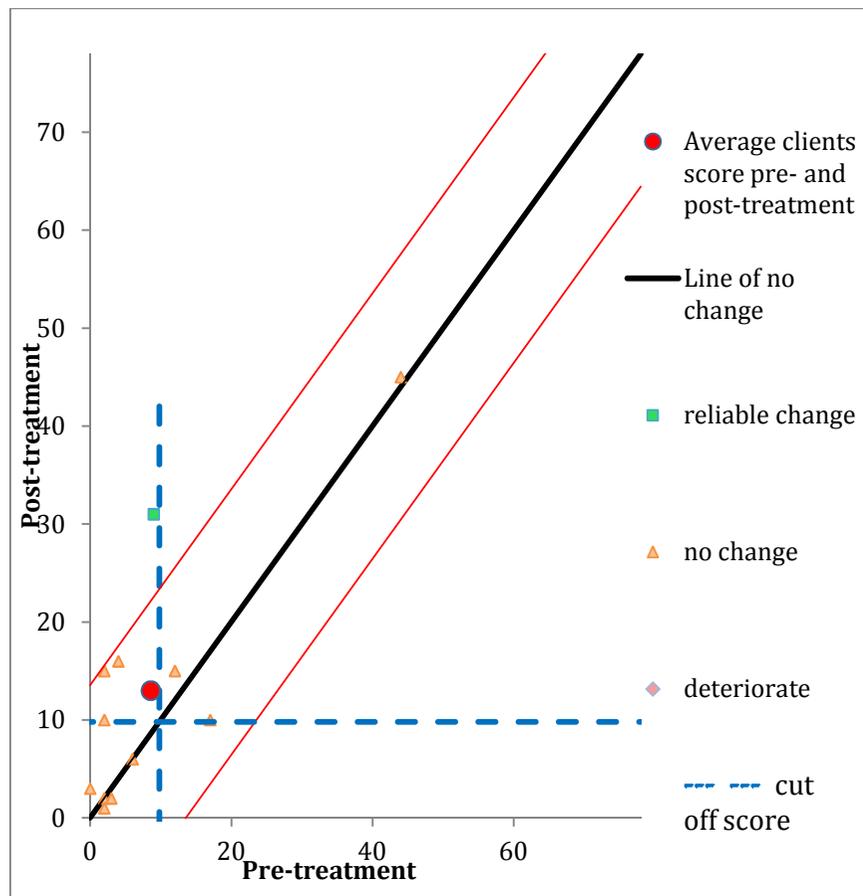
Wait-List Control
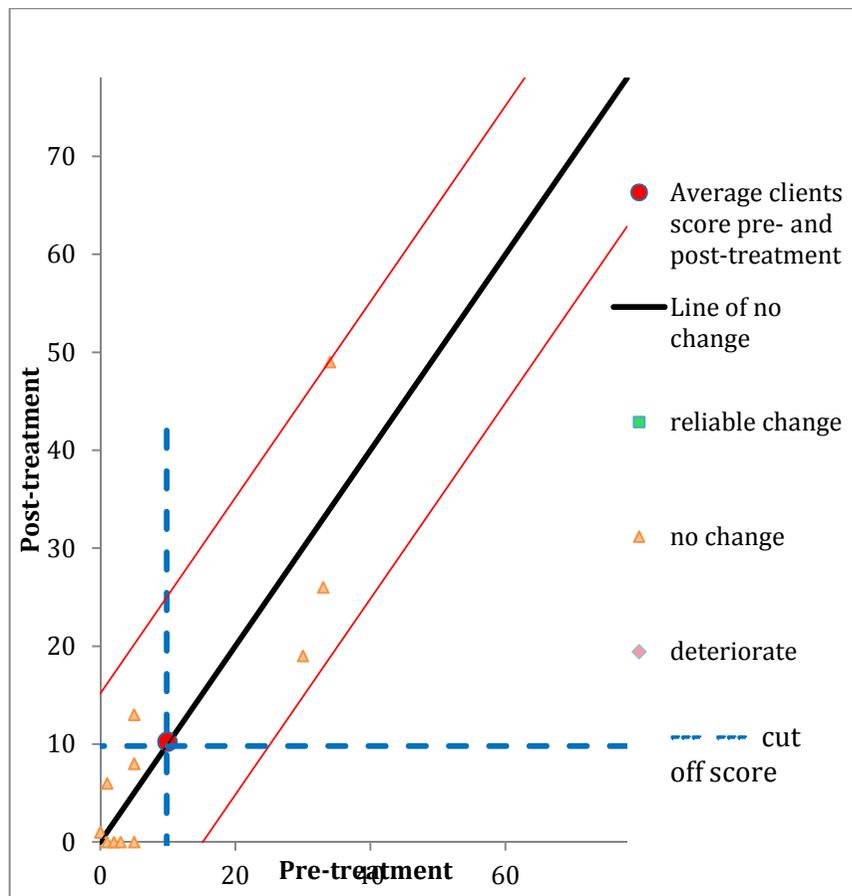
Figure 3.7: The Reliable Change Index for the Treatment and Wait-List Control Groups for Elicited Imitation as measured on Structured Imitation Scale.
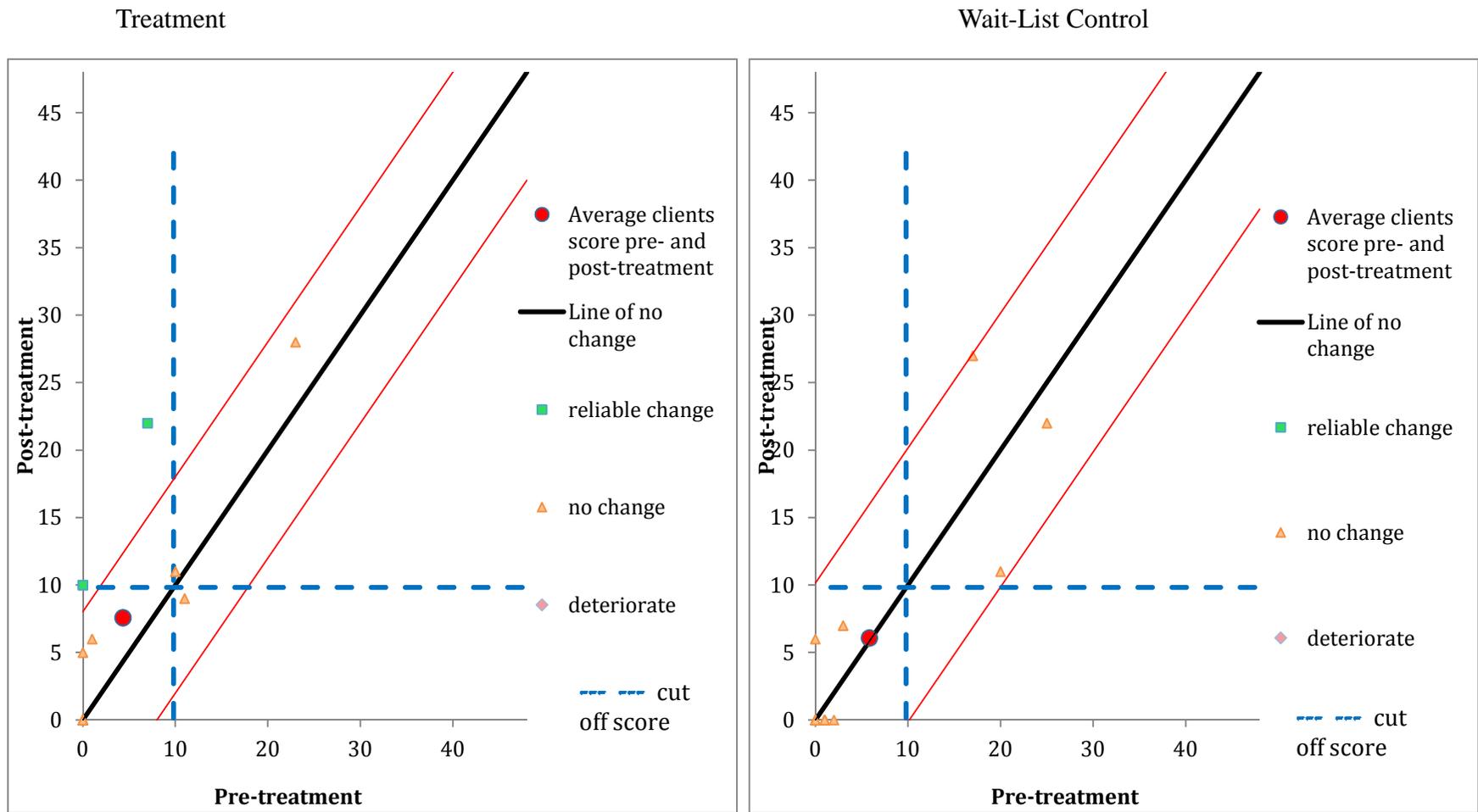
Figure 3.8: The Reliable Change Index for the Treatment and Wait-List Control Groups for Single Bodily Imitation as measured on Structured Imitation Scale.
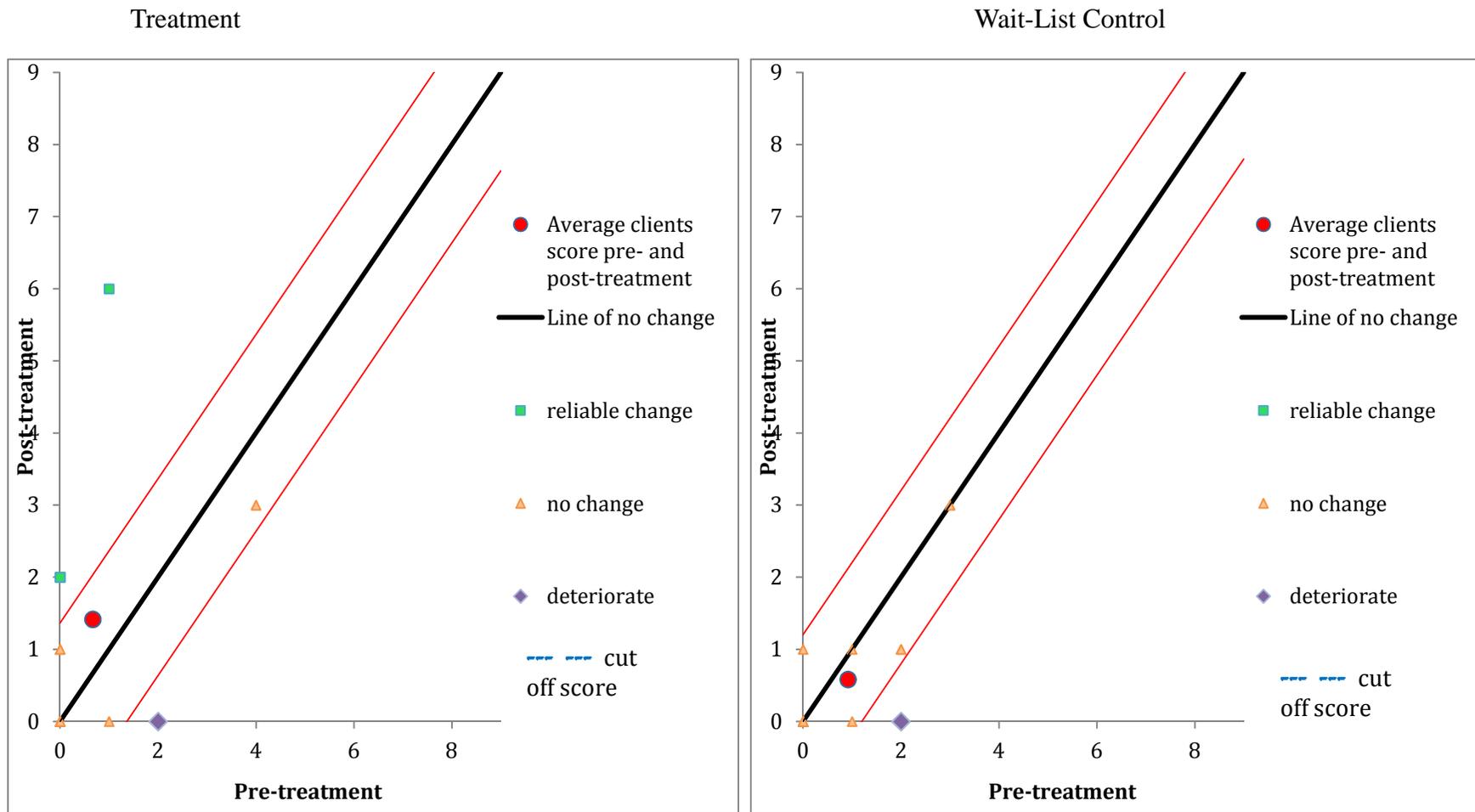
Figure 3.9: The Reliable Change Index for the Treatment and Wait-List Control Groups for Sequential Bodily Imitation as measured on Structured Imitation Scale.
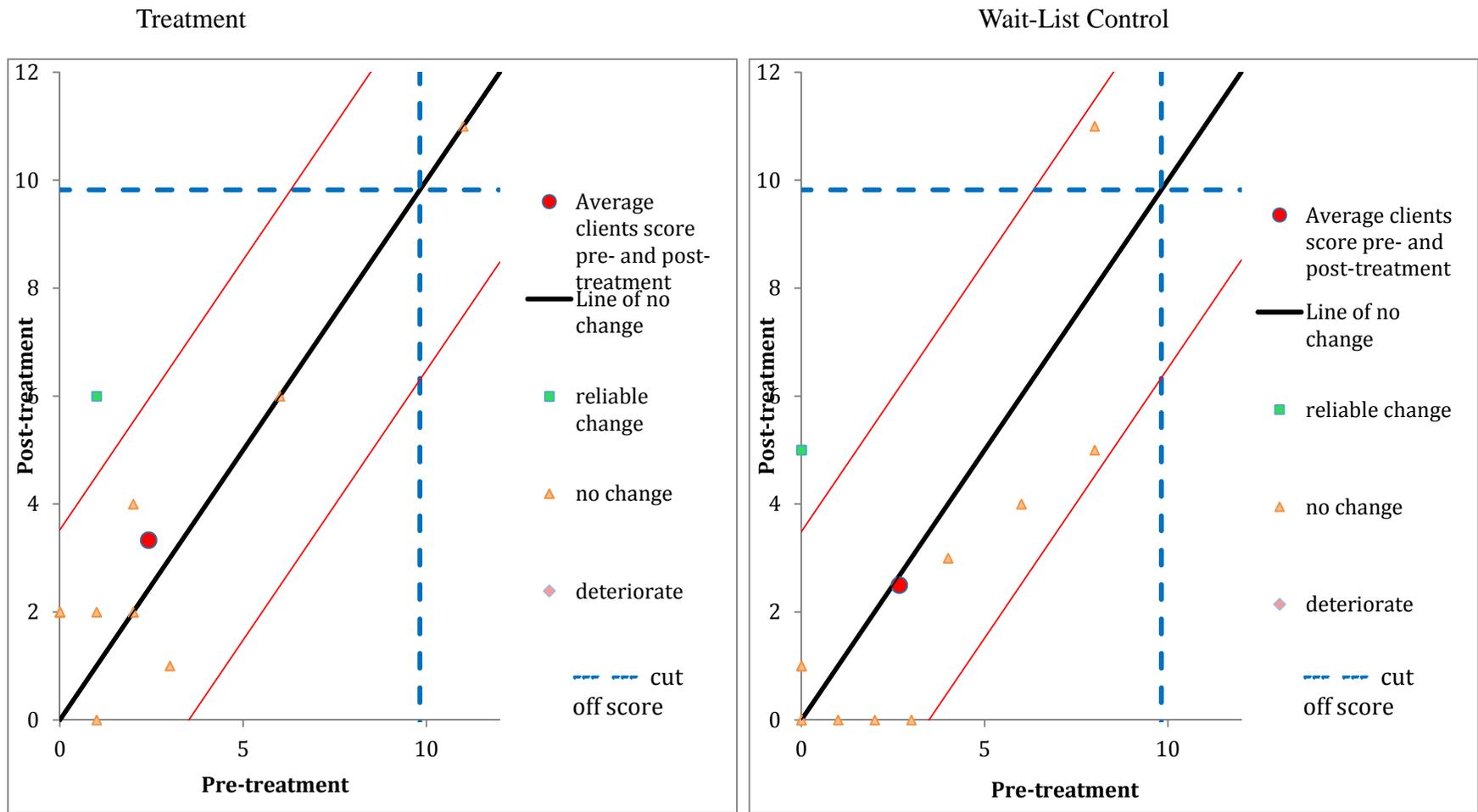
Figure 3.10: The Reliable Change Index for the Treatment and Wait-List Control Groups for Goal-Directed Procedural Imitation as measured on Structured Imitation Scale.
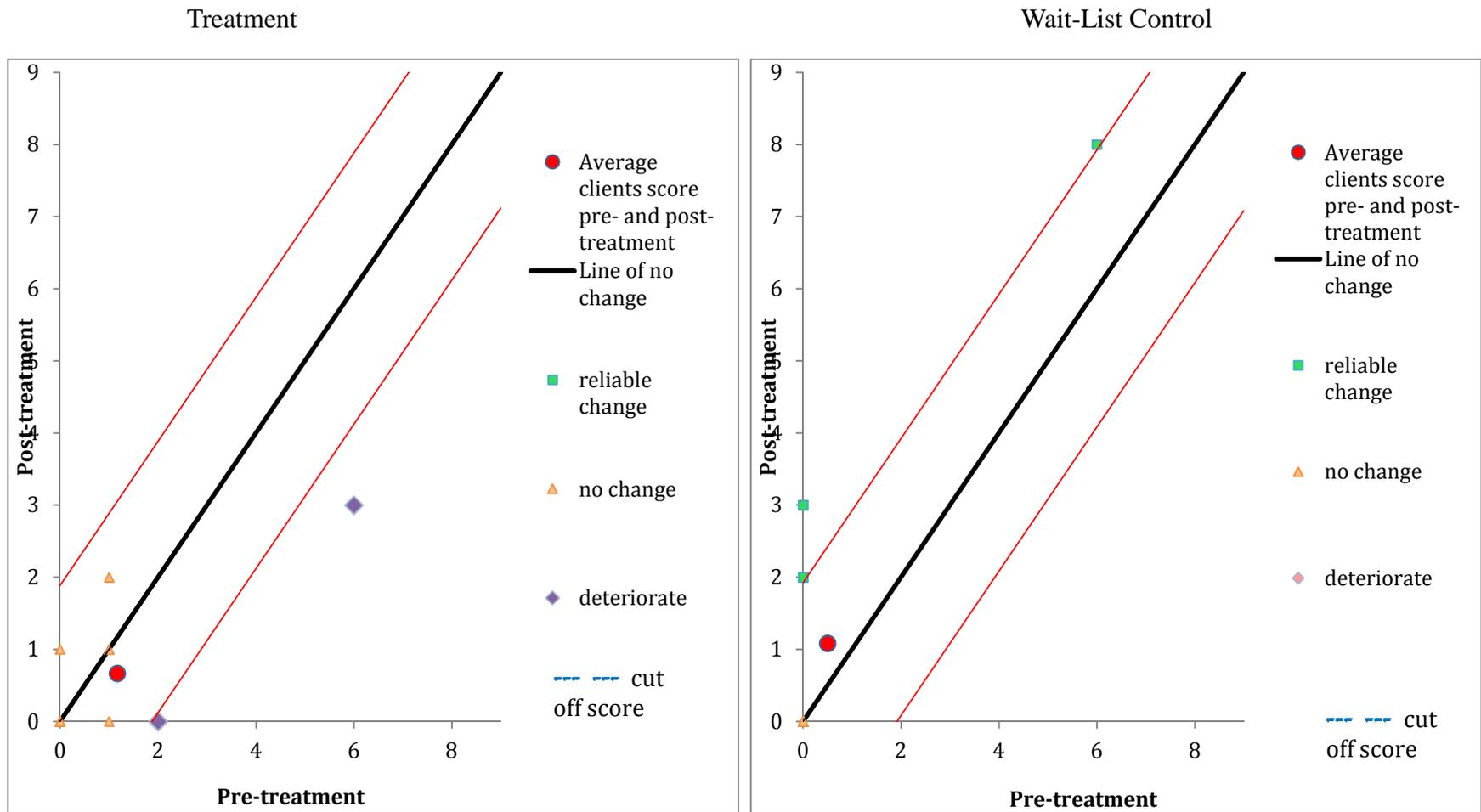
Figure 3.11: The Reliable Change Index for the Treatment and Wait-List Control Groups for Non- Goal Directed Procedural Imitation as measured on Structured Imitation Scale.

3.4. DISCUSSION

This study examined the efficacy of RIT as an early intervention program focused on teaching social imitation skills to children with autism. Behavioural results on spontaneous imitation measure, UIA, provide evidence that RIT improved spontaneous, social imitation significantly with an adult in a play setting in children with autism. Children in the Treatment group showed greater gains in spontaneous imitation, especially object imitation, as compared to the Wait-List Control group. These findings add to the growing evidence base for RIT as an efficacious focused early intervention program for children with autism.

3.4.1. Spontaneous Imitation

The findings show that children with autism who received RIT were able to generalise an acquired skill to a different play-based environment (assessment setting) and a new person (blind assessor). This is important because lack of spontaneity in social interaction and communication has been reported in autism literature (Chiang & Carter, 2008) and the lack of initiation in social interaction also forms part of the key diagnostic criteria for autism (American Psychiatric Association, 2013). Moreover, inability to generalise and spontaneous use of skills that have been acquired have been found to be core issues with some autism intervention programs such that even though children with autism may acquire a skill within treatment, the spontaneous use of it in a different setting is often a challenge (Vismara & Rogers, 2010). Thus, significant gain in spontaneity of imitation is a highly encouraging finding. The UIA also captures play-based social imitation in a back and forth interaction with the examiner when no explicit instruction is given to imitate. This gain in social use of imitation is important in order to help children learn and develop more complex skills and

language (Chiang & Carter, 2008). Previous studies have shown that children with autism are significantly more impaired in social imitation skills than elicited/prompted imitation. The current results show that children in the Treatment group were able to engage more successfully in spontaneous imitation-based dyadic interactions after RIT. Thus, the findings provide support for RIT as an intervention that targets spontaneity and social reciprocity in imitation skills.

3.4.2. Gesture Imitation skills

Although there were significant improvements in object imitation, results regarding gains in gesture imitation skills (Ingersoll, 2010b) were not replicated. Based on the RIT manual, in the current study, object imitation was primarily targeted for seven children in the intervention group while gesture imitation models were introduced much later, post 10 sessions, as these children were found to have low developmental ages and limited play. This specific target of object imitation for more than 50% of the treatment group may have affected the change scores on the gesture imitation scale. Additionally, in the previous pilot RCT of RIT, each child received 30 RIT sessions (Ingersoll, 2010b), while in the present study a total of 20 sessions were given to children in the treatment group. The number of sessions differed between studies primarily because of initial parent feedback suggesting lack of feasibility of more than two sessions per week. This was also demonstrated in retention figures where, out of the 12 families only three agreed to come for sessions more than twice per week. The lower number of total hours of intervention may therefore have had a direct effect on results. Research from behavioural treatment models has shown that number of hours in intervention does have an impact on skill acquisition (Granpeesheh, Dixon, Tarbox, Kaplan, & Wilke, 2009; Virues-Ortega, 2010). Therefore, fewer hours may have been adequate to produce changes in some skills but not all. Additionally, these results suggest that

gesture imitation may be a more complex skill to acquire as compared to action-on-object imitation. This is in line with ASD literature that suggests bodily imitation and gestures, specifically non-meaningful actions, may be more impaired than action-on-objects (Stone et al., 1997; Rogers, Bennetto, McEvoy, & Pennington, 1996; Ingersoll & Meyer, 2011). It may then be possible that children with autism need more targeted hours to learn gesture imitation as compared to action-on-object imitation.

3.4.3. Elicited Imitation skills

With regard to the second hypothesis, the treatment group did not show a significant change in elicited imitation as compared to the control group. There may have been many possible reasons for this. Fewer total hours of intervention may have affected these results suggesting that in order to learn elicited imitation children may need more dedicated hours. Also, RIT is a focused intervention that targets social use of imitation, and elicited imitation may be a skill that has to be targeted specifically in order to see treatment effects. Furthermore, during treatment, children were praised for attempts at imitation while precision of the model was not reinforced. Skills such as attention to task or instruction following were not targeted explicitly. Conversely, the SIA (the measure of elicited imitation) required children to adhere to task, follow basic instruction ("you do it") as well as engage in sustained attention on a table-top activity. The SIA is a 40-item scale with varying levels of difficulty and involving items that ranged from action-on-object imitation to sequential imitation to facial imitation (see Appendix E). Additionally, the scoring of the SIA stresses precision of the model with a lower score given to less precise actions (see Appendix E). Thus, one of the main reasons for differential results in elicited imitation may be the measure used.

3.4.4. Child Characteristics and Individual Change

Evaluating the second aim of the study, child characteristics of social skills and repetitive behaviours were associated with intervention effects in the treatment group while this was not observed for the control group. Also, the RCI data showed that a greater number of children had improved reliably in the treatment group (33%) compared to the control group (8%) on spontaneous imitation skills. During visual inspection for patterns of individual change it was seen that children with low self-stimulatory behaviour tended to respond better on spontaneous imitation. Thus, taken together, these findings suggest that children with greater social difficulties and a higher number of stereotypic and repetitive behaviours, as assessed on the ADOS, were less likely to respond to RIT. This may be the case because social responsiveness is an important first step towards learning to imitate. Imitation in general is known to increase responsivity between partners (Dawson & Adams, 1984; Rogers, 2006). However, children with significantly greater social impairments take longer than their less impaired counterparts to show changes in social responsiveness and imitation (Dawson & Adams, 1984). Furthermore, children who are severely impaired in social interaction skills, children with more stereotyped, repetitive may be less socially responsive in general. In support of this, it was observed that the child who showed significant change on both the spontaneous and elicited imitation measures was the only child in the treatment group for whom therapists noted high levels of social responsivity from the beginning of the intervention. Therefore, responsiveness may be a target before imitation training for children who show greater severity in social difficulties and more stereotypic behaviours and restricted interests. At the same time, these results regarding child characteristics point towards the importance of interventions being individualised. As children with autism show a wide array of strengths and difficulties, understanding which interventions are most effective given child

characteristics will be an important next step (Warren et al., 2011). There is a gamut of treatment options developed for children with autism, many of which are evidence-based. However, non-responders to intervention are often over-looked. Understanding the impact of autism interventions on different children will help move the field in the direction of developing refined interventions which cater to wider profiles as well as helping clinicians decide on an intervention package that may be best for the child characteristics observed.

Finally, this study suggests that low-intensity focused interventions can have an impact on child learning. Only 20 hours of focused intervention over a period of 12 to 14 weeks were able to produce changes in an important aspect of social functioning in children with autism. Future research may therefore focus on understanding and making interventions efficient both in targets and time taken to achieve those targets.

3.4.5. Limitation and Future Directions

The current study was the first external replication trial of RIT, adding to the evidence-base for it being an efficacious intervention impacting social imitation skills for children with autism. However, some limitations remain. A major limitation of the study was the sample size. Small sized studies often lack power and this makes the probability of a Type 1 error high. This could be a possible reason for not finding effects for gesture and elicited imitation. For the current study, power was calculated using the previous effects observed in the pilot RCT (Ingersoll, 2010; Appendix J). Power calculations revealed that minimum of 24 participants were needed in the sample for it to have enough power to detect an effect 80% of the time. However, the sample obtained was highly skewed and variable, and many analyses were not deemed fit. Small samples make interpretation of data often challenging. In the present study, the small sample size did affect interpretation of findings, as it is difficult to say

if gesture and elicited imitation effects were not replicated due to problems with sample or are representative of treatment effects. Therefore, future studies with much larger samples will be crucial in further determining efficacy of RIT.

Hours of treatment time in the present study were fewer than those in previous RIT studies, therefore replication of previous results may have been compromised by this variable as opposed to intervention effectiveness more generally. At the same time, results on spontaneous imitation lend support to RIT being an effective intervention for teaching social imitation skills in a short duration of time. The results suggest that fewer hours in targeted intervention can lead to positive changes in children with autism. Children could not be followed-up after training due to limited resources. Although the results suggest an immediate gain in spontaneous imitation skills, stability of gains is at present questionable. Further, as a blind assessor was used to conduct all test administrations, and therapy and assessment rooms were different, some transfer of skill may be observed in the treatment group. Spontaneous imitation gains show that children were able to generalise to a different setting and to a different/new person. However, generalisation to home and school environments was not assessed and thus transfer of skills to other settings is not completely known.

The present study utilised an adaptation of a standardised imitation assessment. However, due to the nature of the assessment there was emphasis on skills such as attention to task, comprehension of instruction, instruction following and attention regulation. Though these skills were not directly assessed, most children in the sample found the structured nature of the assessment difficult. The nature of the assessment may have then attenuated results as children's abilities may have been masked. In a study looking at the effect of task behaviour on scores on the Mullen Scales of Early Learning, Akshoomoff (2006) found that lower scores on the various domains were associated with higher off-task behaviours. Therefore,

structured tasks may require additional skills, which were not targeted in RIT. To counter this, the assessment was modified based on child requirements and the assessment was conducted sometimes in a cordoned corner of the room or on the floor, but children with lower developmental levels seemed to still perform worse on the task as compared to the UIA. Therefore, the test selected may not have been appropriate for the present sample. Conversely, use of standardised scales is needed in comparisons across studies and ensures generalisability of results. Future studies measuring elicited imitation may use additional measures to assess this skill in order to capture the wide differences seen in the ASD population.

Additionally, the present sample, although highly variable in ethnicity and gender as compared to other studies, largely included children with low developmental ages: most children (22 out of 24) were found to have verbal and non-verbal mental age below 29 months while having a chronological age of 29 months and above (22 out of 24 children). This was not intentional and inclusion and exclusion criteria were broad in terms of developmental level. However, it must be noted that recruitment was a major challenge due to a greater resistance in the community for an autism diagnosis. Thus, children diagnosed early usually present with more severe features.. This limits generalisability of findings to a larger ASD population and would require larger samples with greater variability in developmental levels in order to draw firm conclusions regarding RIT as an effective treatment for children with autism. Conversely, these results are promising, in that children with low developmental levels can also benefit from RIT.

Future studies must focus on full-scale randomised trials looking at use of standardised tools as well as including different real-life measures in order to capture the entire range of behaviour. In addition, follow-up of intervention effects was not possible as part of this study

and studies need to look at maintenance of gains, as stability in spontaneous use of skill is likely to be an important determinant of later development.

SUMMARY AND IMPLICATIONS OF CHAPTER 3

In Chapter 3, effects of RIT on spontaneous and elicited imitation skills were assessed in young children with autism along with examining child characteristics as correlates of outcome. Stratified randomisation produced two well-matched groups –Treatment and Wait-List Control groups. Children with autism in the Treatment group showed significant improvements in spontaneous, social imitation skills, more specifically object imitation, as compared to children in the Wait-List group. No group differences were found on measure of elicited imitation. Also, children with less social difficulties and repetitive stereotypic behaviours as assessed on the ADOS were found to be better responders to RIT. This study has therefore generated the first external replication of RIT demonstrating that RIT may be an early intervention program positively impacting social imitation in children with autism.

The current chapter provided evidence for efficacy of RIT using behavioural measures. In Chapters 4 and 5 two novel techniques of ERP and EEG are employed to examine neurological correlates of observed behavioural changes and changes on global social processing respectively.

CHAPTER 4

THE EFFECT OF RECIPROCAL IMITATION TRAINING ON HUMAN ACTION AND NON-HUMAN ACTION SOUND PROCESSING IN CHILDREN WITH AUTISM

4.1 INTRODUCTION

Imitation typically involves a person replicating their partner's actions as well as goals, thereby acquiring, by observation, a motor behaviour (Vivanti & Hamilton, 2014; Rizzolatti & Fabri-Destro, 2010). Therefore, both observation of action and performance of an action are important aspects of imitation where information from different sensory modalities is transformed into motor representation (Rizzolatti & Fabri-Destro, 2010; Chapter 1 section 1.4.2).

Advances in neuroscientific techniques such as electroencephalography (EEG) and functional magnetic resonance imaging (fMRI), have enabled examination and understanding of the underlying neurological mechanisms associated with social-cognition, advancing our understanding of pathways for both typical and atypical development. Neurological correlates of imitation have been associated with specialised neural networks and mechanisms that underlie perceptual processing of action during action execution and observation. EEG studies have found human action processing reflected in mu rhythm activity of 8-13Hz recorded from the central channels over the sensorimotor cortex (Pineda, 2005; see also Chapter 1 Section 1.4.2). Studies of visual action observation have shown that mu rhythm desynchronisation is associated with action observation and execution over the frontal, central and parietal cortex in both adults (e.g. Muthukumaraswamy, Johnson, & McNair, 2004) and children (e.g. Lepage & Théoret, 2006; Marshall, Young, & Meltzoff, 2011). Thus, the components of imitation, human action observation and execution are reflected in similar neural mechanisms in the brain. However, most studies evaluating human action processing primarily involve visual presentation of action stimuli, whereas action processing involves other sensory modalities as well.

Research into auditory processing of human actions has produced evidence that there may be separate mechanisms involved in the processing of human action sounds versus non-human action sounds. Assessing auditory processing of actions in children, Stefanidou, Ceponiene and McCleery (in review) found that for both 2 to 3 year old toddlers and 4 to 6 year old children, human action sounds produced early sensory as well as late perceptual processing ERP component differences recorded from electrodes over the frontal, frontocentral, temporal, and parietal regions. Conversely, non-human action sounds produced only early sensory component differences in the frontal, frontocentral, and temporal channels. Furthermore, toddlers exhibited right lateralisation for human action sounds in later cognitive components recorded in frontal channels while this activity was bilateral for children. In another ERP study of infant auditory processing of human action sounds, human vocalisations, environmental and mechanical sounds, Geangu and colleagues found that human action sounds were processed differentially to human vocalisations in the temporal regions in 7-month old infants and there was cortical differentiation for 'human sounds' with human-produced sounds (action and vocalisations) showing undifferentiated modulation in the frontal and parietal cortex but differentiated from environmental and mechanical sounds (Geangu, Quadrelli, Lewis, Cassia, & Turati, 2015). Thus, typically, humans have specialised neural networks for human action processing in both visual and auditory domains.

As described in Chapter 1, sections 1.1 and 1.4, autism is a developmental disorder with marked difficulties in social functioning. Neurological studies of individuals with autism examining imitation and human action processing have suggested atypicalities during the execution and observation of hand action (Bernier et al., 2007; Honaga et al., 2010; Martinuea et al., 2010; Nishitani et al., 2004; Oberman et al., 2013; Theoret et al., 2005; Williams et al., 2006; but see also Raymaekers, Wiersema, & Roeyers, 2009; Bernier, Aaronson &

McPartland, 2013; Fan, Decety, Yang, Liu, & Cheng, 2010; see Hamilton, 2013 for a review). To date, the majority of studies related to human action processing in autism have utilised only the visual domain. Only one study has evaluated auditory processing of human actions. Stefanidou (2014) assessed auditory processing of human action versus non-human action sounds in high functioning, 4 to 5 year old children with autism compared to a chronological and verbal age matched typically developing control group. Children were exposed to human action sounds of hands clapping and hands ripping paper as well as non-human action sounds of ocean waves and helicopters. A match-mismatch paradigm was used in which stimuli included human action followed by human action (match) or non-human action (mismatch), and non-human action followed by non-human action (match) or human action (mismatch). Results indicated that 4 to 5 year old high-functioning children with autism demonstrated differences in the processing of human action sounds in the later component (N4), recorded over the parietal region, relative to controls. Specifically, children with autism had a larger response to matched sounds as compared to typically developing children who had a larger response to mismatched sounds, leading the authors to conclude that children with autism did not show a mismatch effect, as seen in the typical group. Thus, neural processing differences in autism may be evident at both auditory and visual levels for human action processing.

There is growing interest in the impact of intervention on neural processing of individuals with autism in an effort to evaluate success of behavioural interventions in altering atypical brain activity in autism (Dawson, 2008). As discussed in Chapter 1 section 1.4.3, autism intervention studies have begun to utilise neurological indices as measures of change, in addition to traditional behavioural assessment. Dawson et al. (2012) for example, employed EEG and ERP as secondary outcome measures in a randomised controlled trial of the Early Start Denver Model (ESDM) intervention. Differences in face processing were

evaluated using ERPs, and it was found that children with autism who received ESDM exhibited shorter latency Nc component responses to face stimuli, which were comparable to a typically developing contrast group and differed significantly from the group of children with autism receiving community interventions. In a study evaluating Pivotal Response Training (PRT), fMRI was used to index changes in social functioning (Voos et al., 2013). The study involved two children who underwent intervention and results revealed that both children showed increases in cortical activation of the fusiform gyrus and other distinct brain regions while viewing biological motion stimuli from pre-training to post-training. A third study evaluating the Program for Education and Enrichment of Relational Skills (PEERS) for adolescents used EEG to evaluate neural correlates of social approach behaviours (Van Hecke et al., 2013). The adolescents who underwent PEERS intervention exhibited greater left frontal EEG asymmetry (associated with increased approach (versus avoidance) tendencies; Coan & Allen, 2003b) compared to a wait-list control group. Similarly, a study involving a theatre-based intervention focusing on development of social skills in 8 to 14 year old adolescents with autism showed changes in ERP components associated with face recognition memory in the treatment group while these changes were not seen in the wait-list control group (Corbett et al., 2014). As discussed in section 1.4.3, all studies described above had major limitations. The lack of a control group, low number of participants, lack of a typical comparison group, and lack of pre-training data suggest that although there may be emerging evidence that behavioural interventions may have some effect on neural functioning, there are no conclusive findings. On the other hand, these studies demonstrate that EEG/ERP and other neuroimaging techniques can help delineate the neural mechanisms and pathways associated with responses to particular behavioural interventions.

Thus, the aim of the current study was to use ERP as a secondary outcome measure in the pilot randomised controlled trial (RCT) of Reciprocal Imitation Training (RIT), described in Chapters 2 and 3. As described previously, RIT is an intervention with a focus on increasing social responsiveness and social imitation skills in young children with autism (Ingersoll, 2010b, 2012; see also Chapter 1 section 1.2.3 and Chapter 3 section 3.2.4). Since RIT focuses on social imitation skills and action processing is an index of imitation, an auditory human action processing paradigm (Stefanidou, Ceponiene & McCleery, in review) was employed. As described in Chapter 1, Section 1.4.2, studies of human action processing have been used to understand imitation difficulties in autism, and the previous study utilizing the same auditory action paradigm found that high functioning 4 to 5 year old children with autism paid significantly less attention to human action sounds compared to typically developing children (as reflected in the N4 ERP component over the frontocentral channels; Stefanidou, 2014). Also, young children with autism showed right lateralisation during human action processing over the parietal region while typically developing children showed left lateralisation during human action sounds condition (Stefandou, 2014). Thus using an established auditory mismatch paradigm (Stefanidou, 2014; Stefanidou, Ceponiene & McCleery, in review), it would be important to see how a targeted imitation-based early intervention may have an effect on auditory processing of human actions in autism. It was, aimed to investigate neurological correlates of behaviour changes in imitation by using ERP methodology to examine auditory human action processing in children who underwent RIT compared to controls. Specifically, differences in the processing of human action and non-human action sounds were of interest, reflected in the differential responses to match versus mismatch stimuli. Owing to excellent temporal resolution of ERPs it was aimed to examine differences in neural processing speed and amplitude at various stages of auditory processing

in the two groups. A second aim was to investigate correlation between ERP responses and changes in imitation skills post-RIT. As discussed in Chapter 3, significant changes were observed in spontaneous imitation only in the Treatment group. Therefore, the study aimed to evaluate whether there were any relationships between neural differences observed for auditory action processing and behavioural outcome on a measure of social imitation, the unstructured imitation assessment (UIA). As this was an exploratory study directional hypothesis could not be made. It was hypothesised that children in the Treatment group will differ significantly from the Wait-List Control group in their processing of mismatch trials for human action sounds at T2. Secondly, it was hypothesised that children in the Treatment group will show greater left lateralisation while children in the Wait-List Control group will show greater right lateralisation over the parietal channels at T2. Third, it was hypothesised that speed of processing (measured through latency) for human action sounds will be faster for children in the Treatment group compared to the Wait-List Control group. Fourth, it was hypothesised that children in the Wait-List Control group will show greater processing of non-human action sounds reflected in greater responses to mismatch non-human action trials compared with the Treatment group. Finally, it was hypothesised that there will be an association between change in imitation scores measured on the UIA and mismatch effect in the human action sound processing.

4.2 METHODS

4.2.1 Design

Children with autism aged two to six years were recruited for the RCT as described in Chapters 2 and 3. After informed signed consent from parents, all children were administered a battery of behavioural measures at T1 (see section 3.2.3 in Chapter 3 for details). Along

with behavioural measures, ERP testing was also conducted (see also Figure 2.1 in Chapter 2). ERP testing was completed after administration of a behavioural measure on the first day of assessments for all children. Child desensitisation procedures were used if parents had reported head sensitivities in order to make the EEG net application easier and to help ensure that the child completed testing. Desensitisation techniques were used for fourteen children in the sample of twenty-four at T1. These families were asked to come back for an extra day of assessments (day 3) in order to complete ERP testing. In summary, after the initial assessments, participants were randomised using a stratified randomisation technique to two groups: Treatment and Wait-List Control group. Children randomised to the Treatment group received 20 sessions of RIT in a period of 12-14 weeks while children in the Wait-List Control group received either no treatment or treatment-as-usual (see Chapter 2 section 2.2 for details). All children were invited post 12-14 weeks after T1 for a second round of assessments, T2. The behavioural battery and ERP testing were repeated. Ten participants required desensitisation to the EEG sensor net at T2.

4.2.2 Participants

Participants were children with autism recruited for the pilot RCT described in Chapter 3 section 3.2.1. All twenty-four children from the RCT were given the opportunity to participate. ERP data were recorded from a total of 18 children at T1 and 21 children at T2. However, ERP data were unusable from approximately 30% of the children at both T1 and T2, due to excessive movement and ocular artefacts. Therefore viable, sufficiently artefact-free data were obtained from a total of 13 children at T1, six children in the Treatment group and seven in the Wait-List Control group; and 15 children at T2, eight children in the Treatment group and seven children in the Wait-List Control group. Out of these children only five children in each group produced viable data at both T1 and T2. Therefore, at the

group level, data at T2 were analysed for outcome results, with data from the 10 participants who produced viable data at both T1 and T2 further examined in order to identify evidence of change associated directly with the intervention from T1 to T2.

As noted in Chapter 3 section 3.2.1, all children met criteria for Autism Spectrum Disorder on the ADOS-G (Lord et al., 2000) at T1. All children in the final sample, except one, also received an independent clinical diagnosis of ASD from a NHS clinician. The one child who had not yet received a clinical diagnosis of autism was under observation of a NHS clinician and the family has been asked to visit the NHS every three months to monitor the child's development. Participant characteristics at T1 are described in Table 4.1. Independent samples t-test and chi-square test showed no differences between groups on chronological age, gender, non-verbal and verbal mental age, ADOS scores or handedness.

Table 4.1: Participant characteristics by group at intake.

	Group M (SD)		χ^2 / t	df	p-value
	Treatment (n=8)	Wait-List Control (n=7)			
Gender (% male)	50%	85.7%	2.14	1	0.14
Chronological Age (in months)	41.5 (16.0)	40.9 (12.7)	0.09	13	0.93
Nonverbal Mental Age	27.4 (12.8)	23.7 (10.4)	0.61	13	0.55
Verbal Mental Age	17.1 (9.5)	18.1 (16.4)	-0.14	13	0.89
ADOS total score	13.5 (4.2)	15.4 (4.1)	-0.90	13	0.39
Handedness (% right-handed)	100%	100%	-	-	-

4.2.3 Behavioural Measures

All participants completed behavioural measures that included descriptive, diagnostic, and behavioural-change measures (for a full description see section 3.2.3, Chapter 3). The Mullen Scales of Early Learning (Mullen, 1995) was used to obtain verbal and non-verbal mental age for the participants while ADOS – G (Lord et al., 2000) was administered at T1 to confirm that all children met the criteria for an Autism Spectrum Disorder. Two behavioural change measures were administered as well: the unstructured imitation assessment (UIA) and the structured imitation assessment (SIA).

4.2.4 Intervention

The primary goal of RIT is to teach children with autism social responsiveness and social imitation. A full description of the intervention is outlined in section 3.2.4, Chapter 3. To summarise, children in the Treatment group received 20 sessions of RIT. All one-hour sessions of RIT involved the child playing individually with two or three different therapists for a duration of 20 minutes each. Every 20 minutes a therapist presented five different sets of developmentally appropriate toys for the children to play with. Object and gesture imitation were targeted in a systematic manner with all the children.

4.2.5 Electroencephalography (EEG) and Event-Related Potentials (ERP) – Novel neurological measures of change

First used by Hans Berger (1929), EEG allows examination of natural electrical brain activity (Luck, 2014). It is a non-invasive technique with excellent temporal resolution (Luck, 2014; Nelson & McCleery, 2008). EEG is a cost-effective and efficient method for recording neurological activity and can be used across the age range (de Haan, 2007; Nelson &

McCleery, 2008). Due to these advantages, EEG has been widely used across populations to further the understanding of brain mechanisms in typical as well as atypical development (de Haan, 2007; Nelson & McCleery, 2008). Although initially researchers focused on changes in continuous EEG, event-related activity, including evoked and endogenous responses, later became the focus for understanding the mental chronometry of human beings (de Haan, 2007; Luck, 2014; Nelson & McCleery, 2008).

Event-related potential (ERP) is the electrical response generated in the brain in response to a discrete stimulus. According to Nelson and McCleery (2008), ERP is "the synchronous activation of electrical fields associated with activity of large proportions of neurons." (p. 1252). As ERPs can be generated without an overt behavioural/verbal response to a stimulus, it allows study of mental processes in infants and young children as well as individuals with limited motor or verbal abilities (DeBoer, Scott & Nelson, 2007). ERPs are collected from the scalp surface by placing scalp electrodes to record responses to the repeated presentation of a stimulus in many trials (Nelson & McCleery, 2008). ERPs are time-locked to stimulus presentation and ERP deflections (positive or negative going components) are believed to reflect cognitive processes associated with sensory and perceptual skills (DeBoer et al., 2007). Typically, early components have been associated with sensory processing while later components with perceptual and cognitive processing though there is evidence that some early components may be impacted by conditions under which stimulus is presented and based on relevance of stimuli, early sensory responses are either enhanced or supressed (Hillyard, Teder-Sälejärvi & Münte, 1998).

One disadvantage often cited for EEG/ERP is the relatively poor spatial resolution (Luck, 2014). However, advances in high-density arrays and use of techniques such as source analysis have allowed for better understanding of the scalp distribution and activity sources

(Nelson & McCleery, 2008). Combining EEG/ERPs with other brain imaging sources has also evidenced success in understanding brain mechanisms involved in EEG (de Hann, 2007). As EEG/ERPs can reflect perceptual processing reliably as well as changes in brain development, and are relatively easy to use with young children, they can provide a reliable neurological measure of change to early intervention. Given the aim of examining possible effects of changes through RIT in brain activity of very young children with autism, both EEG and ERP techniques were determined to be suitable neuroscientific measures. This chapter focuses on an ERP assessment while Chapter 5 utilises EEG to evaluate neural mechanisms associated with RIT.

There are various stimulus presentation methods that have been used in ERP assessments. For the purpose of this study, a mismatch paradigm, Repeated Auditory Mismatch (RAMM; Stefanidou, Ceponiene & McCleery, in review), was used. It is based on the principle of brain response to habituation, that is, as the brain habituates to a stimulus, presentation of an odd/novel stimulus leads to a greater neural response. Thus, responses to the second (odd) stimulus are of interest. The paradigm was designed to evaluate auditory human action processing in young children and has been previously used in autism research (Stefanidou, 2014).

4.2.6   Rapid Auditory Mismatch Paradigm

In the RAMM paradigm two types of auditory stimuli were presented: sounds produced by human actions and non-human actions (Stefanidou et al., in review). There were two distinct human action sounds of simple human action (clapping), and human action-on-object (ripping of paper). The non-human action sounds comprised an object sound (helicopter) and an environmental sound (ocean waves). All auditory stimuli were extracted from the digital

video clips of actions and each sound type had four different exemplars (Stefanidou et al., in review). All stimuli were presented as .wav files (16 bit, 44.1Hz sampling) having a mean duration of 1020 ms (range: 790 to 1250 ms) and both human and non-human action sounds were equalised to 65dB (Stefanidou et al., in review).

The ERP paradigm was implemented using E-Prime software (Schneider, Eschman, & Zuccolotto, 2002). There were four types of trials presented in a randomised order, each with a 25% probability. For descriptive purposes, the trial types were labelled and defined based on the second stimulus presented in the trial and whether it was a match or mismatch of the preceding sound: (a) *Human action Match trial*, where human action sound was followed by human action sound (e.g. ripping paper sound followed by ripping paper sound); (b) *Human action Mismatch trial*, where non-human action sound was followed by a human action (e.g. ocean wave followed by ripping paper sound); (c) *Non-human action Match trial* which involved two consecutive non-human action sounds (e.g. helicopter blades sound followed by helicopter blades sound); (d) *Non-human action Mismatch trial* where human action sound was followed by a non-human action sound (e.g., clapping sound followed by helicopter blades sound; see Figure 4.1; Stefanidou et al., in review). In the match trials, although the perceptual category of the stimuli was the same, they were different exemplars of the same type of sound (e.g. clapping sound 1 followed by clapping sound 2). In the mismatch trials, the clapping sounds were always paired with helicopter sounds and paper-ripping sounds were paired with ocean waves sounds. Within each trial, the inter-stimulus interval was 150ms while the inter-trial interval varied between 900 to 1200ms (Stefanidou et al., in review). Epochs were time-locked to the second stimulus with a stimulus interval duration of -100 ms (before the second auditory stimulus) to 700 ms (after the second stimulus). The

entire paradigm was run for approximately 30 minutes, with a single block of approximately 570 trials (Stefanidou et al., in review).
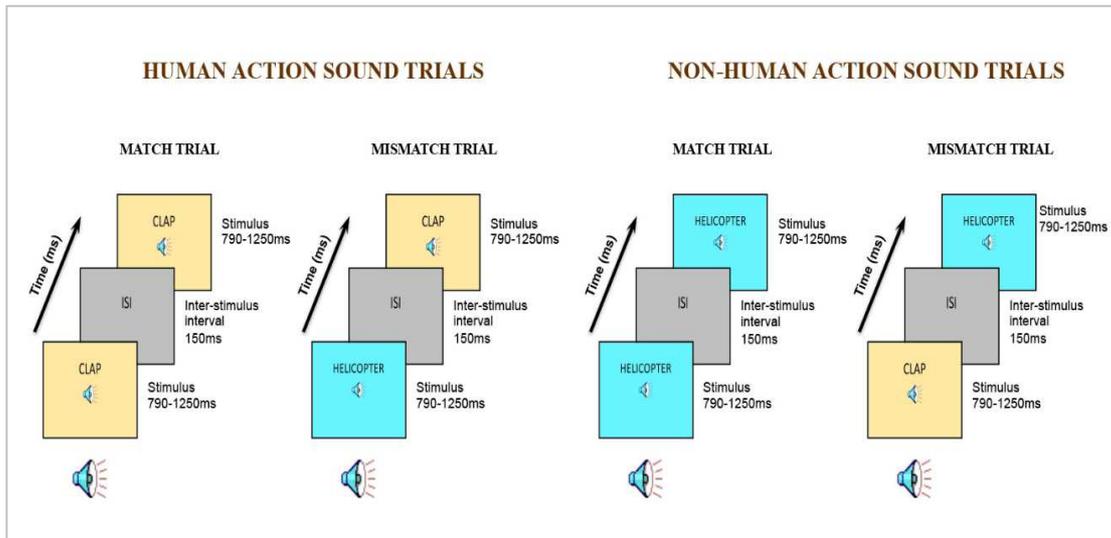
Figure 4.1: Rapid Auditory Mismatch Paradigm, taken from Stefanidou, Ceponiene and McCleery (in review)

4.2.7   ERP Recording Procedure

Before the ERP recording, a researcher played with different hats with the child in a playroom to desensitise the child to wearing the net on their head. During play, head size was measured using a tape measure and participants were given a choice of children's movies which they could watch during the ERP recording: Peppa Pig©, Cars©, Dinosaurs©, Thomas the Tank Engine© and Winnie-the-Pooh©. The videos that children could choose from remained the same across participants. ERP recording was conducted in a sound-attenuated EEG/ERP testing room. All participants sat approximately 60 cm from the screen and audio speakers. Except for three children who sat on their own, all participants sat on their parent's lap. Before the net application, all participants were shown audio-visual clips of each human

action and non-human action sound stimulus used in the experiment. Each clip was played twice in order to familiarise the participant to the source of sound generated (Figure 4.2). Once the child had watched each clip, sensory toys were used to distract the child while the EEG Sensor Net was placed on the participant's head. Following the net application, during the experiment, the chosen DVD was played without sound while the ERP experimental sound stimuli were played in the background via speakers (Stefanidou, 2014). Thus, the participants listened to the human-action and non-human action sounds passively while their brain activity was recorded in the form of event-related potentials. None of the children's movies included visuals of any of the sound stimuli in the ERP experiment. If children became fidgety, bored or upset, sensory toys were used to distract and keep them still. ERP recording lasted approximately 30 minutes or was discontinued earlier if the child got upset. The EEG/ERP testing protocol and procedures were the same at T1 and T2.
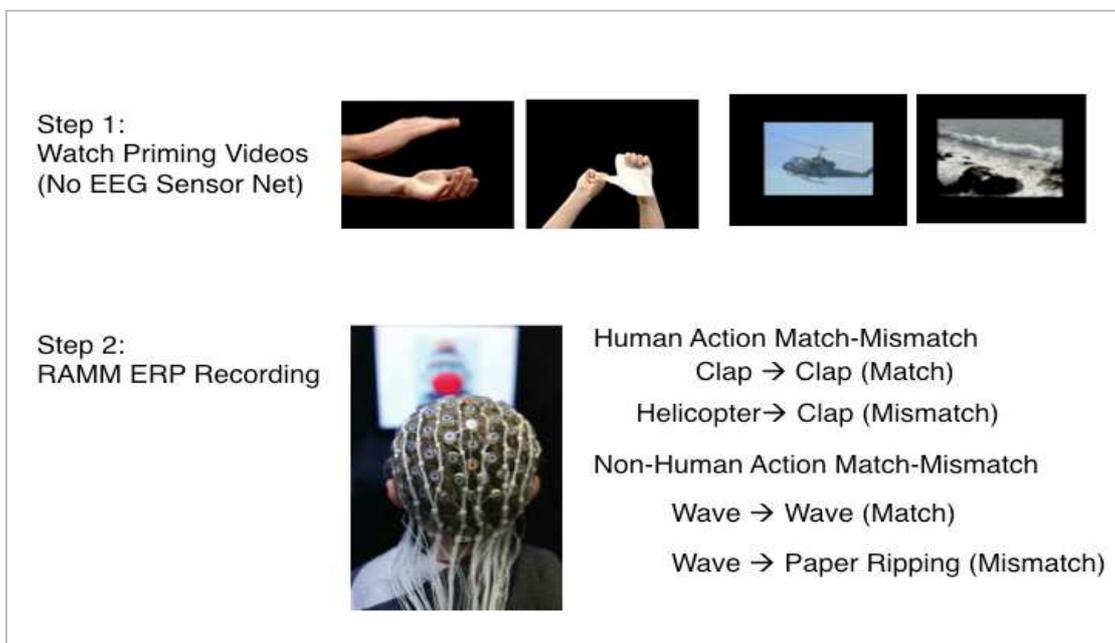
Figure 4.2: Steps followed during ERP recording, taken from Stefanidou, Ceponiene and McCleery (in review).

4.2.8 ERP Analysis

A high density, 128-channel Hydrocel Geodesic Sensor Net (HCGSN, Electrical Geodesics Inc., Eugene, Oregon) was used to record brain electrical activity (Tucker, 1993). This sensor net allows for quick and easy application and therefore is preferable for both young children and atypical populations (Nelson & McCleery, 2008). EEG was referenced to a single vertex electrode Cz (sampling rate = 500 Hz) during recording, and all bioelectrical signals were recorded using EGI NetStation amplifiers with an input impedance of less than 100 kΩ (Stefanidou, 2014; Stefanidou et al., in review).

The ERP analysis as described in Stefanidou (2014) was followed. All ERP data was analysed by the researcher and two trained student research assistants. Due to the nature of ERP analyses, biases in editing process are highly unlikely. However, while both research assistants were kept blind to group allocation, the author was not blind, and thus biases in ERP analyses could not be completely controlled for.

All data were filtered offline using a band-pass filter of 0.1 to 40 Hz. Data were then segmented to epochs using NetStation 4.5.1. software (Electrical Geodesics). All epochs were time locked to the second auditory stimulus in the trial, with a stimulus interval of -100 ms to 700 ms and organised by trial type. An automated artefact detection tool was used to process data and identify bad channels. Segments were marked bad if they contained more than 12 bad channels or contained eye movements or eye blinks. Channels were marked bad if the amplitude varied more than 150 μV from minimum to maximum. Subsequent to this automated artefact detection, each trial was also visually examined individually to identify and discard data with ocular or motor artefacts that were not identified by the automatic artefact detection procedure. All children whose data are included produced a minimum of 30 viable ERP trials per condition (Table 4.2). Independent samples t-test revealed no group

differences on the mean number of artefact-free trials per condition (Table 4.2). Data in bad channels contained in trials with fewer than 12 bad channels were replaced using a spherical spline interpolation algorithm (Srinivasan, Nunez, Tucker, Silberstein, & Cadusch, 1996). Individual participant data were averaged and then re-referenced to an average reference. All files were baseline corrected to a 100 ms pre-stimulus interval.

Table 4.2: Mean (S.D.) of artefact free trials on human-action and non-human action sound conditions.

Condition	Treatment (*n*=8)	Wait-list Control (*n*=7)	*t (13)*	*p-value*
Human Action Sounds				
Match	48.4 (14.4)	43.0 (6.0)	0.92	0.38
Mismatch	47.5 (10.4)	43.4 (6.6)	0.89	0.39
Non-Human Action Sounds				
Match	49.9 (11.5)	46.3 (8.9)	1.27	0.29
Mismatch	50.4 (13.9)	43.1 (6.3)	0.67	0.52

Electrode locations and time windows for analysis were chosen based on the previous findings of Stefanidou, Ceponiene & McCleery (in review) and Stefanidou (2014) as well as visual inspection of grand average ERP data. Frontal, central, and parietal sites were chosen for analysis with 25 frontal electrodes (eight left and right and nine middle), 10 central and 24 parietal electrodes (eight electrodes each in left, middle and right, Figure 4.3). As waveforms revealed only one clear early peaking component between 40-180ms, P1 (frontal and central sites) and N1 (parietal), peak latency was analysed for this one component. Subsequently, the

same time windows were chosen across all three areas: 180-310ms, 310-440ms, 440-570ms and 570-700ms. The mean amplitudes across time windows were analysed between conditions and groups.
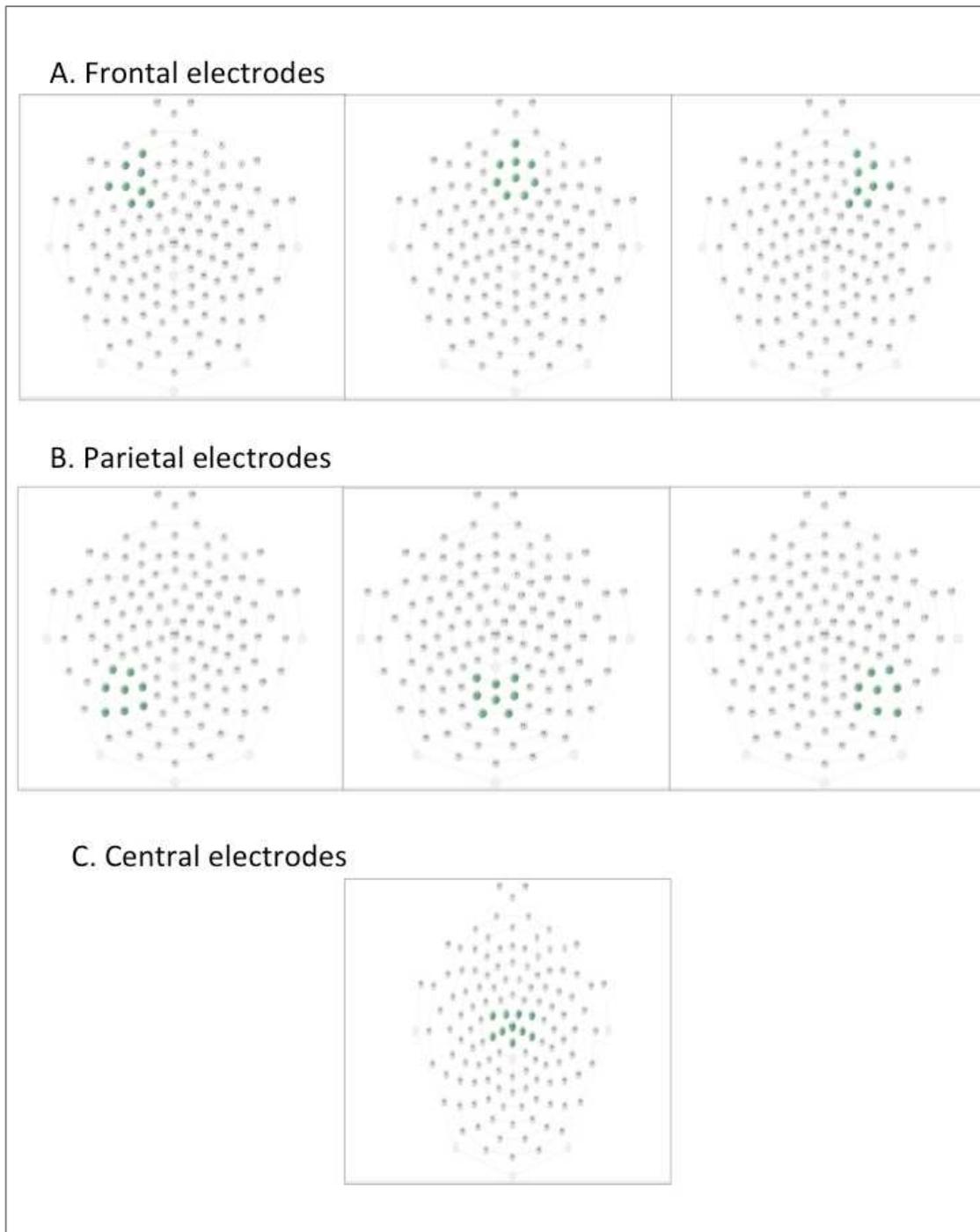
Figure 4.3: Montage selected for analysis. A. Left, middle and right Frontal electrodes selected for analyses. B. Left, middle and right Parietal electrodes selected for ERP analyses. C. Central electrodes selected for analyses.

Human action and non-human action sounds were analysed separately for a mismatch effect. This was the strategy adopted because previous research has shown that there are different brain mechanisms involved in processing of human action and non-human action sounds (Guisti et al., 2010; Lloyds-Fox et al., 2013; Pizzamiglio et al., 2005) and the aim of the study was to look at the effect of intervention on both these conditions. Also, the condition of the trial, match or mismatch, was of interest because a mismatch response would demonstrate attention orienting to novel/unexpected stimuli. A mismatch effect was deemed to be evident when there was a greater brain response to mismatch trials than match trials (mismatch - match = mismatch effect).

4.3   RESULTS

Repeated measures ANOVAs were conducted on mean amplitudes of all time windows and peak latency for the P1/N1 (40-180ms). Only T2 data were used for these analyses. All results violated Mauchley's test of Sphericity and therefore, Greenhouse-Geisser adjusted values are reported. Pairwise comparisons and planned t-tests using Bonferroni corrections[8] were used for post-hoc analysis.

Individual participant data analysis was also carried out to confirm group data findings of T2 (outcome) data. Individual participant data was analysed only for those regions where group differences were found in order to have an experimentally controlled approach. To

---

[8] The SPSS manual provides syntax for Bonferroni correction that can be used with pairwise comparisons and t-tests. This syntax was applied for each comparison.

answer question about change through treatment, exploratory analysis was conducted between groups at T1 and T2.

4.3.1 Human Action Sound Processing

In order to evaluate neural processing speed and amplitude of the early sensory component, P1 mean amplitude and peak latency were analysed using between-subjects repeated measures ANOVAs with condition (match, mismatch stimuli) as a within-subjects factor and group (Treatment, Wait-List Control) as the between-subjects factor for the central channels revealing no significant effects (Appendix H). A similar repeated-measures ANOVA was carried out for the frontal (P1) and parietal (N1) areas with condition (match, mismatch) and hemisphere (left, middle, right) as within-subjects factors and group (Treatment, Wait-List Control) as a between-subjects factor. No significant effects were found over the frontal region (Appendix H). There was a main effect of hemisphere for both mean amplitude (F $(1,13) = 5.63$, $p < 0.01$, $\eta_p^2 = 0.30$), and peak latency (F $(1,13) = 3.57$, $p = 0.04$, $\eta_p^2 = 0.22$) of N1 over the parietal channels suggesting hemispheric differences in processing speed and amplitude of N1 in the parietal region.

To evaluate perceptual auditory processing differences in human action sounds, a between-subjects repeated measures ANOVA with condition (match, mismatch) and time (different timing windows: 180-310ms, 310-440ms, 440-570ms, 570-700ms) as a within-subjects factors and group (Treatment, Wait-List Control) as the between-subjects factor was carried out over all three areas: frontal, central and parietal. For the frontal and parietal regions, as hemispheric activity was of interest, an additional within-subjects factor of hemisphere (left, middle, right) was included in the ANOVA.

Analysis revealed a significant condition x group effect for the central channels (F (1,13) = 21.21, $p < 0.01$, $\eta_p^2 = 0.62$) indicating group differences in match versus mismatch trials (Figure 4.4). Furthermore, a significant condition x time interaction was found over the central region (F (1,13) = 4.03, $p = 0.04$, $\eta_p^2 = 0.24$) suggesting difference in processing time of match and mismatch trials. Pairwise comparisons using Bonferroni correction were calculated in order to understand the interaction effects. There was a significant difference in ERP response to match trials in the Wait-List Control group (M = 1.51μV, $S.E.$ = 0.7) as compared to the Treatment group (M = -0.86μV, $S.E.$ = 0.6) over the central channels (p = 0.03). Post-hoc analysis also showed that there was a significant difference in ERP response during the mismatch trials in the Treatment group (M = 1.12μV, $S.E.$ = 0.6) as compared to the Wait-List Control group (M = -0.99μV, $S.E.$ = 0.7; p = 0.04). Planned pairwise t-tests also showed that within groups there was a significant difference between processing of match and mismatch human-action sounds (t (7) = -2.56, p = 0.04 for Treatment group and t (6) = 4.75, p <0.01 for the Wait-List Control group; Figure 4.5).

These results suggest a significant difference in processing of match and mismatch trials between the Treatment and Wait-List Control group at T2, as evidenced by an opposite pattern of ERP activity for match and mismatch trials between groups (Figure 4.5).
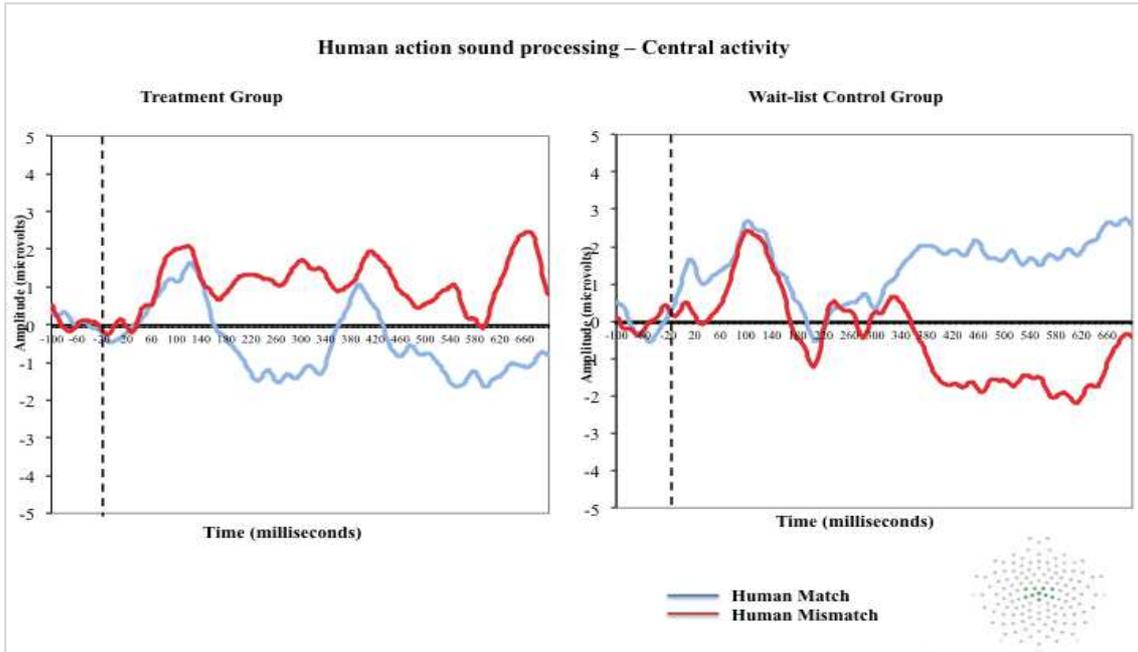
Figure 4.4: ERP waveforms showing activity over the central electrodes in the Treatment and Wait-List Control groups for human action sound processing at T2.
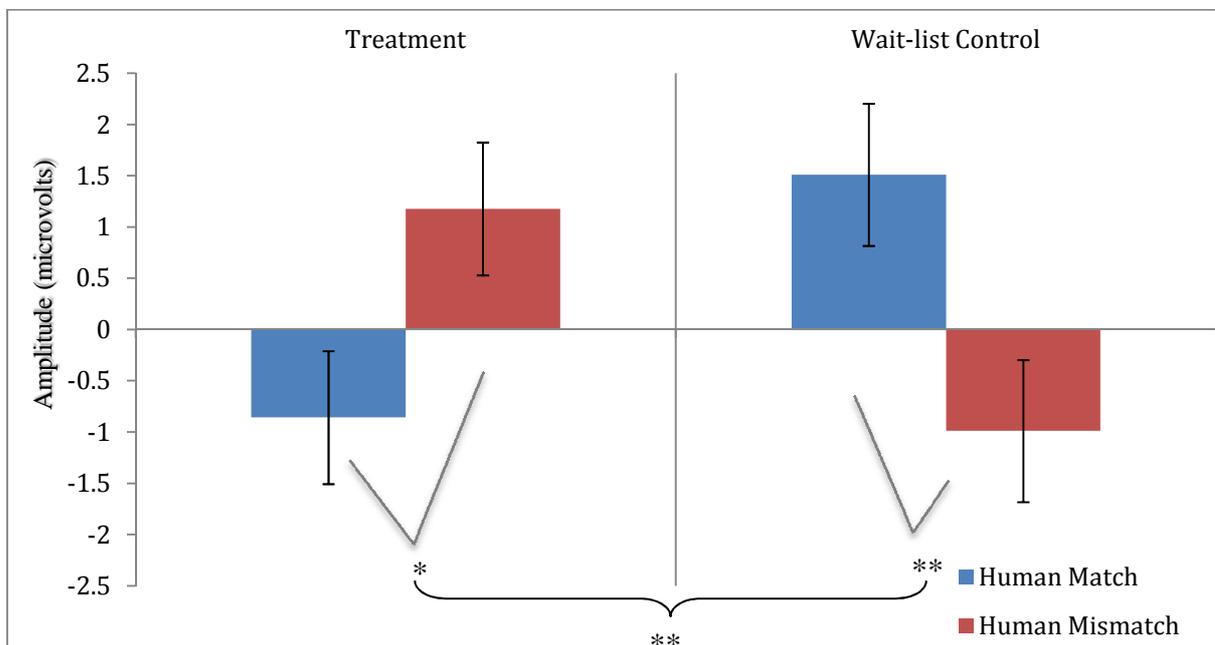
Figure 4.5: Graph showing significant difference between the Treatment and Wait-List Control group in ERP response to matched and mismatched trials for human-action sound processing at T2. Error bars represent standard error.

Pairwise comparisons of processing differences across timing windows of the two conditions showed that the interaction effect was driven by larger positive response to match trials at 310-440ms ($M = 0.8\mu V$, *S.E.* = 0.5) as compared to response at 180-310ms ($M = -0.43\mu V$, *S.E.* = 0.5; $p < 0.01$).

Thus, over the central channels, group differences in human action processing were observed with the Treatment and Wait-List control group showing opposite patterns of ERP responses at T2.

No significant interaction effects were observed over the frontal region (Appendix H), while over the parietal region a significant main effect of hemisphere ($F(1,13) = 8.4$, p< 0.01, $\eta_p^2 = 0.4$); condition x hemisphere x group interaction ($F(1,13) = 3.93$, p = 0.04, $\eta_p^2 = 0.23$); and condition x hemisphere x time interaction ($F(1,13) = 3.3$, p = 0.03, $\eta_p^2 = 0.2$) were found. Post-hoc analysis revealed that the condition x hemisphere x group effect was driven by differences in hemispheric processing of the mismatch trials in the Wait-List group. The Wait-List Control group had a larger negative response to the mismatch trial over the middle-parietal channels ($M = -1.9\mu V$, S.E. = 1.0) as compared to the left parietal channels ($M = 1.12\mu V$, S.E. = 0.9; p <0.01). This difference was not significant when compared to the right hemispheric parietal region ($M = -0.91\mu V$, S.E. = 1.3; p = 0.07). Hemispheric differences in processing were not found in the Treatment group.

Thus differences in processing were observable over the parietal channels for human action auditory processing between Treatment and Wait-List groups. Visual inspection of data also showed that the primary difference in processing between the two groups was over the middle parietal channels for the mismatch trials (Figure 4.6).

Paired contrasts for the condition x hemisphere x time interaction revealed that this effect was driven by greater activity for the mismatch trials in the left hemisphere in the later

two timing windows of 440-570ms and 570-700ms. There was a greater positive response to mismatch trials at 440-570ms on the left channels (M = 1.14µV, S.E. = 0.7) as compared to the middle channels (M = - 0.83, S.E. = 0.9; p <0.01), and the channels over the right parietal hemisphere (M = -0.93µV, S.E. = 1.1; p = 0.03), both of which had a large negative ERP response. Similarly in the last time window of 570-700ms there was again a larger positive response on the left hemisphere (M = 1.78µV, S.E. = 0.8) as compared to the middle channels (M = - 0.58µV, S.E. = 1.0; p =0.02) and right hemispheric channels (M = - 0.48µV, S.E. = 1.1; p <0.01) where there was a smaller negative response.

Overall, in line with our first hypothesis that children in the Treatment group will differ significantly from the Wait-List group in their processing of mismatch trials for human action sounds at T2, the results suggest that children in the Treatment group differed from the Wait-List group in mean amplitude of ERP responses over the central and parietal channels. Secondly, it was hypothesised that children in the Treatment group will show greater left lateralisation while children in the Wait-list group will show greater right lateralisation over the parietal channels at T2. No differences in lateralisation were found in the two groups. Third it was hypothesised that speed of processing (measured through latency) for human action sounds will be faster for children in the Treatment group compared to the Wait-List Control group. However, no group differences in speed of processing of match or mismatch trials was found.
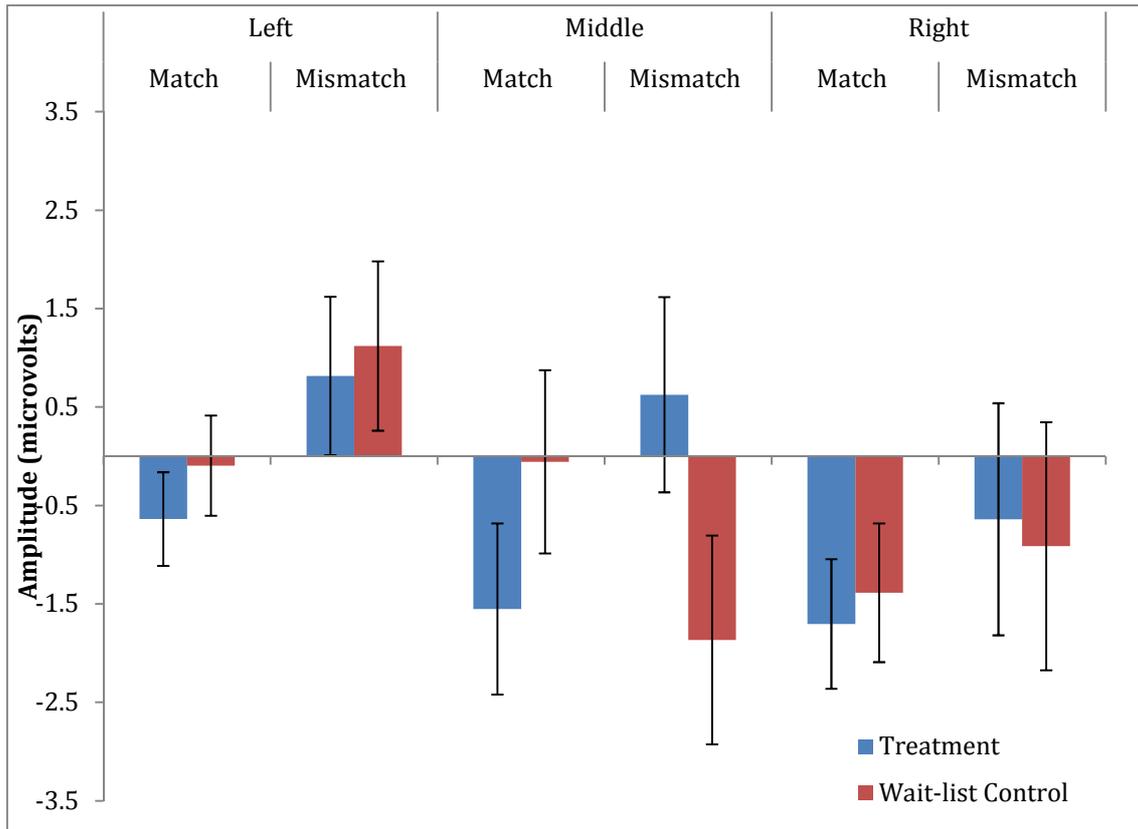
Figure 4.6: Graph showing significant difference between the Treatment and Wait-List Control group in ERP responses to matched and mismatched trials for human-action sound processing over the three different areas of the parietal cortex at T2. Error bars represent standard error.

From these analyses only differences in activity could be evaluated however it is not clear whether the differences were associated with treatment. The next set of analyses were, therefore, carried out to answer questions regarding differences in ERP activity through treatment.

4.3.1.1 Individual Participant Data Analysis: T1 and T2 Comparison

To examine the effect of intervention on change in ERP responses, T1 and T2 data were compared for participants who produced artefact-free data at both time points. In order to do so, difference scores were calculated for mean amplitudes of match and mismatch trials (i.e. mismatch – match = mismatch effect) for both time points T1 and T2. This was done only for the central and parietal regions for which significant effects for condition and group were found. Comparing the pre- and post-treatment data was important to understand whether the difference in ERP response between groups seen at outcome were associated with intervention or influenced by pre-intervention neural responses in the brain.

Figure 4.7 shows the mean difference scores for the central region. An opposite pattern of development in the Wait-List Control group compared to the Treatment group is evident. At T1, three children in the Treatment group have a negative difference, suggesting greater response to match trials, while three children in the Wait-List group have a positive difference, suggesting greater response to mismatch trials. Also, two children in the Treatment group had a greater response to mismatch trials and two children in the Wait-List group showed a greater response to match trials. At T2, three children in the Treatment group have a greater response to mismatch trials, one child had a slightly lower mismatch effect and one child had a smaller response to match trials. All children in the Wait-List group show a greater response to match trials.
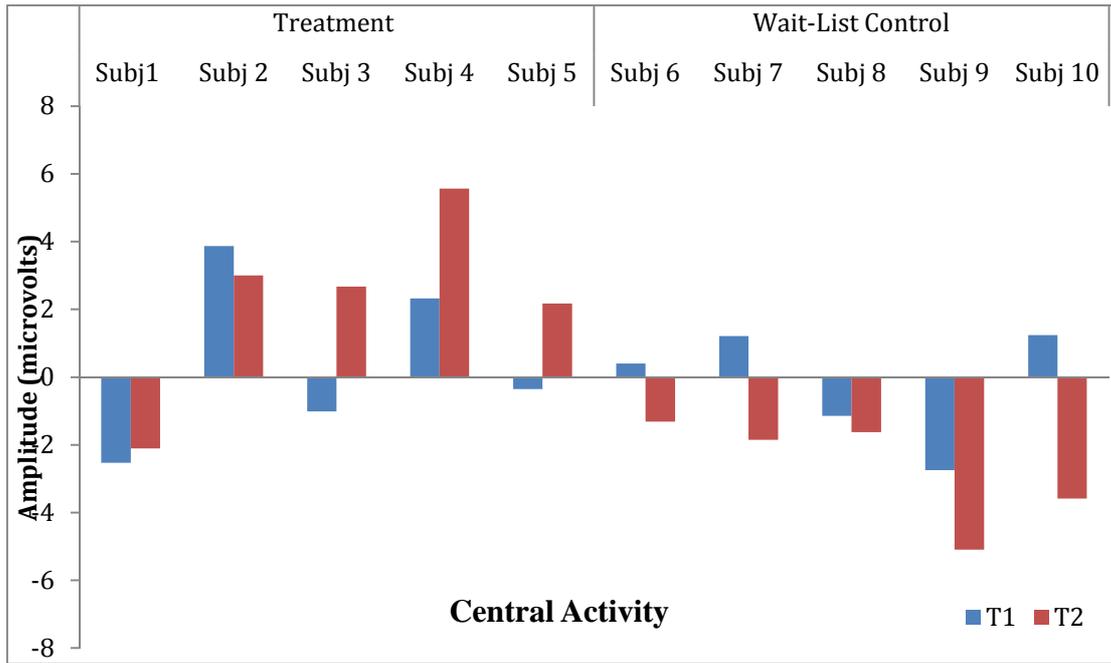
Figure 4.7: Individual participant data showing mismatch effect for each participant at T1 and T2 for the Treatment (n=5) and Wait-List Control group (n=5) over the Central channels.

Comparing the data of participants at a group level, a consistent opposite ERP response pattern was found between the Treatment and Wait-List Control group for the central channels (Figure 4.8). Even though a mismatch effect for both the Treatment and Wait-List group was found to be marginally different at T1, there were no statistically significant differences (Appendix H for supplementary analyses). Even when more participants were included in the samples at T2 the ERP responses at a group level were similar for change data and outcome data (Figure 4.8).
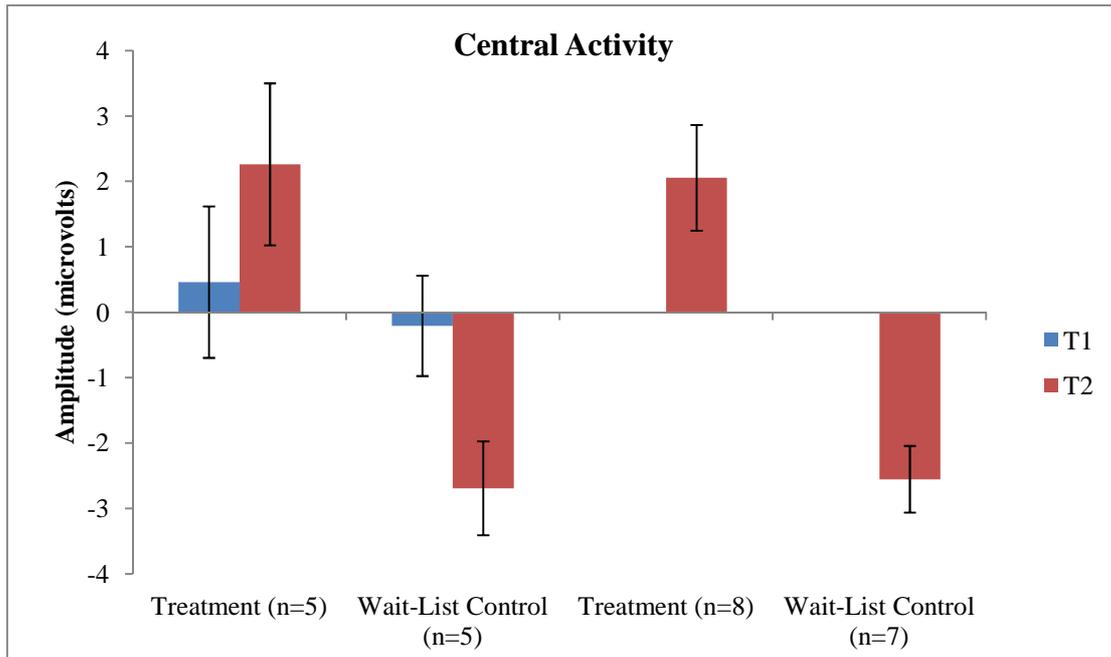
Figure 4.8: Mismatch effect seen in the Treatment (n =5) and Wait-List Control (n =5) group at T1 and T2 (change), and mismatch effect seen in Treatment (n = 8) and Wait-List Control group (n = 7) at only T2 (outcome), over the Central region for human action sound processing. Error bars represent standard error.

In the parietal region, results were more mixed for the Treatment group (Figure 4.8). In the Treatment group, participant 1 showed a reversal in activity from T1 to T2 over the left and middle areas of parietal cortex, participant 2 showed greater activity to match trials at both T1 and T2 while participant 3 and 4 showed greater response at T2 for mismatch trials. Participant 5 showed a reversal in ERP response from greater match processing to greater processing of mismatch trials over the left hemisphere only from T1 to T2. In the Wait-List Control group, there was a more consistent response across participants (Figure 4.9). A reversal in response was seen from T1 to T2 for all participants with a greater response to mismatch trials observed at T1 and this changed to a greater response to match trials at T2

over the middle and right parietal channels. <u>Thus, the patterns were mixed for the Treatment group but contrasted with a consistent pattern for the Wait-List Control participants.</u> At a group level (Figure 4.10), the Treatment and Wait-List Control group showed opposite patterns of activity at T1 but statistically these differences were not significant (Appendix H). At T2, group level outcome results were representative of individual participant means from a smaller sample, except in the right parietal channels (Figure 4.10).
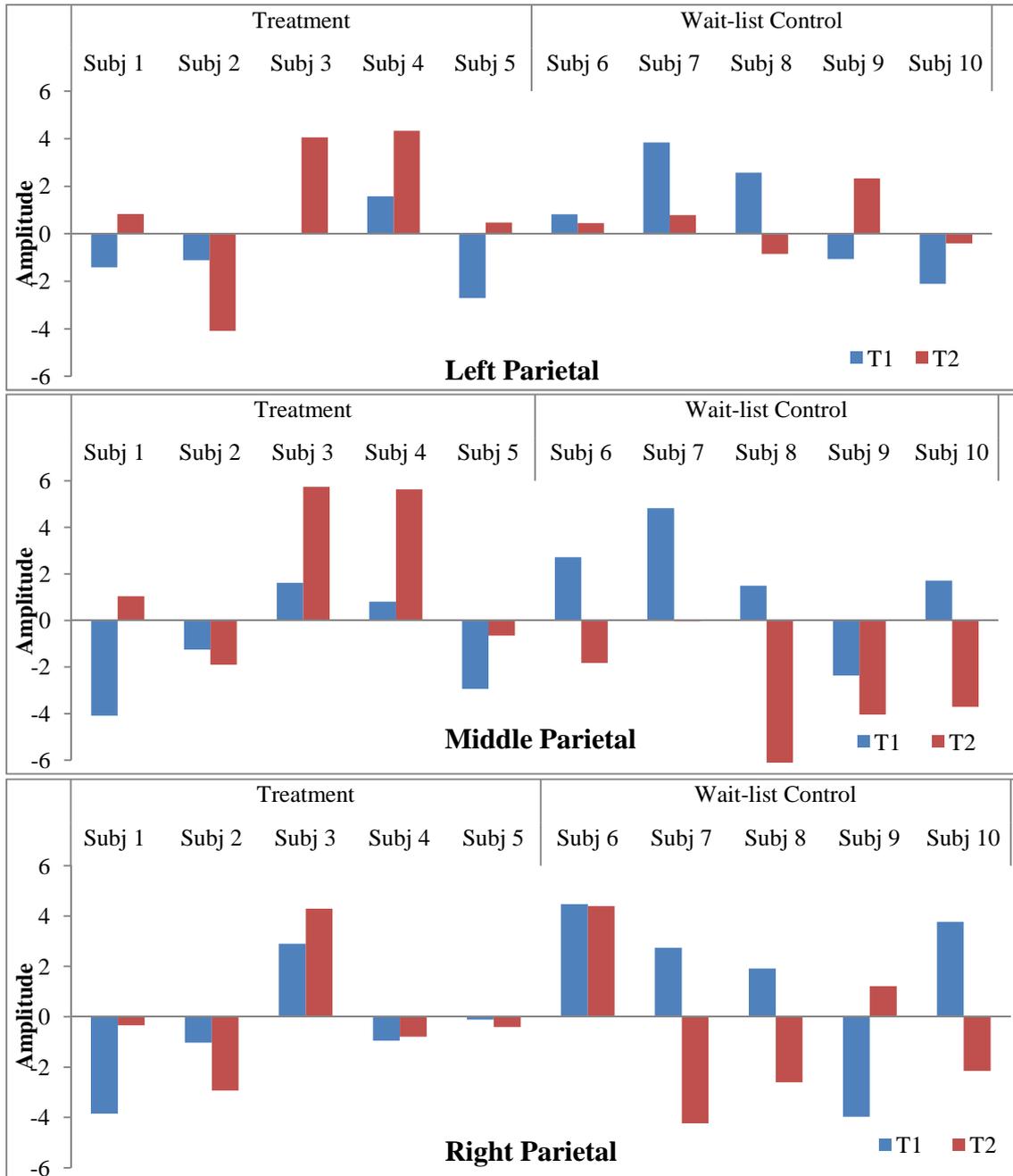
Figure 4.9: Individual participant ERP responses for human action sounds over the left, middle and right parietal region for Treatment and Wait-List Control groups at T1 and T2.
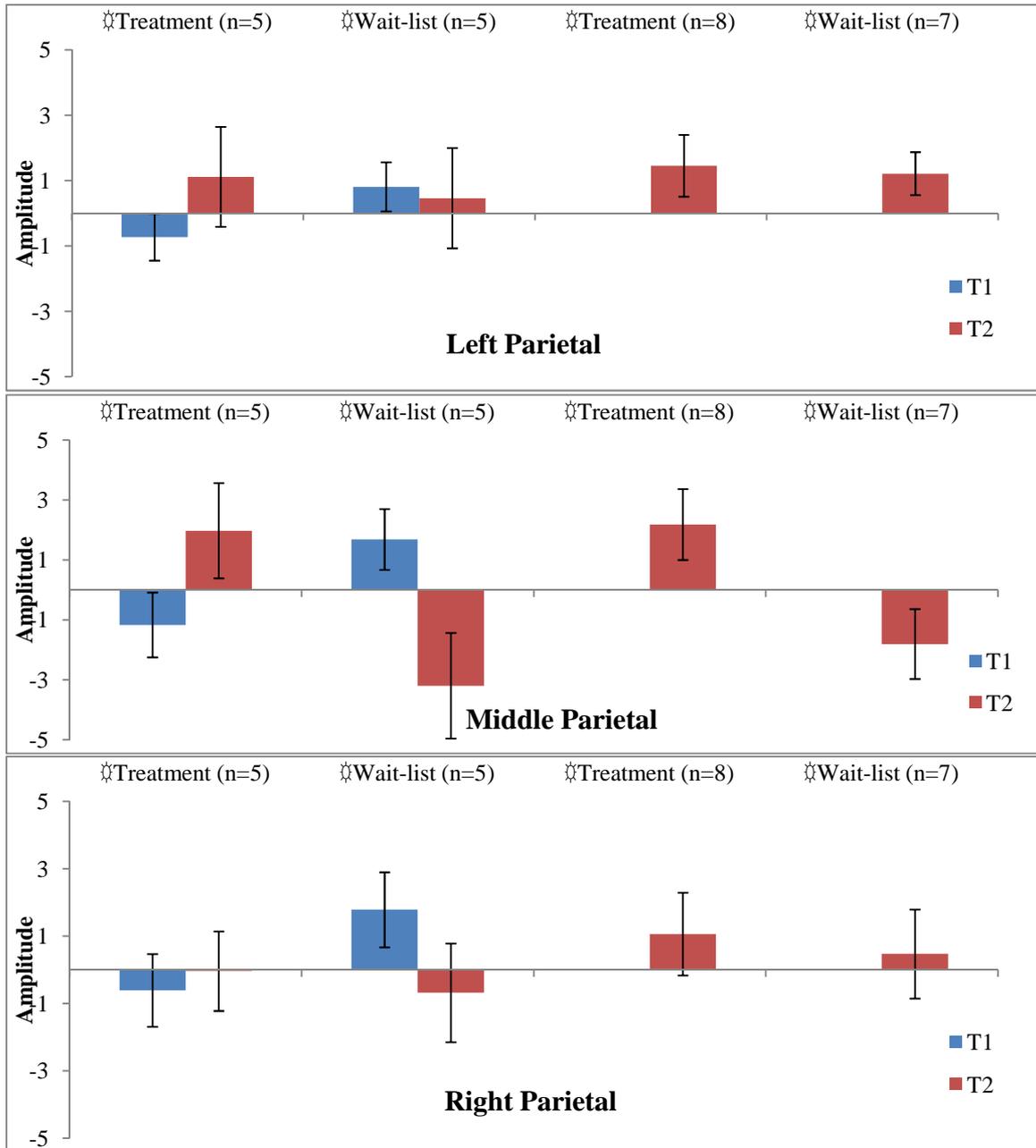
Figure 4.10: Mismatch effect seen in the Treatment (n =5) and Wait-List Control (n =5) group at T1 and T2, and mismatch effect seen in Treatment (n = 8) and Wait-List Control group (n = 7) at only T2 (outcome), over the parietal region for human action sound processing. Error bars represent standard error.

Any interpretation of results from mismatch effect data was difficult as results showed differences at T1 between groups. The mismatch effect was calculated by subtracting match from mismatch trials, but this method does not help us in analysing responses to individual trial types. It is important to understand if the groups truly differed at T1 in the match and mismatch trials individually, and if there was any pattern of change in the groups on each trial type. The next set of analyses was carried out to look for these answers.

4.3.1.2 *Group Data Analysis: T1 and T2 Comparison*

Even though the sample size of each group was small, in order to compare T1 and T2 data repeated measures ANOVA was conducted to explore possible evidence of change over time through RIT. The mean of the four timing windows (from 180-700ms) for each human action trial for each participant was calculated and compared. No difference was found between the Treatment and Wait-List Control group match and mismatch trials at T1 for the central channels (Appendix H). Therefore, in contrast to findings from mismatch effect data, individual trial type did not differ at T1 for the central channels (Figure 4.11). However, a significant difference was found for the match trials between groups at T1 for the parietal region (see Appendix H).

A between-subjects repeated measures ANOVA with condition (match, mismatch) and time (T1, T2) as a within-subjects factors and group (Treatment, Wait-List Control) as a between-subjects factor was conducted for the central electrodes (see Appendix H for details). A significant group x condition x time interaction was found (F (1,8) = 14.33, p <0.01, η_p^2 = 0.64). Post-hoc comparisons showed that there was a significant difference in the Wait-List Control group for the match (M = 2.0μV, *S.E.* = 0.9) and mismatch trials (M = - 0.68μV, *S.E.* = 0.96) at T2 (p =0.03). In the Treatment group there was a trend towards significance for

difference in mismatch (*M* = 1.8μV, *S.E.* = 0.96) and match (*M* = -0.46μV, *S.E.* = 0.9) responses at T2, (*p* = 0.056). <u>These results are consistent with the outcome results and suggest that even though similar activity was observed at T1 for the two trial types, differential processing is observed at T2 for the two groups suggesting a probable impact of RIT on the Treatment group (Figure 4.11).</u> The Treatment group shows an opposite pattern of ERP activity for match trials and enhanced activity for mismatch trials from T1 to T2. The Wait-List Control group shows enhanced activity for match trials and a reverse pattern of activity for the mismatch trials (Figure 4.11).
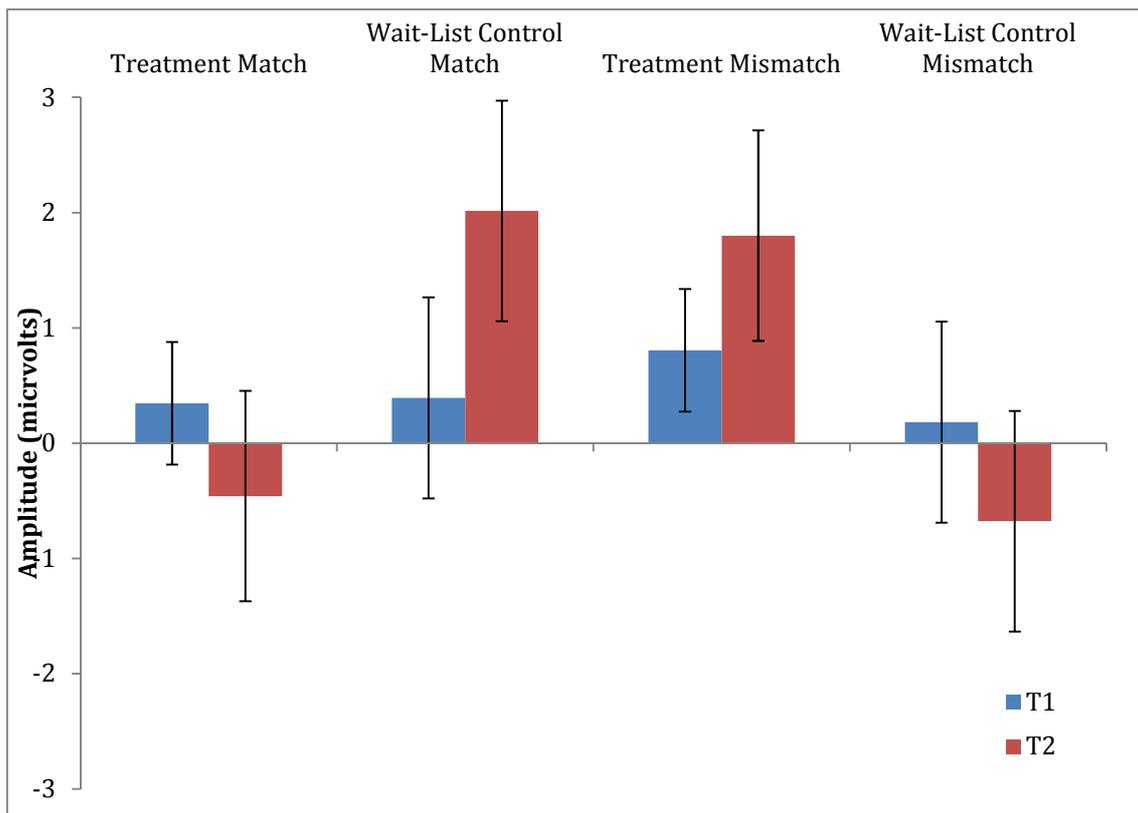
Figure 4.11: ERP response to match and mismatch trials for the Treatment (n=5) and Wait-List Control group (n=5) at T1 and T2 over the central channels. Error bars represent standard error.

A between-subjects repeated measures ANOVA with condition (match, mismatch), hemisphere (left, middle, right) and time (T1, T2) as a within-subjects factors and group (Treatment, Wait-List Control) as a between-subjects factor was conducted for the parietal electrodes (see Appendix H for details). A significant group x condition x time interaction (F $(1,8) = 6.82$, $p = 0.03$, $\eta_p^2 = 0.46$) and a group x condition x time x hemisphere interaction (F $(1,8) = 7.34$, $p = 0.01$, $\eta_p^2 = 0.48$) were found. Post-hoc analysis found a significant difference between the Treatment and Wait-List group in the human action match trials at T1 in the middle parietal region ($p = 0.04$; for details see Appendix H). Also, the Wait-List Control group showed a significant difference between the match and mismatch trials in the middle parietal region at T2 ($p = 0.05$), while no difference was observed in the Treatment group and these findings are consistent with the outcome results (Appendix H). Thus for the parietal region, it is difficult to interpret differences on match trials as groups differed at T1. For the mismatch trials, results are consistent with previous results of group differences in activity over the mid-parietal channels.

Thus, outcome data, individual participant data and change over time group data suggest differences over the central and middle parietal channels between groups for human action sound processing.

4.3.1.3 Correlation Analysis

To assess possible associations between behavioural effects of treatment and brain activity post-treatment, a correlational analysis was conducted. Ideally, a meditational or regression analysis would be preferable. However, due to the small sample size these types of analyses were deemed inappropriate. In order to examine treatment effects, change scores

from T1 to T2 of spontaneous imitation as measured on the Unstructured Imitation Assessment were used (details in Chapter 3 section 3.2.3.4.1). Only spontaneous imitation scores were used in the analysis because, as reported in Chapter 3, treatment effects were observed only for spontaneous imitation and not elicited imitation. The brain activity of interest was the 'mismatch effect', that is the difference in response to matched and mismatched stimuli. Therefore, differences between the mean amplitude of the two conditions (matched vs. mismatched) were calculated.

Parametric correlations were computed between mean amplitude difference (mismatch effect) in regions in which significant group effects were observed and spontaneous imitation change scores. Therefore, correlations were analysed only for the central and parietal regions in the human action sound condition.

A significant correlation was observed between object imitation change scores and mean amplitude differences in the central region ($r_{15} = 0.65$, $p < 0.01$), suggesting that a bigger change score on the imitation assessment was associated with a larger mismatch effect. No other correlation was found to be significant for either the central or parietal region (Table 4.3).

Table 4.3: Correlations between spontaneous imitation change scores and mean amplitude difference for human-action sounds (n=15).

	Central	Parietal Left	Parietal Middle	Parietal Right
Spontaneous Imitation Total	0.50	0.10	0.20	0.11
Object Imitation	0.65[**]	0.07	0.42	0.13
Gesture Imitation	0.06	0.09	-0.18	0.02

**Correlation is significant at 0.01 level (2-tailed).

Additionally, correlations were also calculated for pre-treatment characteristics of chronological age, ADOS domain and total scores, and post-treatment ERP responses in the central and parietal regions as results from Chapter 3 indicated an association between child characteristics pre-treatment and response to RIT. There was no association found between any pre-treatment characteristics and difference ERPs in either the parietal or the central area (Appendix H). Thus mismatch effect observed in both the Treatment and Wait-List group was not associated with pre-treatment child characteristic.

4.3.2 Non-Human Action Sound Processing

In order to examine differences in processing of non-human action sounds between Treatment and Wait-List Control group, between-subjects repeated measures ANOVAs were conducted for P1/N1 and subsequent timing windows.

A between-subjects repeated measures ANOVA with condition (match, mismatch) as a within-subjects factor and group (Treatment, Wait-List Control) as a between-subjects factor was conducted to analyse P1 mean amplitudes and peak latencies for the central channels, and revealed no significant effects (Appendix H). A similar repeated-measures ANOVA was carried out for the frontal and parietal areas with condition (match, mismatch) and hemisphere (left, middle, right) as within-subject factors and group as a between-subjects factor. No significant effects were found for the parietal region (Appendix H). There was an interaction effect of condition x group for the mean amplitude of P1 over the frontal channels (F (1,13) = 5.75, p = 0.03, η_p^2 = 0.31) suggesting differences between groups across conditions for P1. However, paired contrasts using Bonferroni correction did not show any significant effects.

Rest of the timing windows were analysed for perceptual processing differences using a between-subjects repeated measures ANOVA with condition (match, mismatch) and time

(four different timing windows: 180-310ms, 310-440ms, 440-570ms, 570-700ms) as a within-subject factor and group (Treatment, Wait-List Control) as between-subjects factor over the central area and no significant effects were found (Appendix H), <u>suggesting specificity of response to human action sounds in the central region.</u> In both the frontal and parietal regions, between-subjects repeated measures ANOVAs with condition (match, mismatch), hemisphere (left, middle, right) and time (different timing windows) as a within-subject factor and group (Treatment, Wait-List Control) as between-subjects factor were conducted.

In the frontal region, significant time x group (F (1,13) = 5.78, p <0.01, η_p^2 = 0.31) and condition x time (F (1,13) = 6.43, p <0.01, η_p^2 = 0.33) interaction effects were found. Paired contrasts, using Bonferroni corrections, revealed that for the Wait-List Control group there was a larger negative response in the first time window, 180-310ms (M = - 0.66µV, $S.E.$ = 0.8) as compared to the second time window, 310-440ms, where there was a large positive component (M = 0.98µV, $S.E.$ = 0.7; p = 0.02). The activity then remained positive throughout the stimulus presentation as seen in Figure 4.12. The Treatment group, however, showed no significant differences in timing (Figure 4.12). The condition x time interaction was driven by significant difference in processing of the mismatch trials (M = - 1.30µV, $S.E.$ = 0.6) as compared to match trials (M = 1.14µV, $S.E.$ = 0.7) in the last timing window of 570-700ms (p = 0.03).

Therefore timing differences between groups suggest greater perceptual processing in the Wait-List Control group compared to the Treatment group over the frontal channels.
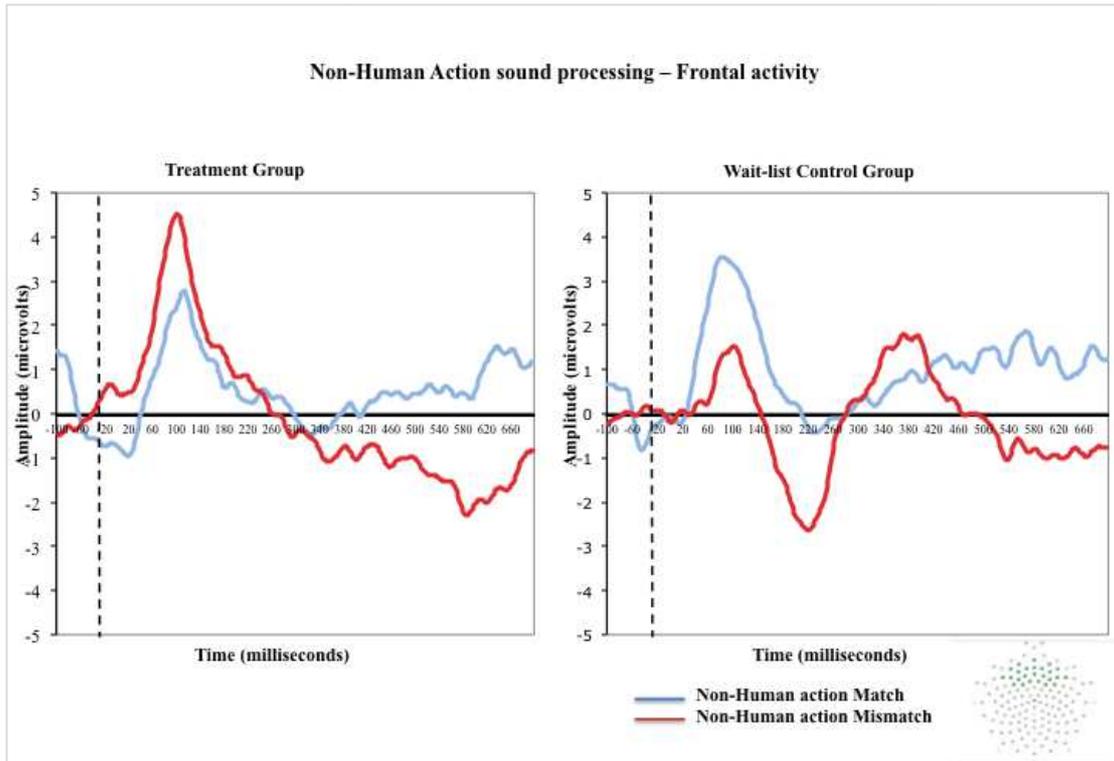
Figure 4.12: ERP waveforms for the Treatment and Wait-list Control group for the Non-Human action sounds condition over the Frontal channels at T2.

A significant group x time interaction was observed for the parietal channels ($F_{(1,13)}$ = 3.53, p = 0.04, $\eta p2$ = 0.21). Post-hoc analysis using Bonferroni correction showed that greater differences in the Wait-List Control group in the first, 180-310ms (M = 0.5µV, S.E. = 0.5) and the second timing window, 310-440ms (M = - 0.93µV, S.E. = 0.5) were driving the interaction effects (p = 0.01). No such timing differences were seen in the Treatment group (Figure 4.13).

These results suggest that there was greater perceptual processing of non-human action sounds in the Wait-List Control group while the Treatment group showed early sensory processing but perceptual processing was not evident of non-human action sounds.
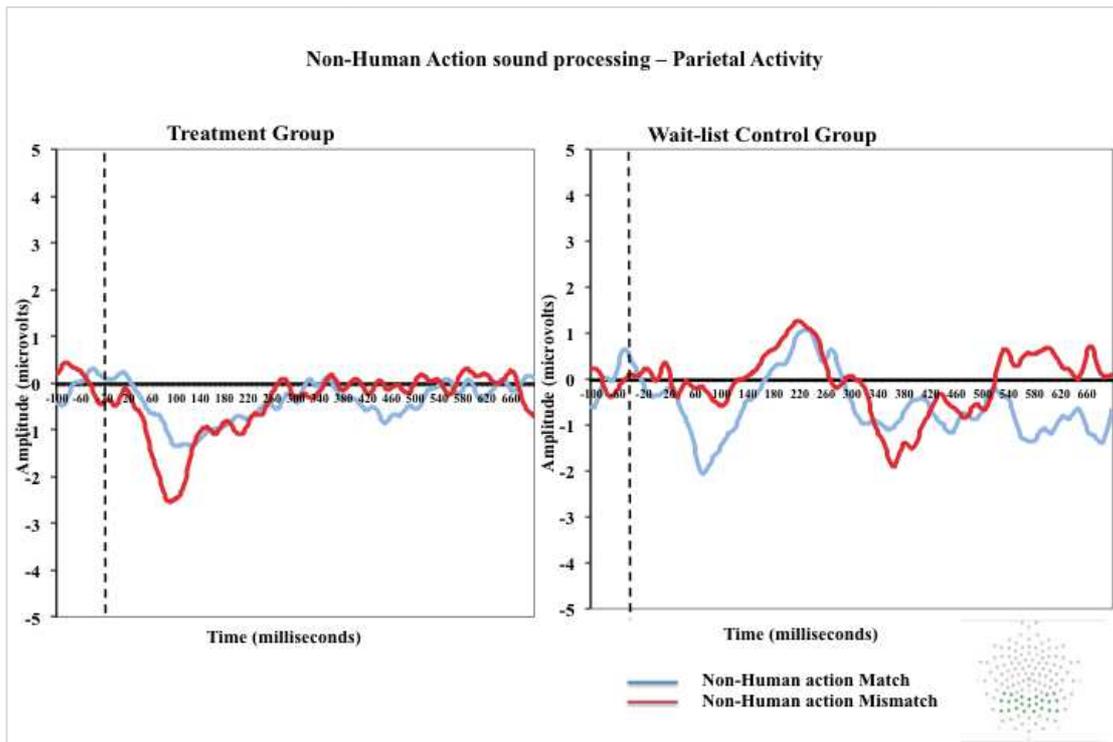
Figure 4.13: ERP waveforms for the Treatment and Wait-list Control group for the Non-Human action sounds condition over the Parietal channels at T2.

4.3.2.1 Individual Participant Data Analysis: T1 and T2 Comparison

Mean difference scores were analysed for frontal and parietal regions, as significant group differences were observed in these two areas for non-human action processing. Furthermore, as group differences were observed based on time, mean difference scores for non-human action match and mismatch trials were plotted for both groups based on individual timing windows irrespective of hemispheric activity.

Frontal ERP responses to match and mismatch non-human action sounds show mixed results for individual participants across groups (Figure 4.14). Four out of five participants in the Treatment group showed a greater response to mismatched non-human action sounds at

T1 across the four timing windows while a greater response to matched trials was seen at T2 especially in the last timing window of 570-700ms (Figure 4.14). In the Wait-List group two children showed positive mean difference at T1 and continued to show greater response to mismatch sounds at T2 while the rest of the three children showed a reverse pattern of greater response to matched non-human action sounds.
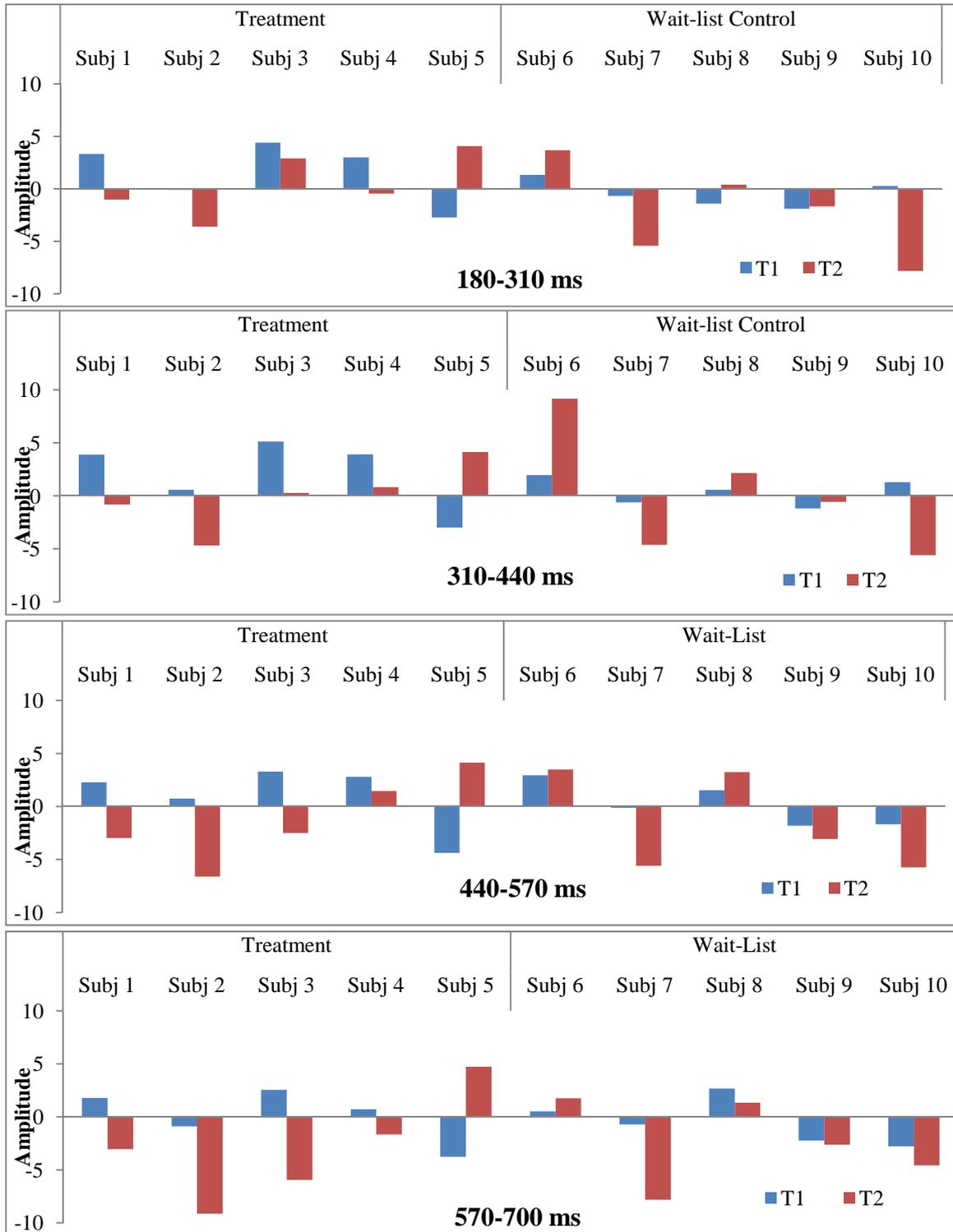
Figure 4.14: Mean difference scores for individual participants in the Treatment (n =5) and Wait-List Control group (n = 5) for Frontal ERP responses to matched and mismatched non-human action sound trials in the four different timing windows at T1 and T2.

With regard to ERP responses over the parietal region, similar responses were observed in the first two time windows of 180-310ms and 310-440ms in both the Treatment and Wait-List Control group where, at T1, all children in the Treatment group showed greater response to match trials and most children (four out of five) in the Wait-List group showed greater response to mismatched trials; at T2 three children in the Treatment and Wait-List group showed larger responses to mismatched trials (Figure 4.15). In the third time window three children in the Treatment group had larger response to match trials while three children in the Wait-List group had larger response to mismatch trials at T1. This changed to four children in the Treatment group having a positive mean difference and three children in the Wait-List group with a positive difference suggesting greater response to mismatch trials. However, ERP responses in the last timing window of 570-700ms showed that all children in the Wait-List group had greater response to mismatched non-action sounds at T1 and T2, three children in the Treatment group had larger response to match sounds at both T1 and T2 while two children showed similar activity to the Wait-List group of greater response to mismatched trials.
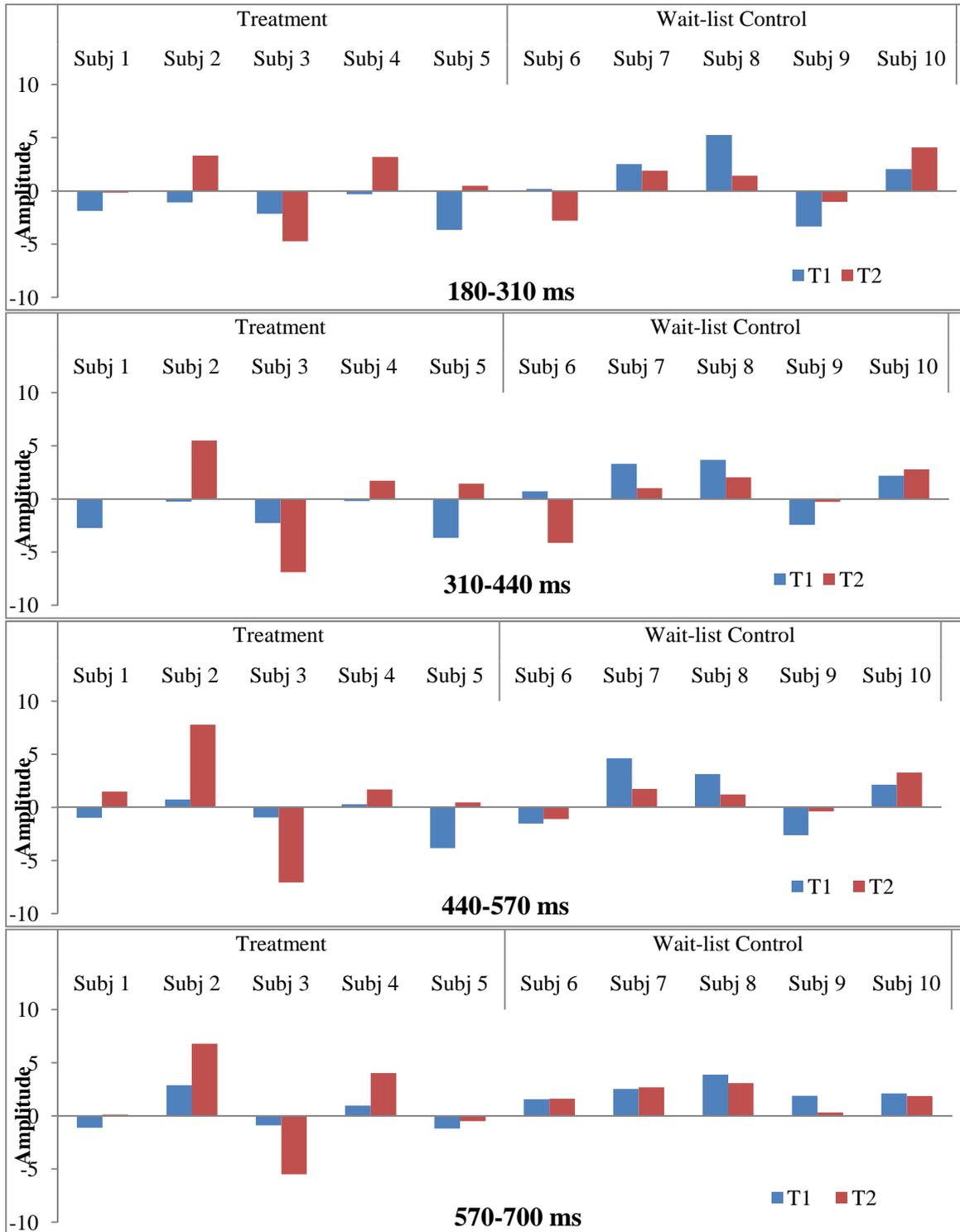
Figure 4.15: Mean difference scores for individual participants in the Treatment (n =5) and Wait-List Control group (n = 5) for Parietal ERP responses to matched and mismatched non-human action sound trials in the four different timing windows at T1 and T2.

4.3.2.2 Group Data Analysis: T1 and T2 Comparison

Similar to the analysis for human-action sounds, change in processing was assessed for non-human action sounds for both the groups. As group differences were found based on timing windows, the mean for each timing window was calculated by averaging ERP activity across left, middle and right electrodes for the frontal and parietal regions. No difference was found between the Treatment and Wait-List Control group match and mismatch trials at T1 (see Appendix H).

A between-subjects repeated measures ANOVA with condition (match, mismatch), ERP time windows (180-310ms, 310-440ms, 440-570ms, 570-700ms) and time (T1, T2) as the within-subjects factor and group (Treatment, Wait-List Control) as the between-subjects factor was conducted for the Frontal and Parietal electrodes. No significant group differences were found for the parietal electrodes (for details see Appendix H). A significant group x ERP time window x time interaction was found for the frontal channels (F (1,8) = 9.92, p <0.01, η_p^2 = 0.55). Post-hoc analysis showed a significant difference in the Wait-List Control group for time window 3 (440-570ms) between T1 (M = -0.49μV, $S.E.$ = 0.7) and T2 (M = 1.64μV, $S.E.$ = 0.5; p =0.02); and time window 4 (570-700ms) between T1 (M = -0.93μV, $S.E.$ = 0.8) and T2 (M = 1.13μV, $S.E.$ = 0.4; p =0.05). No such differences were observed for the Treatment group.

Thus overall results for non-human action processing suggest early sensory processing of non-human action sounds in both the groups, however greater perceptual processing, as evidenced by differential processing across timing windows, was observed in the Wait-List Control group over the frontal and parietal channels. In other words results suggest that children in the Wait-List control group were attending to and processing non-human action

sounds more than the Treatment Control group, which showed evidence of early sensory auditory processing.

4.3.2.3 *Correlation Analyses*

Correlation analyses were conducted between non-human action mismatch effect and imitation change scores to see if there was any association between treatment effect and ERP responses to non-human action sounds. Frontal and parietal channels were used in the analysis as group effects were evident in these two areas. Pre-treatment child characteristics of chronological age and ADOS domain and total scores were also examined for correlations with mean amplitude differences. No significant correlations were found between ERP responses and imitation change scores or child characteristics (Appendix H).

4.4 DISCUSSION

The present study aimed to explore neurological changes associated with RIT in children with autism using an auditory processing paradigm measuring ERPs time-locked to matched and mismatched human action and non-human action sounds. The results showed that children in the Treatment group differed significantly from the Wait-List Control group in their response to both matched and mismatched human action stimuli over the central and parietal region at outcome. Mismatch effect data showed that the two groups were different at time 1, however, individual trial type analysis did not show this difference. Specifically, the Treatment group showed a larger positive response to mismatched human trials while the Wait-List group showed a larger positive response to matched human-action sounds. There was also a significant difference in the neural response over the parietal region, where the

Wait-List group showed difference between mismatched human responses over the left and middle parietal cortex while the Treatment group showed no such differences. Individual participant and group analysis of change over time supported these findings. Furthermore, a significant positive correlation was found between object-imitation change scores and mean amplitude difference between mismatched and matched trials, suggesting that a greater increase in spontaneous imitation at T2 was associated with a greater response to human-action sounds. The current results suggest that the two groups indexed human action matched and mismatched sounds differently, suggesting a probable impact of RIT on processing of human action sounds. This was further supported by findings from non-human action sound processing, where greater perceptual processing was observed for Wait-List Control group at T2 but this was not observed for the Treatment group. Thus the treatment group showed a greater response to human action sounds. However, firm conclusions from this dataset are difficult to draw due a very small sample size and high variability in individual participant data.

Differences in responses were observed over the central and parietal area. Although group effects were found for the parietal region, where there was difference in activity between the left and middle parietal regions in the wait-list group and no such differentiation in the treatment group, upon careful observation this result was seen to be a 'carry-over' effect of the central differences. For the wait-list group there was a greater negative response over the middle-parietal region, which was similar to the response over the central channels in this group. Similarly, the treatment group showed a positive going response to mismatched trials over the mid-parietal area that was comparable to the group response over the central channels. Left and right parietal activity for both the groups was in the same direction and comparable in mean amplitude. Therefore, the significant effect found seems to be driven by

the 'carry-over' response of the central activity in the middle parietal region leading to a significant difference between the left and middle areas in the wait-list group. Furthermore, no difference in activity was observed in the central channels during non-human action sound trials suggesting the specificity of response to human action sounds over the central cortex. Additionally, ERP responses over the central channels were also found to be associated with changes through treatment in imitation skills. Thus, there seems to be specificity of response to treatment over the central cortex for human-action sounds. Furthermore, ERP responses in the central area were observed to be in the opposite direction for the treatment and control group post-intervention. Individual participant data suggested that two children in the treatment group showed a reversal of response with a negative mismatch effect at T1 to a positive mismatch effect at T2 while two children showed a greater positive response at T2 compared to T1. Conversely, in the wait-list group all children showed a greater negative mismatch effect at T2 with two children who had a larger response to mismatch trials at T1 later showing larger responses to matching human sounds at T2. Although praxis was not measured in the study, mid-parietal results could not be explained as an effect of differences in praxis because parietal regions were implicated in both human and non-human action sounds, while the effects over central region were observed only during human action sound processing. Thus, the greatest ERP responses for human action sounds were observed over the central channels located over the sensorimotor cortex.

As discussed previously in section 4.1 and in Chapter 1 section 1.4.2, EEG studies evaluating imitation skills have found mu rhythm activity in the central electrodes of C3, CZ and C4 to be associated with mirror neuron functioning (Muthukumarswamy et al., 2004; Oberman et al., 2007; Oberman et al., 2005; Oberman et al., 2013). Moreover, the role of the sensorimotor cortex in the modulation of action observation has been proposed (Pineda, 2005;

2008). Studies involving action imitation training have shown greater mu suppression over the sensorimotor cortex associated with training (Gerson, Bekkering, & Hunnius, 2015; Marshall, Bouquet, Shipley, & Young, 2009; Paulus, Hunnius, Van Elk, & Bekkering, 2012). RIT is an intervention targeting imitation skills in a social context and therefore it is highly likely that activity in the sensorimotor areas was impacted. This also provides preliminary support for the hypothesis that interventions targeting motor synchrony in a social context may be a potential way of increasing social–communication skills (McCleery, Elliott, Sampanis, & Stefanidou, 2013). RIT is an intervention that targets synchronous motor imitation in children with autism in a play based, social, child-led setting. Children who received RIT showed changes in neural responses over the central and mid-parietal channels, areas of the sensorimotor cortex. Dysfunctions in motor movements and skills including observation, planning, execution and integration of motor activity have been reported in children with autism (McCleery et al., 2013; Miyahara, 2013). According to McCleery et al. (2013) motor synchrony and resonance may be an underlying deficit in children with autism associated with early social-communication deficits observed. In a recent study by Gerson and colleagues (2015) active motor training delivered by parents to 10 month old infants led to greater mu-suppression when infants heard sounds of actions learnt post-training (Gerson et al., 2015). Thus, in children with autism early intervention focusing on motor synchrony may be an important pathway towards helping develop reciprocal interaction skills. Results from this study support this notion as well as suggest that RIT may be an effective focused early intervention program targeting motor synchrony and social imitation skills.

Conversely, differences in the processing of non-human action sounds between the two groups were seen in the frontal and parietal channels suggesting timing differences in processing of non-human action sounds in the wait-list group while no such differences were

found for the treatment group. Processing of non-human action sounds was faster in the wait-list group with an earlier negative going component. However, the ERP response in the treatment group did not show such timing differences. Individual participant data did not suggest any trends. Furthermore, there was no correlation observed between imitation change scores and ERP responses. These results provide support to RIT influencing social, human sound processing specifically..

4.4.1   Limitations and Future Directions

This study documents preliminary results suggesting a beneficial impact of RIT on auditory processing of human stimuli in children with autism. However, there were limitations in the study.

A major limitation of the study was the sample size. The small number of participants giving viable EEG data at T1 limits our understanding of any impact RIT may have had on neural functioning. Also, the Treatment and Wait-list Control group participants had variable individual data and differed in activity at T1. Thus drawing conclusions is difficult from the current dataset. Further, due to the highly small sample size, and therefore reduced power to detect an effect, it is possible that other brain regions may have been impacted by RIT and this was not reflected in the present sample due to limited power. The current study only provides a possible suggestion of a brain region that RIT may be influencing. Thus, *replication using larger samples will be crucial to determine if effects seen in the present study are valid, stable and replicable.*

A sample with a broad age range was recruited. Brain activity changes have been suggested between 3 and 4 years of age in children and therefore the results might differ if analysis was segregated by age. However, as the Treatment and Wait-List Control groups

were matched on both chronological and verbal mental age the comparison between the two groups reveal valid, reliable results. Secondly, gender differences have been suggested in ERP responses in this population (Webb et al., 2015). Therefore, the findings may be biased due to analyses of both males and females together. Although group differences were not found for gender, the Treatment group had more females than the Wait-List Control group. This gender difference could not be controlled for or studied as part of this research. This may have affected the results observed and there is a possibility that females may have responded to RIT differently as compared to males at both behavioural and neural level. Future studies must, therefore look at gender effects on treatment changes.

Importantly, source localisation was not included in the study. By looking at only EEG/ERP activity it is often hard to conclude which area of the brain might be implicated in the activity observed. EEG picks up brain activity from the scalp and the source of activity may be from a completely different region than that where the electrodes are placed. Due to limited resources, source localisation analysis could not be conducted and therefore it is not possible to say conclusively that RIT directly impacted mirror neuron and sensorimotor cortex functioning in this group of children with ASD. Source localisation or pairing EEG with other imaging techniques is a next step towards evaluating changes in the responses of specific brain regions to RIT. Additionally, mu rhythm analysis may be supplemented in order to better understand effect of RIT on action processing.

Individual participant data showed that children responded differently to RIT at a neural level. Neural responses are perhaps suggestive of a more permanent impact and therefore looking at those children who did not benefit from intervention at a neural level could prove vital in helping understand autism as well as develop more focused, tailored services. Moreover, in order to assess the impact of changes in neural responses observed through

treatment on the development of children with autism who received intervention, follow-up studies looking at behavioural (language most importantly) and neural development will be important to assess the long-term impact of RIT as an early intervention.

Finally, due to the lack of a typically developing control group it is difficult to conclude regarding the direction of development of the two groups, that is, it is difficult to conclusively say that children in the treatment group 'improved' in response to human action processing. Also, group analysis of T1 and T2 data (change analysis) showed that there was a reversal in response to match trials in the Treatment group, while there was increase in mismatch trial over the central channels from T1 to T2. Without having a typical control group it is difficult to ascertain the impact of RIT, that is, if it led to greater responses in processing of continuous human action sounds or greater attention-orientation response to human action sounds that were preceded by non-human stimuli.

Thus, the present results provide limited preliminary evidence suggesting neural responses associated with RIT, and studies with larger samples and typically developing controls will be needed to conclusively understand the neural-behavioural associations.

SUMMARY & IMPLICATIONS OF CHAPTER 4

This chapter evaluated RIT through the use of a neurological measure, ERP. Changes related to treatment were examined using an auditory processing paradigm, RAMM. Of particular interest was the effect of RIT on human action stimuli. The results found significant differences in ERP activity between the Treatment and Wait-List Control group for the central and mid-parietal channels for human-action sound processing post-intervention. These results were also associated with behavioural changes in imitation in response to treatment. Further,

results from change through intervention data (T1 and T2 analysis) demonstrated changes in processing through treatment. Also, results from non-human action processing highlight the specific impact of RIT on social sounds compared to non-social sounds. Thus, the results provide preliminary evidence of neural correlates of imitation skill changes in children with autism. Furthermore, as the present sample showed significant developmental delay and intellectual disability (Chapter 3), the results are promising for this population of children with autism.

The next chapter extends on these findings and uses another EEG methodology and paradigm to evaluate the effects of RIT on social and non-social processing. The chapter will therefore add to the evidence for the efficacy of RIT as an effective early intervention program for children with autism at both a behavioural and neural level.

CHAPTER 5

THE EFFECT OF RECIPROCAL IMITATION TRAINING ON SOCIAL

AND NON-SOCIAL PROCESSING IN CHILDREN WITH AUTISM

5.1 INTRODUCTION

Humans are highly social beings and research has shown that just a few days old infants pay more attention to social than non-social stimuli (Nelson, 2001; Puce & Bertenthal, 2015). Researchers have proposed that there is a specialised network of brain regions involved in social processing, popularly known as the 'social brain' hypothesis (Adolphs, 2009; Grossman & Johnson, 2007, see also Chapter 1 section 1.4.1). Advances in neurological research into both visual and auditory social processing have demonstrated that infants and children exhibit specialist neural responses to faces (De Haan & Nelson, 1999; Halit, De Haan, & Johnson, 2003; Johnson, 2005; Taylor, Batty, & Itier, 2004), facial emotions (Grossmann, Striano, & Friederici, 2005, 2006), eye gaze detection and monitoring (Farroni, Johnson, & Csibra, 2004; Reid & Dunn, 2015), human actions (Marshall & Meltzoff, 2011; Oberman, Pineda, & Ramachandran, 2007; Reid, Csibra, Belsky, & Johnson, 2007), and speech sounds (Kuhl & Rivera-Gaxiola, 2008). These findings provide support for the hypothesis that there may be separate neural mechanisms for social stimuli from early in life (see also Chapter 1 section 1.4.1).

Due to several advantages of electroencephalography (EEG) over imaging methods, including its non-invasive nature, excellent temporal resolution, low cost, easy applicability for varied populations, and portability, the method has gained popularity as an effective tool for understanding brain mechanisms, detecting biomarkers of pathology and monitoring treatments (Loo, Lenartowicz, & Makeig, 2016; Nelson & McCleery, 2008, see also Chapter 4 section 4.2.5). EEG oscillations are produced through synchronous firing of large groups of neurons. Rhythmic oscillations with particular associations have been observed across various frequency bands including low frequency delta (1-3Hz) and theta (4-7Hz) bands, and higher

frequency alpha (8-13Hz), beta (13-30Hz), and gamma (greater than 30Hz) bands. These frequency bands seem to change throughout development (Gasser, Verleger, Bächer, & Sroka, 1988; Marshall, Bar-Haim, & Fox, 2002) and each band has been associated with various aspects of social-cognitive functioning.

Both theta and alpha bands, in particular, have been studied in relation to human social processing. For example, theta activity has been associated with affective states and emotions (Bekkedal, Rossi, & Panksepp, 2011; Knyazev, Slobodskoj-Plusnin, & Bocharov, 2009) and memory (Burgess & Gruzelier, 1997; Gevins, Smith, McEvoy, & Yu, 1997; Sauseng, Klimesch, Schabus, & Doppelmayr, 2005) in typical development. According to Miller (1991) theta rhythm modulation can be triggered through socially significant and novel stimuli (as cited in Orekhova, Stroganova, Posikera, & Elam 2006). Orekhova et al., (2006) found that in typically developing infants and children, theta oscillations in different regions of the brain were associated with different stimulation conditions, with toy exploration leading to an increase in theta activity over frontal and temporal areas of the scalp, and hearing adult speech leading to increases in theta activity over parietal areas, suggesting a difference in regions for social and non-social processing. Similarly, Jones and colleagues examined alpha and theta activity whilst 6 and 12 month-old infant participants watched social and non-social movie stimuli as well as live social interaction and object play conditions (Jones, Venema, Lowy, Earl, & Webb, 2015). Greater theta activity was associated with the social conditions of both viewing a social movie as well as a live social condition over the frontal, parietal, and temporal regions as compared to the object condition, while alpha activity was only modulated by the naturalistic social interaction condition (Jones et al., 2015). Additionally, Orekhova and colleagues showed that greater theta activity was observed

in infants when engaging in a game of peek-a-boo with an examiner compared with passive observation of an object or adult (Orekhova, Stroganova, & Posikera, 1999).

Likewise, alpha band frequency modulation recorded from electrodes over the left and right frontal cortices has been associated with perception of emotion in typically developing children (Coan & Allen, 2004; Davidson, 1992) as well as a state and trait marker for approach-withdrawal tendencies (Coan & Allen, 2003a; Davidson, 1988, 2004; Sutton & Davidson, 1997). Alpha suppression specifically, that is, lower alpha activity, is associated with greater neural processing/activation (Coan & Allen, 2003a,b). Alpha asymmetry over the frontal cortex is related to affective stimuli, and is considered a trait and state marker such that an increased trait tendency to approach or state tendency to respond to positive affective stimuli is associated with greater left frontal asymmetry (i.e., reduced alpha power in the left versus right hemisphere; Coan & Allen, 2003b; Coan & Allen, 2004). Alpha frequency recorded over the central region, typically referred to as the mu rhythm (8-13Hz), is found to be associated with human action observation and participant action execution and has been linked to the mirror neuron network (Marshall & Meltzoff, 2011; Muthukumaraswamy, Johnson, & McNair, 2004; Oberman et al., 2007; Pineda, 2005; see also Chapter 1 section 1.4.2. and Chapter 4 section 4.1.). Oberman and colleagues in a study showed that mu suppression was modulated by the degree of social interaction while viewing actions (Oberman et al., 2007). The non-interactive condition of individuals tossing the ball showed least mu rhythm suppression in adults and maximum mu suppression was observed in interactive condition of individuals throwing the ball at each other and to the participant (Oberman et al., 2007), thus adding to evidence for alpha activity being modulated by social stimuli. Therefore, in typical development, social stimuli evoke precise neural responses (as evidenced by differential EEG activity), which are clearly distinguishable from responses to

non-social stimuli. Also, both theta and alpha band frequencies can distinguish social and non-social processing reliably, as both bands seem to be modulated by social processes.

Autism Spectrum Disorder (ASD) is a disorder of social-communication functioning, where symptoms emerge early in life and can significantly impact quality of life of the individual. Atypical neural functioning in autism has been put forth and further supports the hypothesis of 'social specialisation' in different brain regions. Atypical responses in brain activity have been noted in this population for both low and high level auditory and visual processing of social stimuli (Belger, Carpenter, Yucel, Cleary, & Donkers, 2011; Jeste & Nelson, 2009; Shultz, Jones, & Klin, 2015; Chapter 1 section 1.4.1). Neurological differences between children and adults with autism and typically developing controls have been observed in biological motion recognition and processing (Hirai et al., 2014; Klin, Lin, Gorrindo, Ramsay, & Jones, 2009; Kröger et al., 2014), face processing (Aoki, Cortese, & Tansella, 2015; Campatelli, Federico, Apicella, Sicca, & Muratori, 2013; Dawson et al., 2005), eye gaze processing (Grice et al., 2005; Pelphrey, Morris, & McCarthy, 2005), imitation skills (Bernier et al., 2007; Shih et al., 2010), human action processing (Martineau et al., 2008; Oberman et al., 2005) as well as speech processing (Groen, Zwiers, van der Gaag, & Buitelaar, 2008; Kujala, Lepistö, & Näätänen, 2013).

EEG research has also found atypical neural oscillations in several of the frequency bands described above in ASD (Billeci et al., 2013; Coben, Clarke, Hudspeth, & Barry, 2008; Dawson et al., 1995; Orekhova et al., 2014; Stroganova et al., 2007). Support for atypical EEG activity comes from resting-state EEG studies and task-based studies. Dawson and colleagues compared resting-state EEG of five to eighteen year old children with autism with a set of typically developing controls matched on age and another set of controls matched on receptive language, in various frequency bands during eyes-open resting-state EEG. They

found that children with autism had reduced EEG power in the frontal and temporal regions in delta, theta, and alpha frequency bands as well as reduced power in the left hemisphere compared to the right (Dawson et al., 1995). Similarly in sustained visual attention conditions (blowing bubbles and watching a moving fish video), Stroganova et al. (2007) found that there was a lack of leftward asymmetry in the central and frontal regions and atypical leftward hemispheric asymmetry in the temporal region in alpha frequency in boys with autism aged between three to eight years compared to typically developing boys. Additionally, longitudinal studies of infants and infant siblings at-risk for autism have found deviance primarily in mean alpha PSD and frontal alpha asymmetry (Gabard-Durnam, Tierney, Vogel-Farley, Tager-Flusberg, & Nelson, 2013; Orekhova et al., 2014) where developmental trajectories from 6 to 24 months showed a significant difference between low- and high-risk infants at 6 months on all EEG frequency bands but this difference was not significant at 24 months for any frequency band but alpha and gamma bands (Tierney, Gabard-Durnam, Vogel-Farley, Tager-Flusberg, & Nelson, 2012). Similarly Orekhova et al. (2014) found that EEG alpha band hyper-connectivity in high-risk infants was associated with a diagnosis of autism at 36 months. Thus, atypical activity, especially in the alpha frequency band, has been consistently observed in multiple resting-state EEG studies.

Task-based studies have also shown atypical processing in autism. A face processing study found lesser theta activity and greater alpha suppression in individuals with Asperger syndrome compared to controls when viewing photographs of human faces (Yang, Savostyanov, Tsai, & Liou, 2011). Further, Martineau and colleagues examined theta and alpha frequency variations between 5 to 7 year old children with autism and typical controls during four visual conditions: blank white screen (no stimulation), picture of lake (no movement condition), video of waterfall (non-human movement condition) and woman

performing scissor movements with her legs (human movement condition) (Martineau et al., 2008). They found that in the low theta band (3-5.5Hz), control children showed greater desynchronisation during human movement condition while no difference in spectral power was observed across conditions for children with autism. Also, lateralisation differences were observed between the two groups with children with autism showing atypical lateralisation (Martineau et al., 2008). Similarly, a small number of studies examining auditory processing in autism have found that individuals with autism have atypical theta activity in the auditory cortex when listening to speech sounds (Jochaut et al., 2015) and attenuated delta, theta and alpha activity in the central region when viewing a cartoon video with sounds (Machado et al., 2015). Taken together these studies provide EEG evidence for atypical social processing mechanisms in autism, especially in the theta and alpha frequency bands, which are typically associated with social processing.

EEG studies in children with autism to date have not used naturalistic stimuli to investigate social processing differences. Examining EEG activity during naturalistic social processing would help understand underlying neural mechanisms during everyday social interactions in children with autism. Furthermore, EEG studies of children with autism have either employed visual or auditory stimuli separately while everyday interactions involve integration of sensory modalities, especially visual and auditory. No EEG study yet (to the researcher's knowledge) has investigated social processing differences in alpha and theta activity during the observation of naturalistic social interactions using videos of social stimuli (integrating visual and auditory senses) in children with autism. Thus, the first aim of Study 1 was to evaluate differences in children with ASD and typically developing children in alpha and theta frequency bands during a social condition, with adults reading nursery rhymes, versus a non-social condition, with colourful shapes moving on the screen producing

associated sounds. Naturalistic video stimuli were chosen over live interaction as it ensured standardisation of stimulus presentation across participants and therefore afforded a more experimentally well-controlled method. In order to help determine the specificity of any observed atypicalities in alpha or theta activity, associations between autism symptoms and alpha and theta frequencies were examined. Finally, as changes in EEG activity have been noted based on differences in IQ and language (Webb et al., 2015), differences between children with autism and a subset of verbally matched typical control children were examined (sample taken from the chronological age-matched sample).

As described above, social difficulties in autism are highly prevalent at both behavioural and neurological levels. Many early intervention programs have therefore focused on targeting social difficulties in this population. As noted in Chapter 1 section 1.4.3, EEG has been previously used to evaluate early intervention programs for children with autism such as the Early Start Denver Model (Dawson et al., 2012) and the Program for the Education and Enrichment of Relational Skills (PEERS) intervention (Van Hecke et al., 2013). Both studies produced emerging evidence suggesting that autism-specific social-communication interventions, which produce positive effects on behaviour, can also have significant impact on neural activity in individuals with autism (see Chapter 1 Section 1.4.3 for a detailed discussion).

As noted in Chapter 1 section 1.2.3, Reciprocal Imitation Training (RIT) is a social-communication intervention targeting social imitation skills in children with autism. RIT has a growing evidence-base for impacting not only imitation skills but also other social behaviours including language, joint attention, emotion regulation and social-emotional functioning (Ingersoll, 2010b, 2012; Ingersoll & Gergans, 2007; Ingersoll & Lalonde, 2010;

Ingersoll, Lewis, & Kroman, 2007; Ingersoll & Schreibman, 2006; Ingersoll, Walton, Carlsen, & Hamlin, 2013; Wainer & Ingersoll, 2013a). In Chapter 3 and 4 specific changes in social imitation associated with RIT from both behavioural and neural perspective were evaluated. As RIT may have an impact on general social functioning, the aim of Study 2 was to use EEG as a secondary outcome measure as part of the pilot randomised controlled trial (RCT) described earlier in the thesis (see Chapters 2 and 3), to evaluate neural changes in global social processing that may be associated with RIT. Thus, Study 2 aimed to examine changes in processing, reflected in alpha and theta frequencies, of social and non-social stimuli in children with autism who underwent RIT as compared with children in a Wait-List Control group.

The studies described in this chapter first evaluated differences in social processing between children with autism and typical children in their alpha and theta activity, and then evaluated neural correlates of change through RIT by investigating EEG alpha and theta frequency changes in children who underwent RIT versus a Wait-List Control group for processing of social and non-social stimuli. First, it was hypothesised that greater theta activity and greater alpha suppression (that is low alpha activity) will be associated with social processing. Second, it was hypothesised that children with autism will differ significantly from typically developing children in both alpha and theta EEG activity during social and non-social processing. Third, it was hypothesised that RIT will have an impact on social processing in children with autism such that there will be a difference in theta and alpha activity between the Treatment and the Wait-List Control groups measured post-treatment. Finally, it was predicted that alpha and theta activity would be associated with autism symptomatology as evidenced by greater social difficulty being associated with less alpha

suppression, and less theta and alpha activity at outcome will be associated with change in imitation skills.

5.2 METHODS

5.2.1 Study 1

This study aimed to evaluate differences in children with ASD and typically developing children in alpha and theta frequency bands during a social versus a non-social condition.

5.2.1.1 Participants

Thirty, sixteen months to six year old typically developing children were recruited through the Infant and Child Lab database at University of Birmingham and a total of thirty-nine, two to six year old children with autism were recruited. Thirty-seven children with autism were recruited, primarily as part of the pilot-RCT described in Chapter 2 and 3, from the Greater Birmingham region of United Kingdom through various parent support groups and word of mouth. Two children with autism were recruited as part of another project taking place in the Infant and Child Lab through the PEACH Network in Berkshire, United Kingdom (now known as Child Autism, UK). Parents of children who were eligible, were initially contacted via phone and once they verbally agreed to participate in the study, were invited to the University of Birmingham. All parents were asked to read and sign the University of Birmingham Internal Review Board (IRB) approved study consent and a video consent form (Appendix B).

Typically developing children were excluded from the study if: (a) they met or were above the cut-off for ASD on the autism-screening questionnaires, (b) they had extreme

prematurity at birth (3+weeks), (c) there was any primary sensory impairment (such as hearing loss), (d) there was a known presence of a genetic disorder or a seizure disorder. Typically developing children were not excluded if they came from families speaking two or more languages as most of the ASD sample recruited was exposed to two or more languages at home. Of the thirty children, five children did not complete behavioural assessments and three children did not complete EEG testing and therefore their data were excluded from the study. Furthermore, due to a technical problem with video recording of the EEG of two children, those EEG data were also discarded. Therefore, a final sample of twenty typically developing children was included in the study. EEG data were analysed for high frequency noise, motor and ocular artefacts. A minimum of 45 seconds of good EEG data recording was decided as the cut-off for power spectral density (PSD) analysis. Artefact-free data were obtained from seventeen of the twenty children finally included in the sample (85% inclusion rate).

Exclusion criteria for children with autism were the same as that described in Chapter 3, Section 3.2.1, as children were primarily recruited for the RCT. For the purpose of this study, data at T1 from the RCT were of interest. Therefore, data from those children who dropped out from the RCT after T1 assessments were included in the sample. By eliminating children who met the exclusion criteria and those who did not complete the behavioural or EEG assessments, a total of sixteen children comprised the final sample for the present study. Artefact-free data were obtained from twelve of the sixteen children (75% inclusion rate).

Therefore, the current analysis is based on EEG data from seventeen typically developing children (TD group) and twelve children with autism (ASD group) matched on chronological age (CA-matched groups). Independent samples t-test revealed no significant

group differences for chronological age (t = -0.59, *p* = 0.56), equal variances assumed (see Table 5.1 for participant characteristics).

Table 5.1: Participant characteristics of chronological age (CA) matched TD and ASD groups.

	Group *M (SD)*						χ^2 / t	df	*p*
	ASD (*n*=12)			TD (*n*=17)					
	M	**S.D.**	**Range**	**M**	**S.D.**	**Range**			
Chronological Age (in months)	43.8	17.3	24-75	39.3	21.6	16 - 83	-0.59	27	0.56
Gender (% male)	75%	-	-	76.5%	-	-	0.01	1	0.93
Handedness (% right-handed)	100%	-	-	88%	-	-	1.52	1	0.22
Nonverbal Mental Age	28.1	13.0	15-57	39.3	20.7	16.5-68.5	1.64	27	0.11
Verbal Mental Age	18.7	12.3	4-40	36.7	19.9	12.5-65.5	2.79	27	0.01
Q-CHAT	67.5	10.7	67-68	28.7	9.2	21 - 43	-5.67	6	<0.01
SCQ total score	23.5	2.2	15-30	6.4	4.9	4 - 12	-10.04	19	<0.01

As EEG activity is impacted by verbal abilities, a subset of children from the same sample were matched on verbal mental age (VMA-matched groups), ten children with autism and twelve typically developing children. Independent samples t-test and chi-square test revealed that the two groups were comparable on both verbal and non-verbal abilities (Table 5.2 for participant characteristics of the VMA-matched groups).

Table 5.2: Participant characteristics of verbally matched ASD and TD children.

	Group M (SD)						χ^2 / t	df	p
	ASD (n =10)			TD (n = 12)					
	M	S.D.	Range	M	S.D.	Range			
Chronological Age (in months)	45.6	18.5	24-75	30.1	16.1	16-58	-2.10	20	0.05
Gender (% male)	80%	-	-	83.3%	-	-	0.04	1	0.84
Handedness (% right-handed)	100%	-	-	92%	-	-	0.87	1	0.35
Nonverbal Mental Age	29.5	13.4	16-57	29.9	13.5	16.5-64.0	-0.8	20	0.94
Verbal Mental Age	21.5	11.5	7.5-40.5	27.5	15.4	12.0-56.5	-1.03	20	0.32
Q-CHAT	67.5	10.7	67-78	28.7	9.2	21 - 43	-5.67	6	<0.01
SCQ total score	24.4	5.4	15-30	6.4	0.5	6 - 7	-7.27	11	<0.01

5.2.1.2 Behavioural Measures

5.2.1.2.1 Autism Screening Measures

Two age-appropriate, Level 1 autism-screening questionnaires (García-Primo et al., 2014), the Social Communication Questionnaire (SCQ) and the Quantitative Checklist for Autism (QCHAT) were administered to both participant groups.

The Quantitative Checklist for Autism (QCHAT; Allison et al., 2008) is a brief autism-screening tool for eighteen to twenty-four month old toddlers suspected of autism. It is a parent questionnaire that assesses the child on social and communication difficulties and any

repetitive behaviours and interests. The Q-CHAT scores from one child in the typically developing group were not obtained as family did not complete the questionnaire during assessment and then moved to a different country shortly after the assessment was completed. None of the children in the TD group met the cut-off for 'suspicion' of an Autism Spectrum Disorder (score of over 50), whereas all children in the ASD group met the cut-off (Table 5.1 and 5.2).

The Social Communication Questionnaire – Lifetime Edition (SCQ; Rutter, Bailey, & Lord, 2003) is a widely used autism screening measure for children over 4 years, which has further been found to have high sensitivity (93%) for children from 2 years to 6 years of age (Allen, Silove, Williams, & Hutchins, 2007). The SCQ was therefore administered to all children over 2 years. The SCQ is a parent questionnaire assessing social and communication difficulties in children suspected with autism. A cut-off score of 15 and over is suggestive of Autism Spectrum Disorder. All but one family completed the SCQ (for reasons stated above), where no child in the TD group had a score of more than 11 but all children in the ASD group had a score of over 15 (see Table 5.1 and 5.2 for details).

5.2.1.2.2 Mullen Scales of Early Learning

The Mullen Scales of Early Learning (MSEL; Mullen, 1995) is a standardised developmental assessment for children evaluating both verbal (receptive and expressive language) and non-verbal skills (gross motor, fine motor and visual reception). Each domain gives a t-score as well as age equivalents. Due to intellectual delay in children with autism, age-equivalent scores for both groups were used. Verbal and Non-verbal mental ages were generated by calculating the mean scores from receptive and expressive language domains for verbal mental age (VMA), and fine motor and visual reception domains for non-verbal mental

age (NVMA). Independent t-tests for the CA matched groups showed no significant difference between the two groups on NVMA but a significant difference on the VMA (Table 5.1). When matched for VMA, no significant group difference was found for VMA and NVMA (Table 5.2).

5.2.1.2.3 Autism Diagnostic Observation Schedule – Generic

The Autism Diagnostic Observation Schedule – Generic (ADOS-G; Lord et al., 2000) is a semi-structured, standardised, play based assessment that measures social and communication difficulties as well as stereotyped, repetitive behaviours associated with ASD. In the present study, the ADOS was administered only for the ASD group, in order to determine and/or confirm that children met the criteria for an Autism Spectrum Disorder. Modules 1, 2 and 3 were administered for the present sample and all children met the criteria for Autism Spectrum Disorder. From the twelve children in the final sample, eight had an outside clinical diagnosis of an Autism Spectrum Disorder and four were in the process of receiving a diagnosis.

5.2.2 Study 2

This study aimed to examine changes in neural processing, reflected in alpha and theta frequencies, of social and non-social stimuli in children with autism who underwent RIT as compared with children in a Wait-List Control group.

5.2.2.1 Participants

Twenty-four two to six year old children with autism were recruited for the pilot RCT as described in Chapter 3 Section 3.2.1. EEG data for social and non-social processing were

collected at both T1 and T2. At T1 thirteen children participated in the EEG assessment, out of which nine children (five in the Treatment group and four in the Wait-List Control group) produced 45 seconds or more of artefact-free EEG recording per condition (social, non-social). At T2 eighteen children participated in the EEG assessment and 45 seconds or more of artefact-free recordings were obtained for both conditions from fourteen children: seven from the Treatment group and seven from the Wait-List Control group. Of these children, only four children in each group produced viable EEG data at both T1 and T2. Therefore, due to a small sample size, T1 and T2 data were examined at the individual participant level, with only T2 data analysed at a group level using group design statistical tests. Independent samples t-test revealed no significant differences between the two groups at T1 on chronological age, VMA, NVMA, or ADOS scores (Table 5.3). However, chi-square t-test on gender showed significant differences between groups with 4 females in the Treatment group while the Wait-List Control group included only males (Table 5.3).

Table 5.3: Participant characteristics by group at T1.

	Group *M (SD)*						χ^2 / t	df	*p*
	Treatment **(*n*=7)**			**Wait-List Control** **(*n*=7)**					
	M	**S.D.**	**Range**	**M**	**S.D.**	**Range**			
Gender (% male)	43%	-	-	100%	-	-	5.6	1	0.02
Handedness (% right-handed)	100%	-	-	100%	-	-	-	-	-
Chronological Age (in months)	44.7	16.1	26-72	47.4	14.3	34-70	-0.33	12	0.75
Nonverbal Mental Age	29.0	13.4	18.5-57.0	25.5	10.0	14.5-43.5	0.56	12	0.58
Verbal Mental Age	17.4	10.2	4.0-34.5	20.2	16.2	5.5-53.5	-0.39	12	0.71
ADOS Total score	14.3	3.5	11-20	14.0	4.8	8-21	0.13	12	0.90

5.2.2.2 Behavioural Measures

Behavioural measures were administered at T1 and T2 to index cognitive, language, and imitation abilities. All of the behavioural measures administered are described in Section 5.2.1.2 and in Chapter 3, Section 3.2.3. Mullen Scales of Early Learning (Mullen, 1995) were administered to evaluate non-verbal and verbal mental age, ADOS-G (Lord et al., 2000) was administered to determine criteria for Autism Spectrum Disorder and two imitation change measures were administered to assess spontaneous and elicited imitation in children with autism.

5.2.2.3 Intervention

All children in the Treatment group received Reciprocal Imitation Training (RIT) for 20 sessions over 12 weeks (for a detailed description of RIT see Chapters 1 and 3). To summarise, children with autism received training for a total of 20 sessions, two to three times a week. Each session lasted one hour and included the child interacting with two or three therapists individually over 20-minute periods. Social imitation, specifically object and gesture imitation, was targeted along with social responsivity and social reciprocity.

5.2.3   EEG Assessment[9]

The studies described in this chapter used stimuli developed by Graham (2014), and have been reported in similar studies examining EEG activity in infants and children (Christou et al., 2015; Graham, 2014.) The stimuli were comprised of separate thirty second video clips of people *reading* nursery rhymes (social videos) and colourful digitally-produced objects moving around the screen producing contingent sounds (non-social videos). All videos were recorded using a digital camera with a resolution of 720 x 576 colour pixels and were then transferred to Windows Movie Maker where they were edited into 30 seconds epochs (Graham, 2014). All videos were recorded at a data rate of 768 kilobytes per second (kbps), total bit rate of 89kbps and frame rate of 25 frames per second (Christou et al., 2015). Sound tracks for the social video were transferred to Audacity (version 1.3.12, 2010) where they were normalised to ensure maximum and minimum amplitude remained the same across videos (Graham, 2014). Sound was recorded at an audio bit rate of 128 kbps and stereo-audio sample rate of 44kHz (Christou et al., 2015). Video recordings and sound tracks were then combined in Windows Movie Maker (version 2.6, 2010). Recordings of screensavers from

---

[9] For a review of advantages of EEG in evaluation of interventions see Chapter 4 section 4.2.5.

Windows XP (2001) were used to develop the non-social videos (Graham, 2014). The screen recordings were edited using the software Snagit (version 10.0.0, 2010) and sounds accompanying the non-social videos were created and normalised in Audacity (version 1.3.12, 2010) using the same parameters as the social videos (Graham, 2014). Brightness level for all videos was adjusted to 50% (Graham, 2014).

Six minutes of social and non-social video footage respectively was recorded for viewing, that is, total of twelve minutes of video viewing for each participant. Both the social and non-social videos comprised of twelve different thirty-second videos that were counterbalanced within and between participants (Christou et al., 2015). One video segment of thirty seconds was followed by another video segment from the same condition (Figure 5.1). All videos were shown on a computer screen with an average volume of 68dB recorded at the child's head, using 2.1-Hz audio speakers (Graham, 2014).
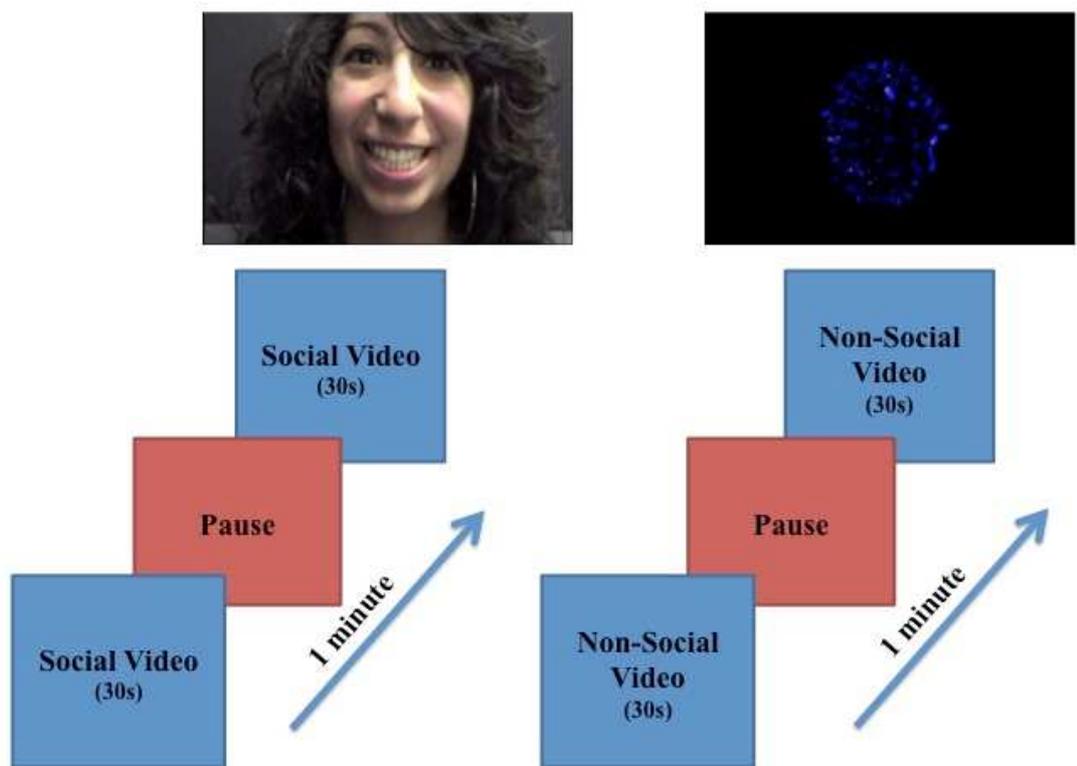
Figure 5.1: Social/Non-Social video processing experiment stimuli presentation.

5.2.4 EEG Procedure and Recording

The researcher first played with regular hats with the child in a separate playroom in order to build rapport and help the child become desensitised to wearing a hat. While playing with the child, head size was measured using a tape measure. EEG was recorded in a separate EEG/ERP recording room. Children either sat on their parent's lap or on their own (with the parent sitting behind them) approximately 70cm away from the computer screen and speakers. During EEG net application children were either given a toy to occupy their hands or were distracted with sound and light toys. Once the EEG net was placed on the child's head, the EEG recording was started and stimuli were presented with the social and non-

social video conditions counterbalanced across participants. Each condition was presented for one minute, with two thirty-seconds blocks separated by a pause (Figure 5.1). Breaks were taken between stimuli viewing if the child was distressed during the EEG recording. A video camera recorded the child's looking behaviour during the EEG recording.

EEG data were recorded continuously using a high density, 128-channel Hydrocel Geodesic Sensor Net (HCGSN, Electrical Geodesics Inc., Eugene, Oregon) referenced to a single vertex electrode, Cz (sample rate = 500 Hz; online highpass filter = 0.1 Hz; Tucker, 1993). EEG data were recorded using Net Station 4.3 data acquisition software and stimuli were presented using E-Prime 2.0 software (Psychology Software Tools, Inc., Sharpsburg, PA). Electrode impedances were kept below 100 kΩ at the time of recording.

5.2.5 EEG Analysis

EEG analysis procedures were similar to those described in Graham (2014) and Christou et al. (2015). All EEG recordings were analysed offline on NetStation 4.5.1 software (Electrical Geodesics). The author and one trained research assistant carried out analysis. The research assistant received extensive training on analysing continuous EEG data including detecting artefacts and differentiating and selecting brain activity data. Data analysed by the researcher and research assistant were balanced across groups with equal number of files being analysed between groups and between each other. Due to the nature of analysing continuous EEG data, biases in the editing process were highly unlikely. However, as the data were analysed by the author, consistent blinding for group allocation of participants was not possible.

Individual participant EEG data were filtered using a high-pass filter of 0.1Hz and a low-pass Notch filter at 50Hz. EEG recordings were then segmented based on epoch (30-

second video clips) and condition (social, non-social), using a clinical segmentation tool. EEG sections and individual electrodes were manually marked bad for each segment if there was participant movement or other artefacts. If a segment had more than 12 electrodes marked bad, the segment was excluded from further analysis. After manual bad channel selection, bad channels in data including 12 or fewer bad channels were replaced using a spherical spline interpolation algorithm (Srinivasan et al., 1996). Subsequently, sections of representative brain activity data (free from any artefacts such as eye blinks) were selected from each segment. Video recording for each segment was also checked wherein only those segments where the child was observed to be looking at the video stimuli were included. All segments were then combined for each condition and, finally, converted to an average reference. Files for each condition for each participant were exported in RAW format for use in a purpose-build MATLAB-based program for data analysis. EEG data were split into one-second epochs using MATLAB program (version 7.1.0). Using a 500-millisecond window with 60% overlap, Fast Fourier Transforms were calculated for each epoch and power spectral density (PSD) values were generated (Christou et al., 2015). PSD is the measurement of amplitude and consistency of synchronous firing of neurons. All PSD values were log transformed for individual frequencies between 3-13Hz.

Previous research suggests that theta activity varies from 3.5-5.6Hz in 12 month old infants to 4-7Hz in 3 to 6 year old children (Orekhova et al., 2006) while alpha activity also modulates developmentally with Marshall and colleagues finding alpha activity to vary between 6-9Hz in infancy to 7-12 Hz in childhood (Marshall et al., 2002). Therefore, there is a degree of overlap in the manner in which the theta and alpha frequency bands are defined in the existing literature (Stroganova & Orekhova, 2007). It has been recommended that frequency bands, especially in early childhood, must be defined in narrow frequencies and

alpha activity has been often defined using two bands: lower alpha of 7-9Hz and upper alpha of 10-13Hz (Klimesch, 1999). Owing to participant ages ranging from 16 months to 6 years in the current study, theta band activity was defined as 3-6 Hz while the alpha band was defined as activity between 7-9 Hz (lower alpha) and 10-13Hz (upper alpha).

Electrode locations were chosen based upon previous research implicating frontal, central and temporal-parietal regions in social functioning in typically developing individuals. Consistent with this, the social brain network has been proposed to include regions of the orbitofrontal cortex (OFC), dorsolateral prefrontal cortex (dlPFC), medial prefrontal cortex (mPFC), a central and parietal mirror neuron network, and the temporal-parietal junction (TPJ), among other regions (Frith & Frith, 2010; Grossmann & Johnson, 2007). Therefore, six left and six right electrodes over the dlPFC and six left and six right electrodes around the OFC were chosen, corresponding to the F3 and F4 electrodes and F1 and F2 electrodes in the international 10-20 EEG coordinate system respectively (Figure 5.2). Additionally, six left and six right electrodes located over the TPJ were selected corresponding to TP3 and TP4 electrode regions, and five left and five right Central electrodes were chosen around the C3 and C4 regions in the international 10-20 EEG system (Figure 5.2). Theta, lower alpha and upper alpha mean PSDs were analysed across each region between conditions and groups. Planned analyses included analysing for each frequency band separately as well. This was implemented as previous research suggests that different regions of the brain and different social processes modulate the theta and alpha bands differently.
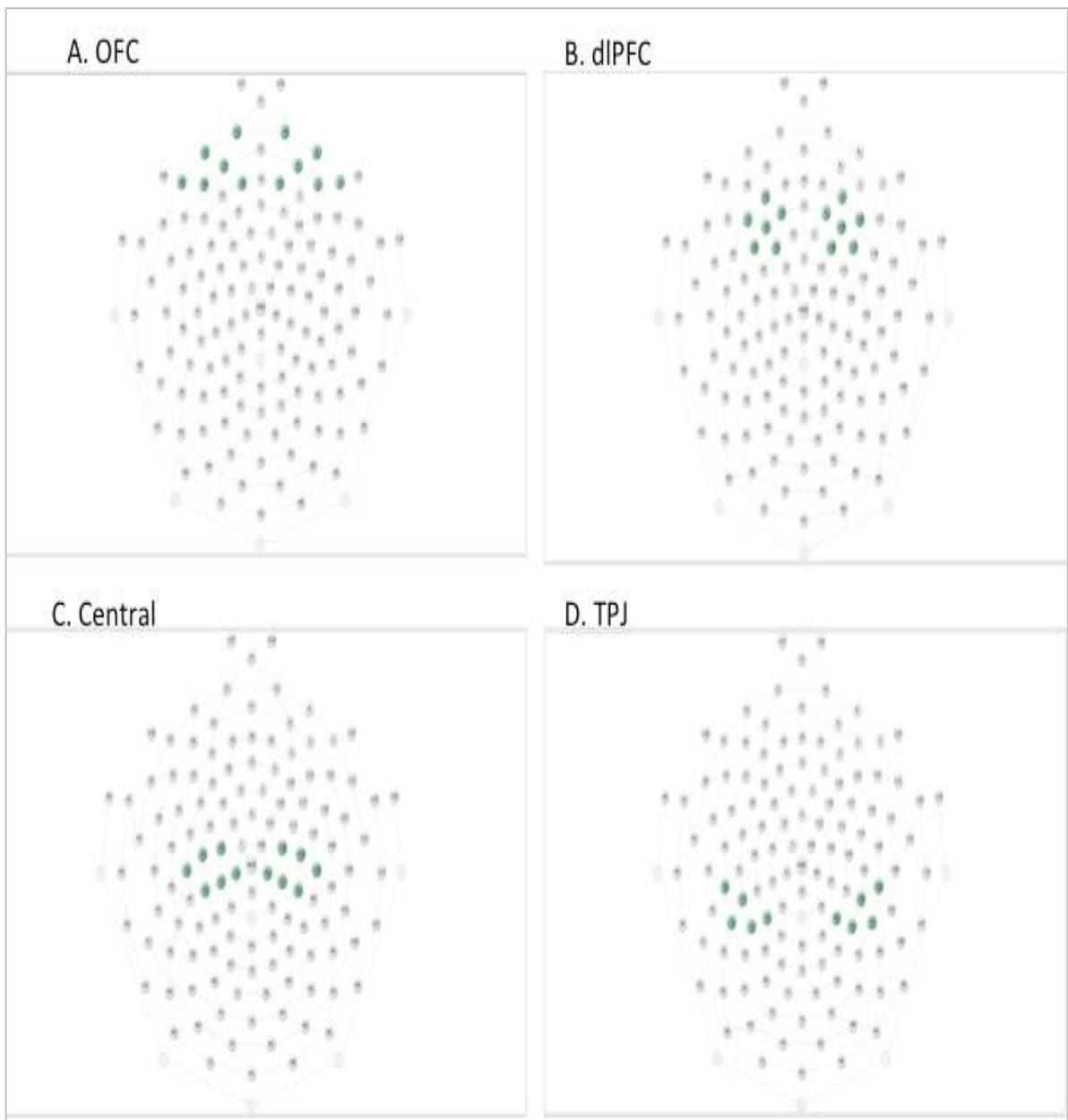
Figure 5.2: Montages selected for analysis. A. Orbitofrontal Cortex (OFC), B. Dorsolateral Prefrontal Cortex (dlPFC), C. Central, and D. Temporal-Pareital Junction (TPJ).

5.3 RESULTS

5.3.1 Study 1: ASD versus TD group

5.3.1.1 Alpha and Theta Activity: CA-matched groups

Children in the ASD and chronological age-matched (CA) TD group produced comparable amounts of EEG data, and independent samples t-test revealed no significant differences in length of artefact-free EEG data (Table 5.4). A Shapiro-Wilk test of normality further revealed non-significant results for mean PSD values, indicating a normally distributed dataset. Parametric tests were therefore performed. All results violated Mauchley's test of Sphericity and, therefore, Greenhouse-Geisser adjusted values have been reported. Mixed ANOVAs were carried out and post-hoc analyses of interaction effects were performed using Bonferroni correction[10]. Post-hoc analyses included pairwise comparisons and planned t-tests.

Table 5.4: Mean length (S.D.) of artefact-free EEG data (in seconds) for the two groups in the two conditions.

Condition	ASD (*n*=12)	TD (*n*=17)	*t (27)*	*p-value*
Social	116.75 (59.2)	135.76 (66.3)	0.79	0.43
Non-Social	140.75 (52)	150.53 (77)	0.38	0.71

It was hypothesised that greater theta activity and greater alpha suppression (that is low alpha activity) will be associated with social processing and that children with autism will differ significantly from typically developing children in both alpha and theta EEG activity

---

[10] The SPSS manual gives syntax for Bonferroni correction that can be used with pairwise comparisons and t-tests. This syntax was applied for each comparison.

during social and non-social processing. In order to evaluate differences between the TD and ASD groups in theta, lower alpha and upper alpha activity while viewing social and non-social stimuli, a five-way mixed ANOVA was conducted with frequency band (mean PSD for theta, lower alpha, upper alpha), condition (social, non-social), region (Central, TPJ, OFC, dlPFC) and hemisphere (left, right) as within-subjects factors and group (TD, ASD) as a between-subjects factor.

This analysis revealed a main effect of region (F (1,27) = 73.59, p <0.01, η_p^2 = 0.73) and frequency band (F (1,27) = 516.92, p <0.01, η_p^2 = 0.95).

A significant interaction was found for hemisphere x condition (F (1,27) = 18.04, p <0.01, η_p^2 = 0.40) suggesting difference in processing of social and non-social stimuli between left and right hemispheres. However, pairwise comparisons using Bonferroni correction did not reveal any significant differences.

Four different interactions were revealed for frequency band: frequency band x condition (F (1,27) = 8.37, p <0.01, η_p^2 = 0.24), region x frequency band (F (1,27) = 16.69, p <0.01, η_p^2 = 0.38), region x hemisphere x frequency band interaction (F (1,27) = 11.56, p <0.01, η_p^2 = 0.30) and condition x frequency band x group interaction (F (1,27) = 5.74, p = 0.01, η_p^2 = 0.18). These interactions supported the previous argument for evaluating frequency bands individually.

Post-hoc analysis using pairwise comparisons with Bonferroni correction for the frequency band x condition interaction revealed that there was a significant difference in mean Theta activity for the social (M = 0.78, $S.E.$ = 0.04) versus non-social conditions (M = 0.75, $S.E.$ = 0.04; p = 0.01).

Pairwise comparisons using Bonferroni correction were also conducted on the region x frequency band interaction to examine differences in activity amongst regions for individual

frequency bands. Theta activity differed significantly between the Central, TPJ, OFC and dlPFC regions (all differences between regions in theta activity significant at $p < 0.01$) revealing highest theta activity over OFC region and lowest theta PSD over the Central channels (Table 5.5). Lower and upper alpha activity over the Central region were significantly different from activity over the TPJ, OFC and dlPFC regions ($p < 0.01$), and OFC activity differed significantly from activity over Central, TPJ and dlPFC region ($p < 0.01$) showing greatest lower and upper alpha suppression in the Central region. However, activity in the TPJ and dlPFC was significantly different from Central and OFC regions ($p < 0.01$) but no difference in EEG alpha activity was found between TPJ and dlPFC region ($p = 0.37$; Table 5.5). Thus, different regions modulated each frequency band differently.

Table 5.5: Mean PSD for theta, lower alpha and upper alpha EEG activity for central, temporal parietal junction (TPJ), orbitofrontal cortex (OFC) and dorsolateral prefrontal cortex (dlPFC) for the whole sample.

Region	Mean Theta PSD *(S.E.)*	Mean Lower Alpha PSD *(S.E.)*	Mean Upper Alpha PSD *(S.E.)*
Central	0.60 (0.04)	0.31 (0.04)	-0.29 (0.04)
TPJ	0.72 (0.03)	0.45 (0.04)	-0.15 (0.04)
OFC	0.91 (0.04)	0.56 (0.05)	-0.04 (0.04)
dlPFC	0.83 (0.04)	0.50 (0.05)	-0.11 (0.04)

In order to understand the three-way interactions for region x hemisphere x frequency band and condition x frequency band x group, further ANOVAs were conducted. These ANOVAs tied with previous planned analyses regarding EEG frequencies being different across regions and conditions. To evaluate the hypothesis regarding differences in social and

non-social processing for theta, lower alpha and upper alpha frequency bands planned analyses were conducted for each band individually. Therefore, mixed ANOVAs were conducted for theta, lower alpha and upper alpha bands with region (Central, TPJ, OFC, dlPFC), condition (social, non-social) and hemisphere (left, right) as within-subjects factors and group (TD, ASD) as between-subjects factor.

5.3.1.1.1 Theta Band Activity (3 – 6Hz)

The mixed ANOVA for theta band activity revealed a significant main effect of region, ($F_{(1,27)} = 93.26$, $p < 0.01$, $\eta_p^2 = 0.78$) and condition ($F_{(1,27)} = 7.17$, $p = 0.01$, $\eta_p^2 = 0.21$). Highest theta activity was observed for the OFC region ($M = 0.91$, $S.E. = 0.04$) and for the social condition ($M = 0.78$, $S.E. = 0.04$).

A significant interaction effect was found for condition x hemisphere ($F_{(1,27)} = 7.18$, $p = 0.01$, $\eta_p^2 = 0.21$). Post-hoc pairwise comparisons using Bonferroni correction found a significantly greater theta activity for the social ($M = 0.79$, $S.E. = 0.04$) condition compared to the non-social condition ($M = 0.75$, $S.E. = 0.04$) in the right hemisphere ($p < 0.01$; Figure 5.3).
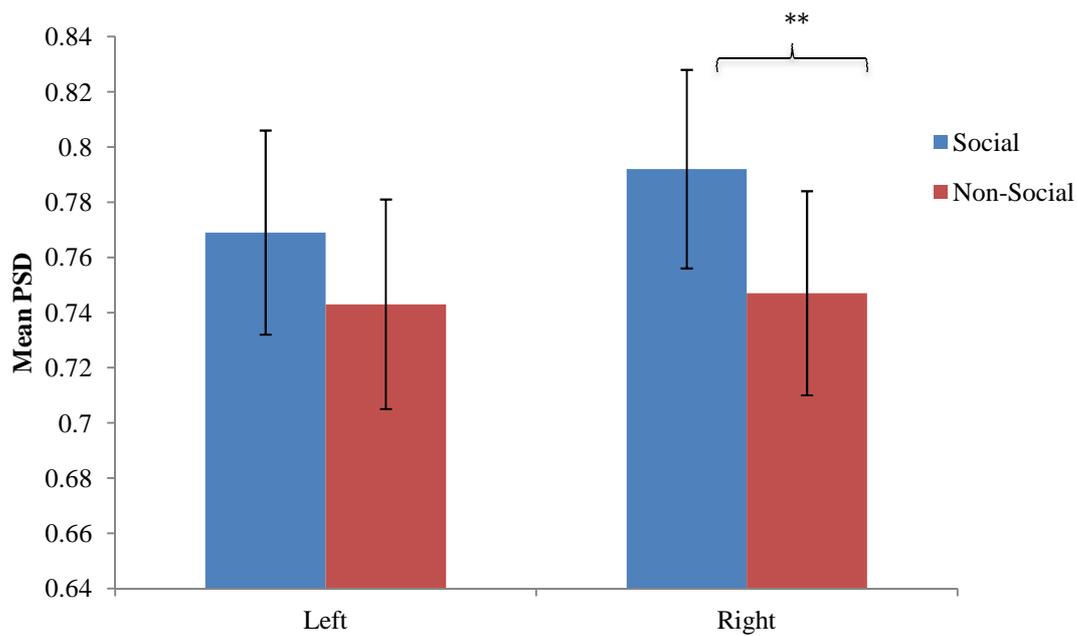
Figure 5.3: Theta power spectral density for the social and non-social conditions recorded over the left and right hemispheres for the whole sample. Error bars represent standard error.

5.3.1.1.2 Lower Alpha Band Activity (7 – 9Hz)

A mixed ANOVA for lower alpha activity revealed a significant main effect of region, (F (1,27) = 46.31, p <0.01, η_p^2 = 0.63). As alpha suppression suggests greater brain activity, lowest alpha activity was observed for the Central region (M = 0.31, *S.E.* = 0.04).

A significant interaction effect was found for condition x hemisphere (F (1,27) = 12.33, p <0.01, η_p^2 = 0.31) however post-hoc pairwise comparisons using Bonferroni correction did not produce any significant differences in activity.

5.3.1.1.3 Upper Alpha Band Activity (10 – 13Hz)

Results of the mixed ANOVA found a significant main effect of region (F (1,27) = 71.35, p <0.01, η_p^2 = 0.73). Lowest upper alpha activity was observed in the Central region (M = - 0.29, *S.E.* = 0.04).

Region x hemisphere interaction was found to be significant (F (1,27) = 4.0, p = 0.02, η_p^2 = 0.13), and post-hoc analysis revealed a difference in hemispheric activity for Central and OFC regions (Figure 5.4). In the Central region greater alpha suppression was observed in the left hemisphere (M = - 0.32, *S.E.* = 0.04) compared with right hemisphere (M = - 0.26, *S.E.* = 0.04; p <0.01). In the OFC region, alpha suppression was also observed in the left hemisphere (M = - 0.06, *S.E.* = 0.05) compared with right hemispheric activity (M = - 0.01, *S.E.* = 0.05; p = 0.05).
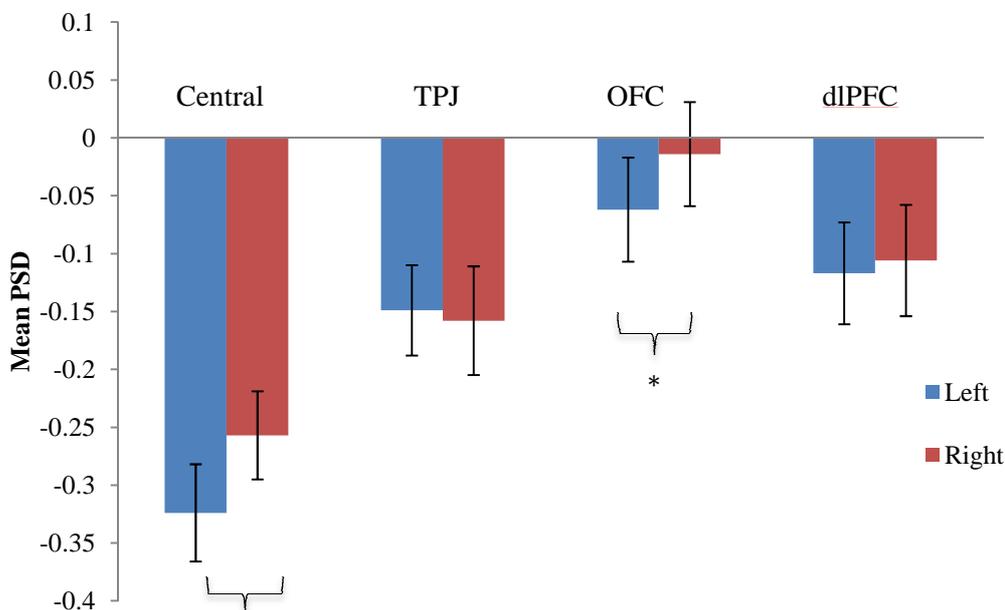
Figure 5.4: Upper Alpha activity recorded over the left and right hemispheres for central, temporal-parietal junction (TPJ), orbitofrontal cortex (OFC), and dorsolateral prefrontal cortex (dlPFC) scalp regions for the whole sample. Error bars represent standard error.

5.3.1.1.4 Condition by Group Interaction

The main mixed ANOVA had initially revealed a condition x frequency x group interaction (Figure 5.5). However, none of the frequency bands individually were able to explain the group interaction. Therefore, another set of two-way ANOVA was conducted for condition x group to explicate the three-way interaction. Neither the main effect of condition (F (1,27) = 2.81, p = 0.11, η_p^2 = 0.09) nor the condition x group interaction (F (1,27) = 0.47, p = 0.50, η_p^2 = 0.02), were significant. Therefore, no conclusive results regarding which differences were driving the three-way interaction of condition by group by frequency band were obtained.

Visual inspection of mean PSDs showed that lower alpha frequency in the TD group was greater in the social condition (*M* = 0.43, *S.E.* = 0.05) compared to the non-social condition (*M* = 0.39, *S.E.* = 0.06). However, for the ASD group, lower alpha in the social condition (*M* = 0.49, *S.E.* = 0.06) was observed to be lesser compared to the non-social condition (*M* = 0.52, *S.E.* = 0.07; Figure 5.5). Thus, even though further statistical analyses did not show the mean PSD differences to be significant, a different trend in the means of lower alpha activity for the two groups was observed.
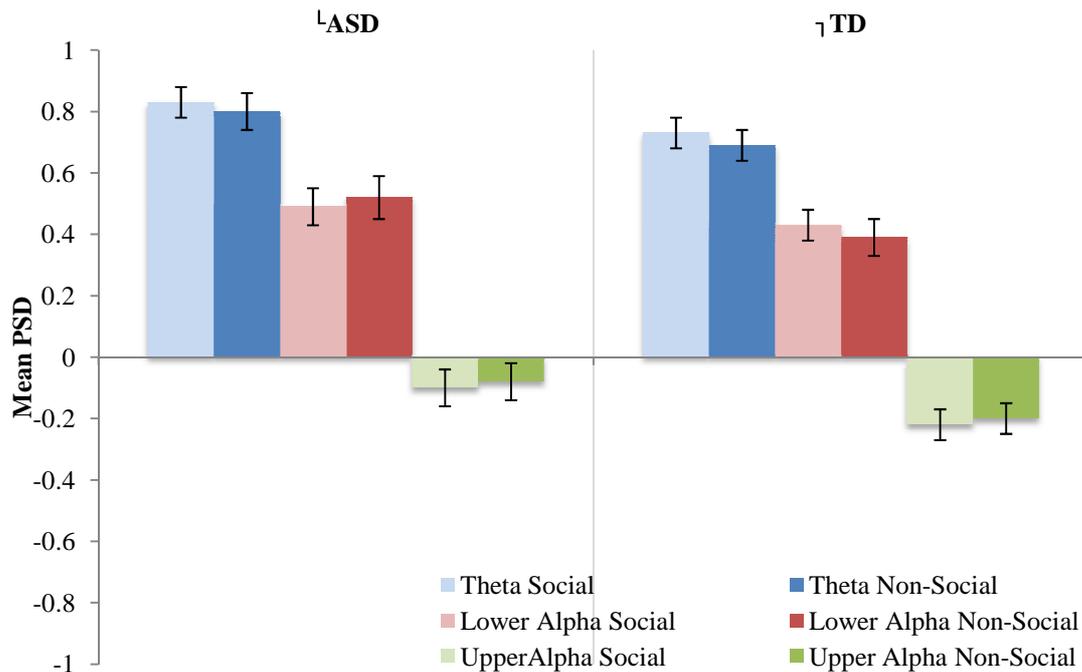
Figure 5.5: Graph showing theta, lower alpha and upper alpha activity for social and non-social condition in the ASD and TD groups. Error bars represent standard error. .

To summarise, first, it was hypothesised that greater theta activity and greater alpha suppression (that is low alpha activity) will be associated with social processing. The present results were able to find that only theta activity was modulated by condition, with greater theta activity associated with social condition. Second, it was hypothesised that children with autism will differ significantly from typically developing children in both alpha and theta EEG activity during social and non-social processing. Even though a mixed interaction effect was found for group differences based on condition and frequency band, post-hoc analysis did not lead to any conclusive findings.

5.3.1.2 Alpha and Theta Activity: VMA-matched groups

As mentioned previously to control for differences in EEG activity based on verbal abilities a sub-group of verbal mental age matched children were analysed for social and non-social processing differences in the theta, lower and upper alpha frequencies. An independent samples t-test revealed no differences in the length of artefact-free EEG data between the ASD and verbal-age matched (VMA) TD groups (Table 5.6). Shapiro-Wilk test of normality revealed non-significant results for mean PSD values indicating normally distributed dataset. Parametric tests were therefore performed. All results violated Mauchley's test of Sphericity and therefore, Greenhouse-Geisser adjusted values have been reported.

Table 5.6: Mean length (S.D.) of artefact-free EEG data (in seconds) for the VMA-matched two groups in the two conditions.

Condition	ASD (*n*=10)	TD (*n*=12)	*t (20)*	*p-value*
Social	127.90 (58.8)	115.42 (62.9)	-0.48	0.64
Non-Social	145.10 (49.5)	128.83 (77.7)	-0.57	0.57

To examine social and non-social processing differences between groups, a mixed ANOVA was conducted with frequency band (mean PSD for theta, lower alpha, upper alpha), condition (social, non-social), region (Central, TPJ, OFC, dlPFC) and hemisphere (left, right) as within-subjects factors and group (TD, ASD) as between-subjects factor. Analysis revealed very similar effects as the CA-matched groups (Table 5.7).

Table 5.7: Summary of five-way ANOVA for verbal mental age matched TD (n=12) and ASD

(n=10) groups.

	F (1,20)	p	η_p^2
Region	49.19	**	0.71
Condition	0.65	0.43	0.03
Hemisphere	1.19	0.29	0.06
Frequency Band	488.89	**	0.96
R x G	1.63	0.22	0.08
C x G	0.14	0.72	0.01
H x G	0.01	0.94	0.00
F x G	2.21	0.12	0.10
R x C	0.40	0.69	0.02
R x H	1.80	0.17	0.08
C x H	7.78	0.01*	0.28
R x F	12.19	**	0.38
C x F	10.25	**	0.34
H x F	1.00	0.36	0.05
R x C x G	1.24	0.30	0.06
R x H x G	0.87	0.44	0.04
C x H x G	0.04	0.85	0.00
R x C x H	0.61	0.53	0.03
R x F x G	0.78	0.48	0.04
C x F x G	2.94	0.07	0.13
R x C x F	1.53	0.22	0.07
H x F x G	0.16	0.81	0.01
R x H x F	11.97	**	0.37
C x H x F	2.23	0.12	0.10
R x C x F x G	1.65	0.20	0.08
R x C x H x G	1.98	0.16	0.09
R x H x F x G	1.56	0.20	0.07
C x H x F x G	0.77	0.47	0.04
R x C x H x F	1.04	0.38	0.05
R x C x H x F x G	0.84	0.48	0.04

**F-statistic significant at p<0.01.
All values shaded grey were significant at p <0.05. R = Region, C = Condition, H= Hemisphere, F = Frequency band, G = Group.

Post-hoc analysis revealed significantly greater Theta activity in the social condition (M= 0.78, *S.E.* = 0.04) compared to the non-social condition (M= 0.75, *S.E.* = 0.04; p = 0.02), and differences in activity between regions for individual frequency bands (see Table 5.8 for mean values). Similar to previous results for the CA-matched groups, Theta activity was found to significantly differ between the Central region compared with OFC, TPJ and dlPFC regions (p<0.01); OFC region compared to TPJ and dlPFC (p<0.01); and TPJ region compared to dlPFC (p = 0.04). In the lower alpha band, a significant difference in activity was found between the Central region compared with OFC, TPJ and dlPFC regions (p<0.01); OFC region compared to dlPFC, (p<0.01); and TPJ region compared to dlPFC, (p <0.01) but was not significant between TPJ and OFC region (p = 0.21). Finally, in the upper alpha band a significant difference was found between the Central region compared with OFC, TPJ and dlPFC regions (p<0.01); OFC region compared to dlPFC (p<0.01); and TPJ region compared to dlPFC (p <0.01) and TPJ and OFC region (p = 0.01).

Table 5.8: Mean PSD for theta, lower and upper alpha EEG activity for central, temporal parietal junction (TPJ), orbitofrontal cortex (OFC) and dorsolateral prefrontal cortex (dlPFC) in the VMA-matched sample for the whole sample.

Region	Mean Theta PSD *(S.E.)*	Mean Lower Alpha PSD *(S.E.)*	Mean Upper Alpha PSD *(S.E.)*
Central	0.61 (0.04)	0.31 (0.04)	-0.29 (0.04)
TPJ	0.74 (0.03)	0.46 (0.04)	-0.15 (0.04)
OFC	0.90 (0.05)	0.54 (0.05)	-0.06 (0.05)
DLPFC	0.82 (0.05)	0.48 (0.05)	-0.13 (0.05)

Planned analyses were conducted on each frequency band. Mixed ANOVAs with region (Central, TPJ, OFC, dlPFC), conditions (social, non-social) and hemispheres (left, right) as within-subject factors and group (TD, ASD) as between subjects factor were conducted (Table 5.9). The results were similar to those for the CA-matched group.

Table 5.9: Summary of four-way ANOVA in theta, lower alpha and upper alpha frequency bands for VMA-matched TD and ASD sample.

	Theta			Lower Alpha			Upper Alpha		
	F (1,20)	*p*	η_p^2	*F* (1,20)	*p*	η_p^2	*F* (1,20)	*p*	η_p^2
Region	59.94	**	0.75	30.45	**	0.60	47.99	**	0.71
Condition	6.28	0.02*	0.24	0.78	0.39	0.04	2.24	0.15	0.10
Hemisphere	0.66	0.43	0.03	1.25	0.29	0.06	1.48	0.24	0.07
R x G	1.15	0.34	0.05	2.09	0.16	0.09	1.22	0.30	0.06
C x G	0.00	0.99	0.00	1.30	0.27	0.06	0.27	0.61	0.01
H x G	0.05	0.82	0.00	0.001	0.98	0.00	0.002	0.97	0.00
R x C	1.70	0.20	0.08	0.54	0.56	0.03	0.40	0.68	0.20
C x H	7.30	0.01*	0.27	6.08	0.02*	0.23	0.24	0.63	0.01
R x H	1.89	0.16	0.09	1.19	0.32	0.06	4.23	0.01*	0.18
R x C x G	1.33	0.27	0.06	0.29	0.72	0.01	2.15	0.10	0.10
R x H x G	1.19	0.32	0.06	0.33	0.74	0.02	1.17	0.32	0.06
C x H x G	0.66	0.43	0.03	0.43	0.52	0.02	0.08	0.78	0.00
R x C x H	1.34	0.27	0.06	0.59	0.57	0.03	0.28	0.72	0.01
R x C x H x G	2.53	0.10	0.11	1.29	0.29	0.06	1.06	0.35	0.05

**F-statistic significant at p<0.01.

All values shaded grey were significant at p <0.05. R = Region, C = Condition, H = Hemisphere, G = Group.

Theta band activity was highest for the OFC region ($M = 0.90$, *S.E.* $= 0.05$) and for the social condition ($M = 0.78$, *S.E.* $= 0.04$). Theta activity differed in the right hemisphere between the social ($M = 0.80$, *S.E.* $= 0.04$) and non-social conditions ($M = 0.75$, *S.E.* $= 0.04$) with greater activity in the social condition. Lower Alpha band activity was lowest in the Central region ($M = 0.31$, *S.E.* $= 0.04$). Post-hoc comparisons did not show any significant difference in hemispheric activity for the two conditions. Upper Alpha activity was also lowest in the Central region ($M = - 0.29$, *S.E.* $= 0.04$). Post-hoc analysis on the region x hemispheric interaction revealed greater left hemispheric alpha suppression ($M = - 0.33$, *S.E.* $= 0.04$) compared to right hemispheric alpha activity ($M = -0.25$, *S.E.* $= 0.04$).

Thus the results provided partial support for the first hypothesis of the study as greater theta activity for social condition compared to non-social condition was observed but no differences in social/non-social processing were reflected in the lower and upper alpha bands. Also, the results for the chronological age-matched sample revealed a complex group interaction for condition and frequency bands, however post-hoc analyses did not reveal any conclusive results regarding which differences were driving the three-way interaction. Furthermore, this interaction was not observed in the verbal mental age matched sub-group. Thus, with regards to the second and third hypothesis of the study, no conclusive results can be found regarding differences in theta and alpha band frequency during social or non-social processing between the ASD and TD groups.

5.3.1.3 *Correlation Analysis*

A last hypothesis of the present study was that alpha and theta activity will be associated with autism symptomatology as evidenced by greater social difficulty being

associated with less alpha suppression and less theta activity. Correlations were conducted to investigate relationships between EEG frequency bands and autism symptomatology as measured on the ADOS domains: reciprocal social interaction, communication, stereotyped behaviours and restricted interests and play, in the ASD group. Pearson correlations were conducted and Holm-Bonferroni sequential correction was used to correct for Type 1 error due to the large number of analyses carried out (Gaetano, 2013; Holm, 1979). Corrected values revealed no significant correlations between EEG activity in any of the three frequency bands and ADOS domain or total scores (Appendix I) suggesting that alpha and theta activity were not associated with ASD symptomatology in the present sample.

5.3.2   Study 2: Treatment versus Wait-List Control Group

The aim of Study 2 was to examine changes in processing, reflected in alpha and theta frequencies, of social and non-social stimuli in children with autism who underwent RIT as compared with children in a Wait-List Control group. Hence, EEG activity in children with autism between the two groups, Treatment and Wait-List Control, was compared on theta, lower alpha and upper alpha frequency bands. Due to the relatively small amount of data obtained at T1, the data analyses were conducted in two ways. First, as a larger number of children produced artefact-free EEG data at Time 2, Mann-Whitney U were carried out to identify group differences in social and non-social processing at outcome. Subsequently, data from a total of eight children (four each from the Treatment and Wait-List Control groups) who produced viable EEG data at both T1 and T2 were examined. Individual participant data were used for descriptive analysis of changes from T1 to T2 in an effort to understand patterns associated with any differences identified between the two groups at T2.

5.3.2.1   Post-treatment Results: Treatment (n=7) versus Wait-List Control group (n=7)

The amount of viable, artefact-free EEG data was found to be similar across the two groups (Table 5.10). Due to the small sample size and variability in the sample, non-parametric analysis was carried out.

Table 5.10: Mean length (S.D.) of artefact-free EEG data (in seconds) for the Treatment (n=7) and Wait-List Control group (n=7) in the two conditions.

Condition	Treatment (n=7)	Wait-List Control (n=7)	t (12)	p-value
Social	100.1 (51.1)	87 .0 (19.8)	0.63	0.54
Non-Social	60.4 (15.0)	61.6 (17.1)	-0.13	0.90

Mann-Whitney U test was conducted for each region (Central, TPJ OFC and dlPFC), condition (social and non-social) and frequency band (theta, lower alpha and upper alpha) to analyse for group differences in processing. Analysis did not reveal any significant differences between Treatment and Wait-List control group for any region, condition or frequency band (Table 5.11).

Table 5.11: Median, range scores and Mann-Whitney statistics for Central, TPJ, OFC and dlPFC regions for theta, lower alpha and upper alpha EEG activity for the Treatment (n=7) and Wait-List Control groups (n=7) in the two conditions at T2.

	Treatment (*n* = 7)		Wait-List Control (*n* = 7)				
	Mdn	Range	*Mdn*	Range	*U*	*z*	*p*
Central							
Theta Non-Social	0.56	0.08 - 0.80	0.66	0.30 – 0.77	24	-0.06	0.95
Theta Social	0.64	0.11 - 0.79	0.70	0.24 – 0.79	21	-0.45	0.66
Lower Alpha Non-Social	0.52	-0.34 - 0.68	0.35	-0.03 – 0.48	15	-1.21	0.23
Lower Alpha Social	0.30	-0.24 - 0.56	0.35	-0.14 – 0.40	24	-0.06	0.95
Upper Alpha Non-Social	-0.17	-0.79 - 0.06	-0.24	-0.55 – 0.05	21	-0.45	0.66
Upper Alpha Social	-0.32	-0.76 – -0.03	-0.20	-0.62 - 0.03	17	-0.96	0.34
TPJ							
Theta Non-Social	0.68	0.13 - 0.89	0.74	0.43 – 0.88	23	-0.19	0.85
Theta Social	0.59	0.25 – 0.88	0.77	0.37 – 0.89	16	-1.09	0.28
Lower Alpha Non-Social	0.63	-0.21 - 0.83	0.43	0.13 – 0.62	22	-0.32	0.75
Lower Alpha Social	0.36	-0.04 - 0.65	0.47	0.03 – 0.56	17	-0.96	0.34
Upper Alpha Non-Social	-0.07	-0.68 – 0.21	-0.11	-0.38 – 0.14	24	-0.06	0.95
Upper Alpha Social	-0.28	-0.58 – 0.02	-0.11	-0.53 – 0.16	15	-1.21	0.23
OFC							
Theta Non-Social	0.99	0.61 – 1.13	0.90	0.69 – 1.11	22	-0.32	0.75
Theta Social	0.96	0.72 – 1.15	0.93	0.77 – 1.08	15	-1.21	0.23
Lower Alpha Non-Social	0.76	0.18 – 0.94	0.53	0.29 – 0.74	24	-0.06	0.95
Lower Alpha Social	0.58	0.35 – 0.81	0.55	0.26 – 0.74	23	-0.19	0.85
Upper Alpha Non-Social	0.08	-0.28 – 0.30	0.05	-0.23 – 0.22	20	-0.58	0.57
Upper Alpha Social	0.07	-0.15 – 0.18	0.15	-0.23 – 0.28	19	-0.7	0.48
dlPFC							
Theta Non-Social	0.87	0.43 – 1.12	0.86	0.63 - 1.05	24	-0.06	0.95
Theta Social	0.84	0.51 - 1.01	0.86	0.66 – 1.01	16	-1.09	0.28
Lower Alpha Non-Social	0.76	0.04 – 0.90	0.49	0.24 – 0.69	24	-0.06	0.95
Lower Alpha Social	0.42	0.17 – 0.77	0.51	0.21 – 0.69	22	-0.32	0.75
Upper Alpha Non-Social	0.01	-0.44 – 0.23	0.03	-0.29 – 0.21	23	-0.19	0.85
Upper Alpha Social	-0.05	-0.34 – 0.13	0.10	-0.27 - 0.23	18	-0.83	0.41

It was hypothesised that RIT will have an impact on social processing in children with autism reflected in difference in theta and alpha activity between the Treatment and the Wait-List Control groups measured post-treatment, however no group differences were found for theta, lower alpha or upper alpha activity at outcome between the Treatment and Wait-List Control group. The findings do not support the hypothesis that RIT had an impact on social or non-social processing in children with autism.

5.3.2.2   Individual Participant Data Analyses: Treatment (n=4) versus Wait-list Control group (n=4)

To investigate the effect of RIT on change in EEG activity, T1 and T2 data were compared for participants who produced artefact-free data at both time points. As the sample size was small, mean scores were calculated for the social and non-social condition for theta, lower alpha and upper alpha activity in each region, at both T1 and T2. Individual participant data are discussed below for each region and frequency band.

5.3.2.2.1   Central

Theta: In the non-social condition, in the Treatment group three out of four children showed higher theta activity at T2 compared to T1 while children in the Wait-List group showed lesser activity at T2 compared to T1 (Figure 5.11). For the social condition, only one child in the Treatment group showed higher theta at T2 compared to T1. All other children in the Treatment group showed lower theta activity at T2 compared to T1 and the same pattern of lower activity at T2 compared with T1 was observed for the Wait-List Control group (Figure 5.11). Thus, Treatment and Wait-List Control group differed in theta activity for the non-social condition from T1 to T2.

Lower Alpha: In the lower alpha band, greater activity was seen at T2 compared with T1 in three out of four children in the Treatment group while all children in the Wait-List Control group showed lower activity at T2 for the non-social condition (Figure 5.11). For the social condition three children in the two respective groups showed lesser lower alpha activity at T2 compared with T1 though this was more pronounced in the Wait-List Control group and lower alpha activity for one child in the Treatment group did not change while one child in the Wait-List Control group demonstrated higher alpha activity at T2 compared to T1 (Figure 5.11). Thus, again the two groups differed in activity in the non-social condition.

Upper Alpha: In the upper alpha band, suppression in activity was observed for both social and non-social condition. Greater upper alpha suppression was observed for the social condition as compared to the non-social condition and in the Wait-List Control group compared to the Treatment group (Figure 5.11).
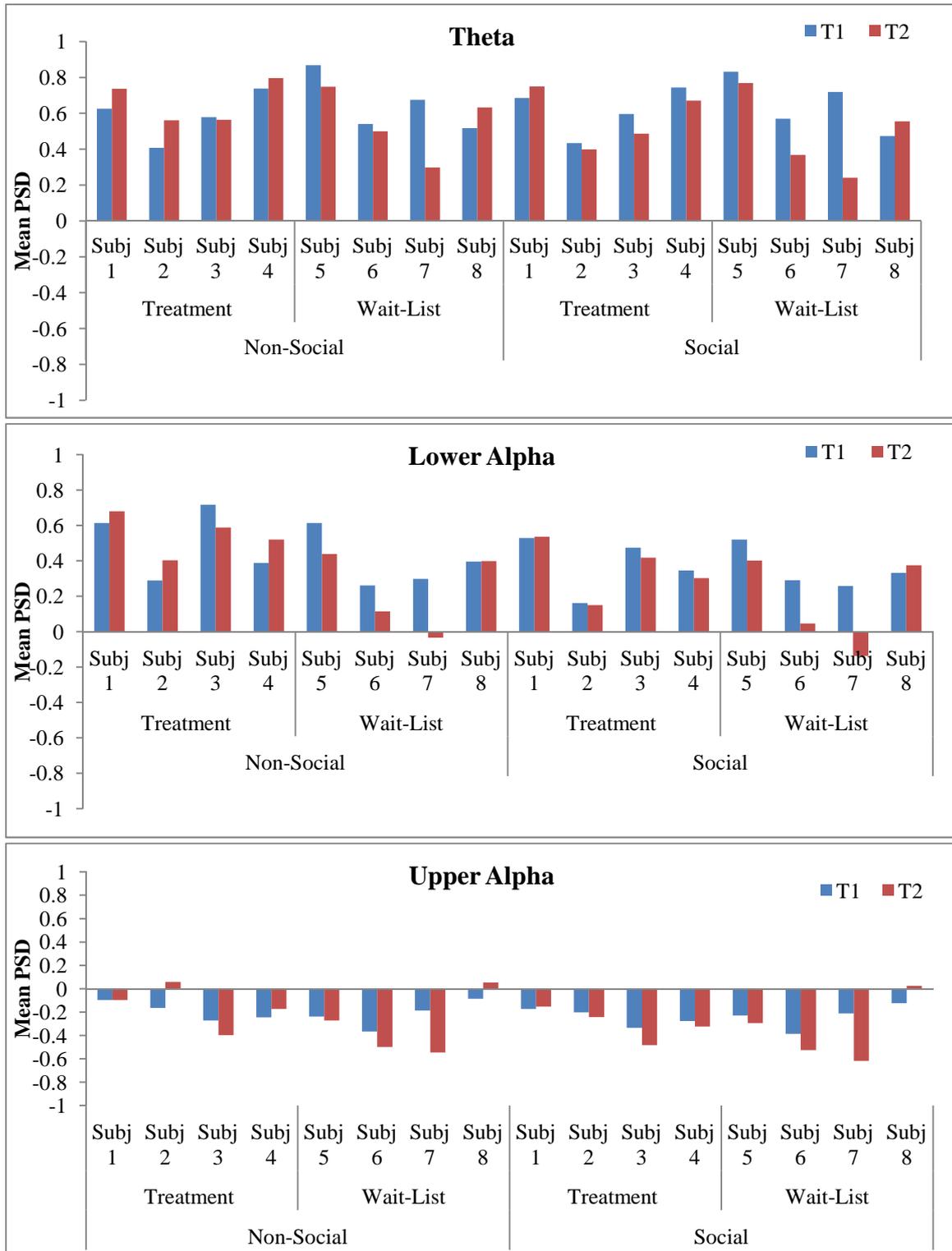
Figure 5.11: Individual participant mean PSDs for Treatment (n=4) and Wait-List Control (n=4) group for the social and non-social condition in theta, lower alpha and upper alpha bands over the Central electrodes.

5.3.2.2.2 Temporal Parietal Junction (TPJ)

<u>Theta:</u> In the TPJ region, all children in the Treatment group showed an increase in theta activity for the non-social condition while two children in the Wait-List group showed increase in activity and two children showed a decrease in theta activity from T1 to T2 (Figure 5.12). In the social condition, three children in the Treatment and three children in the Wait-List Control group showed a decrease in theta activity at T2 and one child in each group showed an increase at T2 compared with T1 (Figure 5.12).

<u>Lower Alpha:</u> In the lower alpha band, for the non-social condition three children in the Treatment group showed an increase in activity at T2 compared with T1 while one child had a slight decrease in activity while three children in the Wait-List group show lower alpha activity at T2 (Figure 5.12). Conversely, in the social condition three children in the Treatment group and Wait-List Control group showed lower activity at T2 while one child in each group had an increase in lower alpha band activity from T1 to T2 (Figure 5.12). Thus, there was a difference in lower alpha band activity between groups for non-social stimuli.

<u>Upper Alpha:</u> In the non-social condition, two children in the Treatment group and one child in the Wait-List Control group had a lesser alpha suppression (lesser alpha activity). All others showed greater alpha suppression at T2 (Figure 5.12). For social stimuli Treatment group showed greater suppression at T2 while three out of four children showed alpha suppression in the Wait-List group.
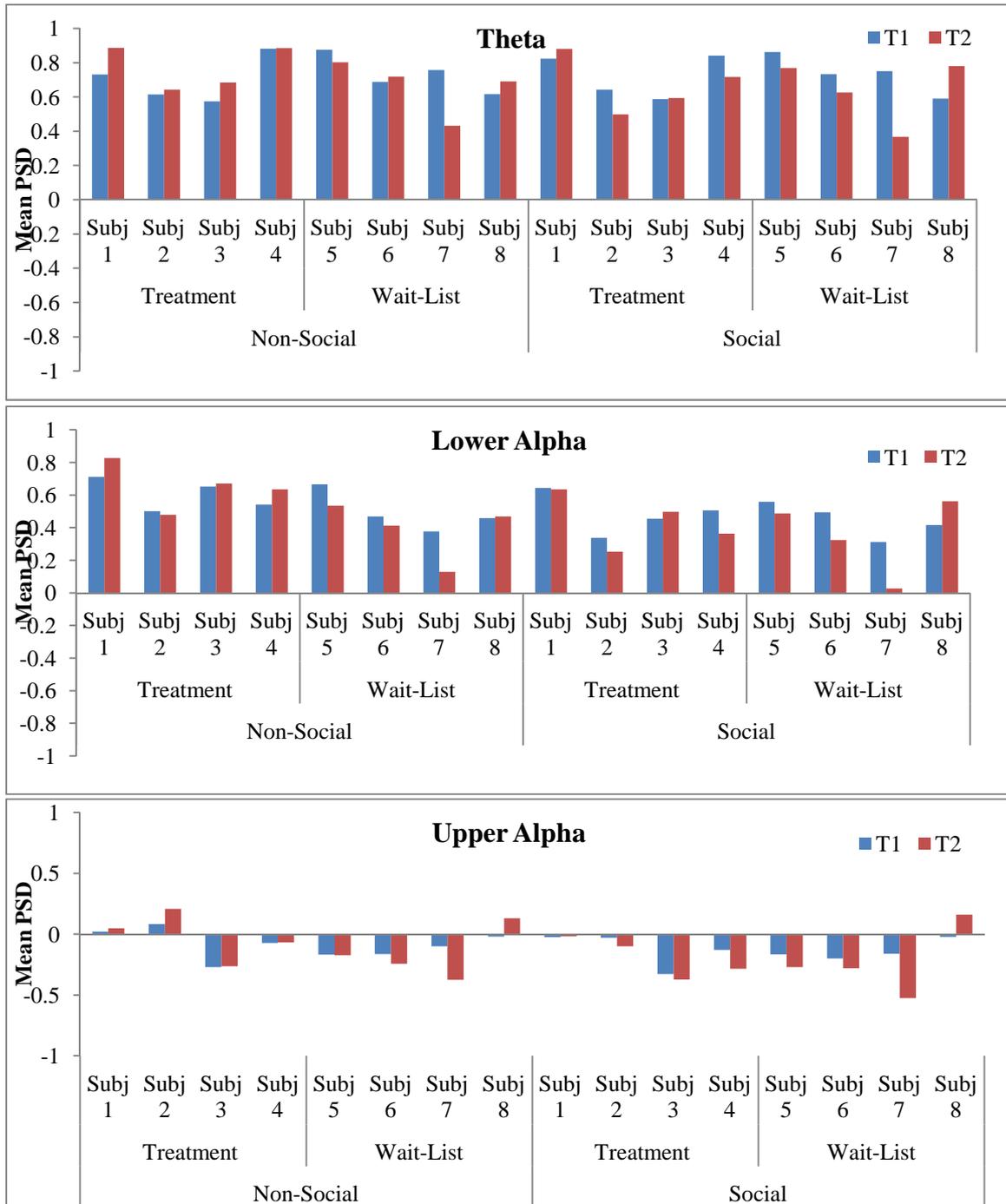
Figure 5.12: Individual participant mean PSDs for Treatment (n=4) and Wait-List Control (n=4) group for the social and non-social condition in theta, lower alpha and upper alpha bands over the TPJ.

5.3.2.2.3 Orbitofrontal Cortex (OFC)

Theta: For the non-social condition, three out of four children in the Treatment group showed higher theta activity at T2 compared with T1. Conversely, two children in the Wait-List group showed lower theta activity at T2 and two children had the same activity at T2 as at T1. For the social condition, there was an increase in theta activity for two children in the Treatment group while all children in the Wait-List group showed a decrease in theta activity at T2 compared with T1. Thus, there was a difference in activity between groups for both social and non-social condition at T2 (Figure 5.13).

Lower Alpha: Three children in the Treatment and one child in the Wait-List group had increased lower alpha activity from T1 to T2 for non-social stimuli (Figure 5.13). For social stimuli, two children in the Treatment group did not show a change in activity from T1 to T2 while the other two children showed a decrease in alpha activity at T2. Conversely, three children in the Wait-List group showed a decrease in lower alpha activity from T1 to T2 while one child showed an increase in activity (Figure 5.13).

Upper Alpha: In the upper alpha band, Wait-List participants showed greater alpha suppression compared with the Treatment group from T1 to T2 in both the conditions (Figure 5.13).
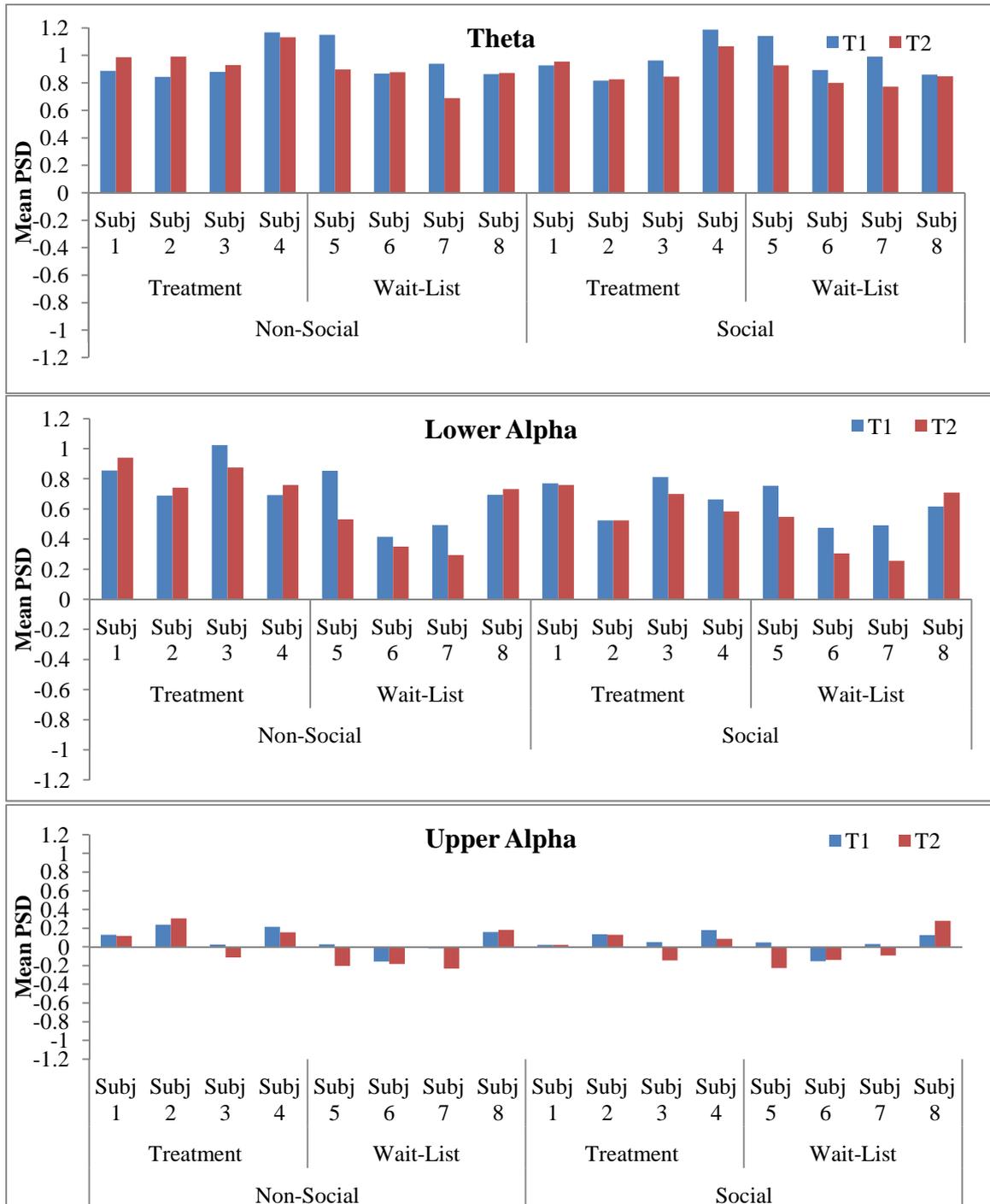
Figure 5.13: Individual participant mean PSDs for Treatment (n=4) And Wait-List Control (n=4) group for the social and non-social condition in theta, lower alpha and upper alpha bands over the OFC region

5.3.2.2.4 Dorsolateral Prefrontal Cortex (dlPFC)

<u>Theta:</u> In the non-social condition, group differences were observed where all children in the Treatment group showed an increase in activity from T1 to T2 while three children in the Wait-List group showed a decrease in activity (Figure 5.14). In the social condition three children in the Treatment group showed lower theta activity from T1 to T2 while one child showed an increase. All children in the Wait-List group showed a decrease in theta activity at T2 (Figure 5.14).

<u>Lower Alpha:</u> In the non-social condition, two children in the Treatment group showed an increase in lower alpha activity from T1 to T2 while activity did not change for one child and one child showed a decrease in lower alpha. On the other hand, three children in the Wait-List Control group showed a decrease in lower alpha activity and activity did not change for one child. For social stimuli, children in the Treatment and Wait-List group showed comparable activity - three children showed decrease in activity at T2 compared to T1 and for one child activity remained the same at T1 and T2 (Figure 5.14).

<u>Upper Alpha:</u> In the upper alpha band, for the non-social condition two children receiving RIT showed an increase in activity while one child showed greater negative activity and there was no change in upper alpha activity for one child. Conversely, in the wait-list group three children showed greater negative activity at T2 compared with T1 and one child showed an increase in activity. For social stimuli, two children in the Treatment group showed greater alpha suppression at T2 while two children did not seem to show any activity in this condition for this frequency band. On the other hand, three children in the wait-list group showed greater negative activity at T2 compared with T1 while one child showed an increase in activity.
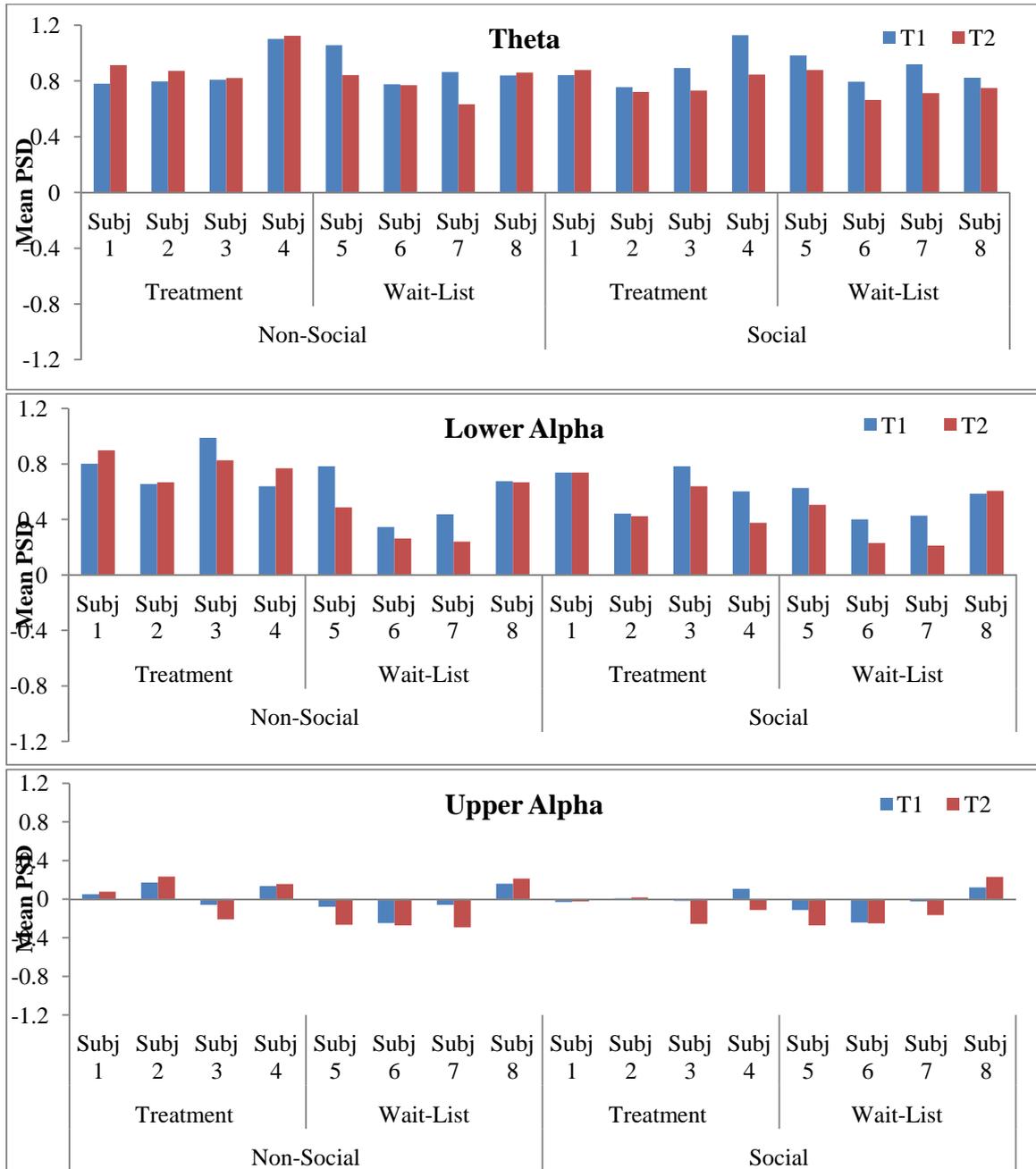
Figure 5.14: Individual participant mean PSDs for Treatment (n=4) and Wait-List Control (n=4) group for the social and non-social condition in theta, lower alpha and upper alpha bands in the dlPFC region.

Thus individual participant data suggests group differences for the non-social condition over time between the Treatment and Wait-List Control group over the central, TPJ and dlPFC.

5.3.2.3 Correlation Analysis

To examine any association between changes in imitation and EEG activity, theta, lower alpha and upper alpha activity for social and non-social condition in the four regions of Central, TPJ, OFC and dlPFC were compared with change scores on Unstructured Imitation Assessment (UIA) using Pearson correlations. Correlation was carried out only for the UIA as behavioural results (discussed in Chapter 3) revealed significant changes only in spontaneous imitation, measured on the UIA. The left and right hemispheric activity was collapsed to give mean PSD values for social and non-social condition for each frequency band and region. In order to control for error, Holm-Bonferroni sequential correction was used (Gaetano, 2013) and correlation analyses did not reveal any significant results (Appendix I).

Thus, for study 2, the results did not support the hypothesis of an impact of RIT on social processing in children with autism, as evidenced by no difference in theta, lower alpha and upper alpha activity between the Treatment and the Wait-List Control groups measured post-treatment as well as when analysed for change through treatment from T1 to T2. Further, no association was found between behavioural effects of RIT and EEG activity.

5.4 DISCUSSION

The two studies described in this chapter examined social and non-social processing in children with autism compared to typical children and whether RIT has an impact on neural responses during social and non-social stimulus processing in children with autism.

5.4.1 Study 1

The first study aimed to identify and examine potential differences in EEG activity in the theta (3-6Hz), lower alpha (7-9Hz) and upper alpha (10-13Hz) bands in children with autism and typically developing children during processing of social and non-social stimuli. It was hypothesised that greater theta activity and greater alpha suppression would be associated with social processing. The study results found greater right hemispheric power spectral density for EEG theta band during social viewing condition compared to the non-social condition, however no difference in alpha suppression was found for social and non-social conditions. It has been suggested that theta band activity may be a more sensitive measure of social processing especially during naturalistic stimuli presentations (Jones et al., 2015) and the current results support this claim. A study by Jones and colleagues found that in typically developing infants, no differences were observed for alpha activity for social versus non-social processing when stimuli were presented in a video format whereas theta frequency was modulated in both live interaction and naturalistic video viewing conditions (Jones et al., 2015). Thus, theta band may be a more sensitive measure of social processing in early childhood compared to EEG alpha band. Furthermore, in the present study, the greatest theta power was observed over the right hemisphere of the OFC region suggesting greater right hemispheric frontal theta activity in young children. In an ERP study examining human action

sound processing in toddlers, greater right lateralisation was observed over the frontal cortex in 2 to 3 year old toddlers compared to the 4 to 5 year old children for human action sound processing (Stefanidou, Ceponiene & McCleery, in review; Stefanidou, 2014). Jones and colleagues examining theta activity also found greater right than left hemispheric activity when comparing social and non-social stimulus processing (Jones et al., 2015) and Orekhova et al. (2006) found right lateralisation in the frontal channels for theta activity in typically developing infants. The present sample had sixteen children (55% of the sample) between 16 months to 36 months suggesting the possibility that the finding of right lateralisation in the theta band may have been influenced by inclusion of a greater percentage of children in the younger age group in the current study. Overall, right frontal theta activity seems to be a possible indicator of social processing in early childhood.

A second hypothesis of the study was that children with autism and typically developing children would differ significantly on theta, lower alpha and upper alpha activity during social and non-social processing. Results for the chronological age matched sample showed that there was a significant interaction between groups, stimulus type and EEG frequency bands, and, visual inspection of mean PSDs suggested that the typically developing group had greater lower alpha band activity during the non-social video condition compared with the social condition, while this pattern was reversed for children with autism with greater lower alpha band activity during the social condition. However, these mean differences did not reach significance in a follow-up analysis. Thus a complex interaction, which is not immediately apparent in the data, may be driving the group differences, and there may be other covert factors driving the significant results. As hypothesised, differences between the two groups were observed in lower alpha activity during social and non-social processing though these differences were not statistically significant. However, the social/non-social

processing differences in the current study were also observed only in the chronologically age-matched groups of TD and ASD children, while these differences were not statistically significant in the verbal age-matched sub-group. Verbal ability, therefore, could be an important factor contributing to differences observed in the chronological age-matched group comparisons. There is a very close relationship between language and social functioning, with development of non-verbal social skills aiding the development of language (Bates & Dick, 2002). It is possible that neural responses to social stimuli may vary based on language abilities and language processing may require social competence. Owing to this complex relationship, it is possible that when the two groups were matched on expressive and receptive language age, differences observed in social processing were negated. This is particularly true given that the social video stimuli utilised in the current study involved people speaking nursery rhymes. Another potential reason for group differences not being observed in the verbal age-match group could be the very small sample size in this particular analysis. Smaller sample sizes create greater error in estimations of the means (i.e., larger statistical variance), and thereby reduce statistical power to identify effects and make it more difficult to draw firm conclusions. A larger verbal age-matched sample will be crucial to determine if the findings of the current chronological age matched comparison are replicated in future studies.

Finally, the study also found greater alpha suppression in the upper alpha band of 10-13Hz over the central region and significantly greater left hemispheric activity compared to right hemispheric activity was observed in this frequency band across participant groups for both the central and OFC regions. Left lateralisation of alpha activity in the central and frontal regions in this study is in accordance with previous literature on alpha band activity (Coan & Allen, 2003a,b; Davidson, 2004; Klimesch, 2012; Stroganova & Orekhova, 2007).

Overall, the current study provides preliminary evidence for verbal ability influencing differential processing for social and non-social stimuli in typically developing and ASD children in EEG theta and alpha bands. It also provides support for theta activity in young children being modulated more during social interaction conditions.

5.4.2   Study 2

The second study aimed to examine differences in theta, lower alpha and upper alpha activity in children with autism who underwent RIT compared to children in a Wait-List Control group. No differences were observed at outcome between the two groups on any frequency band for either condition. These findings suggest that RIT may not impact EEG oscillations during general social processing in children with autism. As RIT is a focused intervention for specifically improving social imitation skills in children with autism, it is possible that RIT had an impact on neural processes associated with imitation skills only (as evidenced by results in Chapter 4) rather than broader impacts upon social processing more generally. This is supported by the existing behavioural literature, which has shown that the focus of an intervention leads to specific results whereas generalisation of skill is often a difficulty in this population (Schreibman, 2000). As RIT focused on social imitation only it is likely that other aspects of social processing and behaviour were not affected. This is also supported by the behavioural findings discussed in Chapter 3 where imitation changes were observed on the spontaneous, social imitation task only and not on elicited imitation tasks. However, previous studies of RIT have produced evidence to suggest that RIT can have significant impact on other aspects of social functioning including language and joint attention skills. Variation in the delivery of intervention between previous studies and the present RCT, for example, fewer intervention hours, may have not only impacted on

behavioural results but EEG activity also. At the same time, differences in participant characteristics and variation in autism aetiology are other factors that may help to explain differential behavioural results and also the potential impact of RIT on EEG activity during social and non-social processing. Further, very small sample size in this study might have limited power in the study to detect an effect, and therefore a higher chance of a Type 1 error suggesting null findings when actually there may have been an effect.

In order to better understand potential differences and any changes in neural activity through intervention, individual participant data at time 1 and time 2 were analysed for the Treatment and Wait-List Control groups. The results suggest some differences between groups in non-social processing reflected in activity in the theta and lower alpha bands recorded over the Central, TPJ and dlPFC regions. However, due to the small sample size it was difficult to analyse data using statistical methods and therefore, no conclusive findings could be reached. .

Overall, no consistent pattern or otherwise conclusive findings were apparent regarding changes in EEG activity associated with RIT intervention, and thus RIT may not influence social processing broadly or generally but, instead, may have a greater impact on specific processing of imitation skills.

5.4.3   Conclusions

Differences in EEG activity during social and non-social processing in the chronologically age matched sample of children with autism and typically developing children were driven by a complex interaction of condition and EEG frequency bands such that no conclusive findings were observed. Analysis of a sub-group of verbal age matched children suggested that differences might be influenced by verbal abilities. With regards to

EEG effects that were consistent across groups, neural activity differences for social versus non-social processing were observed in specific EEG frequency bands, and suggest that theta band activity may be a stronger contender for understanding social attention mechanisms in early childhood. Finally, RIT may not have an impact on the broader functioning of the social brain network more generally and may have more specific effects on imitation networks such as those reflected in the findings of Chapter 4.

5.4.4 Limitations and Future Directions

A main limitation of the current studies was small sample sizes. These restricted the use of more sophisticated analyses, and both the verbal age-matched sample and the RIT intervention versus wait-list samples had low statistical power. This makes interpretation of study results difficult, as it is highly likely that group differences were not observed in the two studies because of small number of participants in the groups. On the other hand, each of the groups in the comparisons were matched on particular key characteristics, such as age, verbal and non-verbal abilities and handedness. Thus variance from confounding factors was minimised in the current samples. However, the current studies only provide an indication of possible effects and in order to conclusively generate reliable findings, replication with larger sample sizes is warranted.

Variability in EEG power spectral density has been proposed based on age and intellectual ability. Frequency band modulation in toddlers may be different from that in the EEG activity of 4 to 6 year olds and children with average to superior intellectual functioning may be different in EEG activity compared to children with intellectual delays and deficits (Webb et al., 2015). In the current study, children with autism with both high and low intellectual functioning were included together and age varied from 16 months to 6 years.

These factors may have been confounders in the study. Challenges in recruitment and resulting sample sizes did not allow more nuanced or informative age-based analyses and therefore all children were pooled together. However, despite these limitations, the chronological age-matched sample was similar in non-verbal skills, and to control for variability in participants due to verbal ability a secondary set of analyses was conducted wherein both the ASD versus typically developing and ASD intervention versus wait-list participant groups were individually matched for verbal mental age and chronological age. This led to comparisons of well-matched samples, increasing the validity of the findings and interpretations.

An important participant characteristic that could not be controlled for as part of the study examining differences in children who underwent RIT and a wait-list control group, was gender. Although the initial sample recruited for the pilot RCT produced two groups that were comparable on male to female ratio (Chapter 3 section 3.2.1), no female participants in the Wait-List Control group produced viable EEG data. Therefore the final sample in the present study included a treatment group with significantly more number of female participants compared to the control group. It has been suggested that gender differences may be observed in EEG activity (Webb et al., 2015). However, due to the sample size, separate analyses of gender differences were not possible and female participants were included in the final sample. Conversely, even though gender differences were present between the two groups, no difference in EEG power spectral density between the Treatment and Wait-List Control group were found. Thus, variability in the sample was high on accounts of both gender and age, and small sample sizes made analyses and interpretation of results highly challenging. Studies with larger sample sizes must therefore be designed to minimise the confounding impact of chronological age and gender, in order to draw firm conclusions

regarding differences in EEG activity between children with ASD and typically developing children, and any possible impact of RIT.

Looking behaviour was not monitored directly as part of the study. Looking time was however, indexed via video recordings, and groups evidenced comparable looking time. A video camera was placed in the recording room to ensure that EEG data analysed corresponded with the child looking at the screen. However, it is possible that children with autism and control groups were looking at different aspects of the adult's face in the social videos, for example. If so, then the children with ASD may have used different neural processing mechanisms while processing social information. This being said, there was no consistent evidence for differences in social or non-social processing differences that might reflect this in the current study.

Finally, the stimuli used in the study were not well matched. The social stimuli had four different adults reading nursery rhymes to children while the non-social stimuli included shapes and objects moving around the screen creating sounds. The two stimuli were not matched on novelty, such that the non-social stimuli were not something that a child would likely observe in everyday life. Viewing time also reflected this as children in all groups had longer lengths of time viewing non-social videos compared to social videos, which suggests that these stimuli may have been more novel for them. There were also physical differences between the two types of stimuli. For example, the background used in the videos was not the same, where social stimuli were filmed against a bright white background and non-social stimuli had a black background. These and other differences in novelty and visuo-physical features could have had an impact on processing mechanisms or processing styles used by the two groups. Conversely, the stimuli are indeed different on aspect of social and non-social factors and are representative of the conditions the researcher was attempting to measure.

Thus, results in general reflect global social and non-social processing. Refined social and non-social measures could be used in the future in an effort to produce a better understanding of differences and similarities in social and non-social processing in children with autism and typically developing children. In order to improve future research, the present stimuli may be redesigned to include better matched social and non-social stimuli. For example, non-social stimuli could be produced using toys that children are familiar with such as musical toys such that novelty of stimuli is reduced. The stimuli in both conditions may also be superimposed on a black background in order to control for visuo-physical features. For social stimuli, variability in facial expressions of adults reading the nursery rhymes must be controlled. Also, different measures on social and non-social functioning to evaluate the impact of RIT may be beneficial to understand if there are other key aspects of social functioning other than imitation that the intervention has an impact on. For example, adding live interaction social and non-social conditions (interaction with a person versus interaction with toys) would produce valuable information on whether neural functioning differs in everyday interactions in autism. Also, resting-phase EEG recordings (which typically require only 2-3 minutes of viable data) will probably be helpful to include in future studies of RIT due to the ease of gathering resting EEG data from such young children as well as many previous studies showing differences in children with ASD and typically developing children on resting-state EEG.

SUMMARY & IMPLICATIONS OF CHAPTER 5

The studies presented in this chapter were designed to help produce a comprehensive picture of social versus non-social processing in autism, first by investigating differences in

processing mechanisms and then examining the effect of intervention on differences in neural processing within an autism group. Even though group differences were found in the age-matched sample, no differences were observed when children with autism and typically developing children were matched on verbal skills. RIT, also, did not appear to have an impact upon social or non-social functioning in children with autism. The study is one of the first in the field to use a naturalistic video paradigm in an effort to examine social and non-social processing differences. The present study is also the first to report data on use continuous EEG and power spectral density as a change measure to look at neural changes in children with autism who underwent RIT compared with a Wait-List Control group.

Chapter 3 focused on behavioural changes observed through RIT and Chapter 4 assessed neural correlates of the imitation changes observed in Chapter 3. The present chapter investigated if RIT could have an impact on a broader index of social processing. All three chapters examined the impact of RIT using different methodologies. Chapter 6 includes a general discussion of findings and concluding remarks.

CHAPTER 6

GENERAL DISCUSSION

6.1   INTRODUCTION

Autism Spectrum Disorder (ASD) is a developmental disorder with social-communication difficulties, and, stereotyped, repetitive behaviours and interests as the key defining features of the disorder. Symptoms are often noticeable early in life and have a lifelong impact on the quality of life of the individual. An early impairment that is known to have later implications on social, communication and cognitive functions is imitation. In Chapter 1 imitation skill impairments in children with autism were discussed. It was argued that impairments in imitation were specific to the social aspect of imitation (Section 1.1.2.2). The association between imitation skill deficits and other social-communication skills was also discussed (Section 1.1.2.2). Social imitation, defined as reciprocal imitation with a purpose of engaging socially and emotionally with a partner, was proposed as an important target skill for children with autism as well as an essential backdrop to the development of more complex social, communicative and cognitive skills.

Early interventions for children with autism were discussed in Section 1.2 Early interventions have been defined in two ways: based on the theoretical model and on the focus of intervention. Based on the various theoretical models, three approaches to early intervention in autism were described: behavioural, developmental and naturalistic developmental behavioural interventions. It was argued that naturalistic developmental behavioural model of early intervention had the most promising results in children with autism (section 1.2.1.3). Early intervention programs have also been classified based on the focus of intervention as either comprehensive or focussed, with the comprehensive programs addressing a wide range of social-communicative and adaptive skills while the focused programs target a specific skill.

As social imitation was recognised as an important early milestone for children with autism, a focused, naturalistic developmental behavioural early intervention, Reciprocal Imitation Training (RIT), was reviewed for evidence supporting its efficacy in teaching children with autism social imitation skills (section 1.2.3). It was argued that RIT has generated a growing body of research demonstrating its effectiveness for having a significant influence on imitation skills, social engagement, language, and joint attention (Ingersoll, 2010b; 2012; Ingersoll & Lalonde, 2010; Ingersoll & Schreibman, 2006). However, a major gap in RIT research was identified as a lack of replication trials in different lab settings and in the community. This had been acknowledged as a major drawback, preventing RIT from being recognised as an evidence-based intervention (Wong et al., 2015).

Behaviour is influenced by and is a product of genetic, neurological and environmental factors. Neurological research has focused on the relationship between brain and behaviour and Section 1.4 of Chapter 1 focused on neurological underpinnings for social processing in human beings. The differences in the processing of social and non-social stimuli in individuals with autism were examined and it was argued that individuals with autism show specific deficits in the 'social brain' network. Along with other kinds of social stimuli, atypical processing of human action in both the visual and auditory domains has been observed (Hamilton, 2013) and in Section 1.4.2 mirror neuron system dysfunctions in children with autism were examined and, neurological underpinnings for imitation skills dysfunctions were discussed providing greater evidence for imitation being a key skill to target in children with autism.

The studies described in this thesis were therefore conducted to fill the gaps identified in RIT research and evaluate the impact of an imitation intervention on neural correlates of imitation and global social processing (see also Figure 1.1).

6.2   AIMS OF THE THESIS

The aims of this thesis were to attempt replication of the previous findings of RIT as an effective intervention for increasing social imitation skills in children with autism, using a randomised controlled trial design, and evaluate possible neurological correlates of behavioural changes observed through RIT. Through the use of EEG and ERP as novel outcome measures, the research aimed to unravel the neural mechanisms modulated by behaviour-based early intervention focusing on social imitation. Thus, by evaluating neural responses to social stimuli in a set of children who underwent RIT, the current research aimed to broaden the approaches used to evaluate interventions as well as identify possible biomarkers for social imitation deficits in children with autism.

6.3   MAIN FINDINGS

6.3.1   Reciprocal Imitation Training Impacts Spontaneous, Social Imitation

In Chapter 3 behavioural change measures were used to investigate the effect of RIT on spontaneous, social imitation skills in children with autism. Two measures of imitation, Unstructured Imitation Assessment and Structured Imitation Assessment, were used to measure changes in spontaneous social imitation and elicited imitation respectively. A quasi-randomised controlled trial (RCT) design was used in which after stratified randomisation based on age and expressive language, children with autism were allocated to either a Treatment group or a Wait-List Control group. The Treatment group received 20 hours of RIT over a period of 12 to 14 weeks. Children were assessed for imitation skills at intake (T1) and after 12 to 14 weeks (T2).

The results showed that children with autism who received RIT had significantly higher scores on spontaneous social imitation skills than children in the Wait-List Control group. However, even though there was an increase in elicited imitation skills from T1 to T2 for the Treatment group, the difference between Wait-List Control and Treatment group was not significant. Thus the study was able to partially replicate previous results of RIT having a significant impact on imitation skills.

The study reported in Chapter 3 was the first external replication trial of RIT and provided support for RIT impacting social imitation skills in children with autism. At the same time the study provided support for naturalistic developmental behavioural interventions as being a successful model for influencing social skills, as well as increasing spontaneity in use of a skill, an area often found to be the most challenging in children with autism (Chiang & Carter, 2008). This study also set the background for further investigation of changes in social imitation skills through RIT by evaluating neural processes associated with imitation and social skills.

6.3.2 Child Characteristics Associated with Imitation Gains

A second aim of Chapter 3 was to evaluate predictors of response to treatment. In Chapter 1 section 1.2.4 it was argued that age, IQ and autism symptom severity pre-treatment, have been previously associated with gains post-treatment in different intervention models. These factors were therefore examined for associations with imitation gains through RIT. Due to small sample size sophisticated analyses were not possible. Correlation analyses revealed that gains in spontaneous, object and gesture imitation were associated with lesser difficulties in reciprocal social skills and fewer stereotyped behaviours and restricted interests (as measured on the ADOS). These results provide initial evidence of possible child

characteristics of responders to RIT. Individual patterns of change were also assessed using the Reliable Change Index to examine children who reliably changed, and therefore benefitted significantly, from RIT. Mixed profiles of children were found in the Treatment and Wait-list Control groups. However, lack of self-stimulatory, repetitive behaviours was one consistent pattern observed in the four children who changed reliably in the Treatment group

6.3.3 Reciprocal Imitation Training Impacts Neural Processing Of Human Action Sounds

In Chapter 4, using the neurophysiological method of event-related potentials (ERP), the effects of RIT on auditory human action processing were examined. Using the backdrop of the pilot quasi-RCT described in Chapter 3, children were assessed at T1 and T2 for ERP changes using a Rapid Auditory Mismatch (RAMM) paradigm (Stefanidou, Ceponiene & McCleery, in review). Outcome data were analysed for group differences at T2 while individual participant's ERP data were analysed descriptively for changes through treatment. Secondary group level analyses were also carried out to determine changes through RIT from T1 to T2.

Children in the Treatment group showed significantly different ERP responses at T2 as compared with the Wait-List Control group over the central and middle-parietal region for human action processing. Individual participant analyses also showed similar results, with the Treatment group showing greater responses to human action sounds as compared to the Wait-List Control group. Furthermore, group analysis of change through treatment was conducted for a subset of children who generated data at both T1 and T2 and similar results were obtained. Finally, correlation analyses showed an association between ERP responses post-treatment and increase in object imitation. Taken together, these results suggest a probable

impact of RIT on the central areas of brain. ERP responses over the central and middle parietal region have been linked to processing in the sensorimotor cortex (Muthukumarswamy et al., 2004; Oberman et al., 2005; Oberman et al., 2007; Pineda, 2005). The sensorimotor cortex has been implicated in imitation skills as well as during mentalizing (Pineda, 2005; Frith & Frith, 2010). Therefore, changes in neural responses over the central and mid-parietal regions are promising.

Thus, there is possible evidence of RIT influencing neural responses to action sound processing suggesting that the behavioural results obtained in Chapter 3 of social imitation gains were also reflected in neural changes in activity associated with action processing.

6.3.4 Verbal ability may modulate Social and Non-Social Processing in Autism Spectrum Disorder and Typically Developing Children

Two studies were described in Chapter 5. The first evaluated processing differences for social and non-social stimuli between children with autism and typically developing children. As discussed in Chapter 1 and Chapter 5, social processing difficulties at a neural level have been reported in children with autism, but to date no study has evaluated neural processing differences using a naturalistic audio-visual paradigm in young children with autism. Thus, the study aimed to examine differences in social (adults saying nursery rhymes) and non-social (objects moving around the screen creating associated sounds) processing in children with autism using EEG oscillation bands as measures of neural activity. Theta (3-6Hz), lower alpha (7-9Hz) and upper alpha (10-13Hz) bands were identified as EEG frequency bands of interest due to their demonstrated relationship with social attention processing (see Chapter 5 section 5.1). A subset of ASD and typically developing children was matched on verbal mental age and additional analyses were conducted to evaluate processing differences.

A complex interaction was found suggesting group differences for condition and frequency band in children with autism and chronologically age-matched controls. However, post-hoc analyses showed no clear statistical results regarding consistent or interpretable group differences. Further, when the same analyses were conducted in the verbal age-matched sample, this interaction was not significant. It was concluded that verbal ability might be a factor determining processing differences in social and non-social stimuli. Therefore, the findings suggest the importance of including language age-matched samples when comparing neural mechanisms in autism as many social processes may be modulated by language.

6.3.5   EEG Theta Frequency associated with Social Processing

Study 1 in Chapter 5 also aimed to evaluate any differences in modulation of frequency bands based on social and non-social processing. The findings revealed that in both the chronological age-matched and verbal age-matched sample, significantly greater right hemispheric theta power spectral density was observed in the social condition as compared to the non-social condition, and theta band frequency was the only frequency significantly related to social functioning. These results were consistent with previous findings of right lateralisation of EEG theta band and greater theta band activity during processing of social stimuli (Jones et al., 2015; Orekhova et al., 2006). Therefore, EEG theta band frequency may be an important marker for social processing in early childhood.

6.3.6   Reciprocal Imitation Training may not impact neural social processing

The second study described in Chapter 5 built on the pilot quasi-RCT described in Chapter 3, by evaluating the impact of RIT on more global neural processing indices of social and non-social stimuli. Using the same naturalistic paradigm as in Study 1 in Chapter 5,

children in the Treatment and Wait-List Control group were assessed for EEG theta, lower alpha and upper alpha activity while watching social and non-social videos. Outcome data were analysed at a group level at T2 while data for individual participants were analysed descriptively for changes through intervention from T1 to T2.

Both at the group and individual level, children in the Treatment and Wait-List Control groups were found to show no differences in processing of social and non-social stimuli. Secondary analyses of group data to determine change through treatment revealed differences in social and non-social processing in the Treatment group at T1. It was therefore difficult to draw any conclusions about the effect of RIT from subsequent analyses that showed differences at T2. It is possible that RIT did not have more general effects on social processing. However, due to differences between groups at T1 and small sample sizes results were difficult to interpret.

Thus in relation to the rationale described in Chapter 1, the studies in this thesis were able to generate more support for RIT as an intervention for influencing social imitation skills as well as producing initial evidence of impact of RIT on neural correlates of imitation.

6.4   LIMITATIONS

6.4.1   Limitations due to Sample Size

A limitation in all studies described in the thesis was the small sample sizes. Due to limited resources and time, final sample in the pilot quasi-RCT described in Chapter 3 included 24 children with autism. Power analysis while setting up the study revealed that a minimum number of 24 children were needed in the study for it to be sufficiently powered

(Appendix J). However, the group obtained was highly heterogeneous. This limited the interpretation of behavioural results. Having larger samples in a randomised trial are known to be advantageous as they reduce heterogeneity and thereby confounding factors that cannot be controlled otherwise. It is, therefore, important for future studies to consider recruiting larger samples to help validate the results of studies described in this thesis.

Studies using ERP and EEG methodology lacked power, as the number of children giving viable EEG/ERP data was even smaller. This greatly impacted interpretation of results as individual participant data was highly variable and consistent patterns were not observed during individual analyses. Thus, all results reported currently provide only an indication of possible impact of RIT. Further, in Chapter 5, power may have impacted study findings greatly. A null effect was obtained on both studies evaluating differences between typically developing children and children with autism, and differences between the treatment and wait-list control group. It is highly likely that these could be because of the small sample rather than a true reflection of the impact of RIT or of similar EEG activity in autism and typical development. Thus, the small number recruited made it difficult to draw conclusions from the studies described in this thesis.

6.4.2 Limitations in Delivery Model

RIT is a manualised intervention for young children with autism, with well-defined aims, fidelity protocols for therapists, as well as delivery instructions and training (Ingersoll, 2008b, 2010b, Ingersoll & Lalonde, 2010). However, there is no defined number of hours recommended for intervention to produce demonstrable effects. Previous studies of RIT have delivered 30 hours of intervention per child (Ingersoll, 2010b, 2012), whereas the present study delivered 20 hours of intervention per child. Several practical reasons prevented the

author from providing the same number of hours as previous studies. Challenges to recruitment were experienced, as early diagnosis is uncommon in the community where the study was based. Also, due to lack of comprehensive services in the West Midlands area of the UK, gaining access to the autism community was a major challenge. Although Birmingham is a base for autism NGOs, such as Autism West Midlands, most cater to older children, adolescents and adults. Therefore, it was only through word-of-mouth that most families were recruited. When the RCT was designed, hours of intervention delivery were kept consistent with previous studies, 30 hours. However, once recruited the initial few families struggled coming to the laboratory and informal feedback from parents highlighted that the commitment required for number of hours per week from families was too high. Furthermore, three families dropped out during intake assessments, stating difficulties in time commitment, and two families dropped out of the study due to the distance required to travel. Taken together, barriers in recruitment and feedback from parents compelled the author to reduce the number of intervention hours to two per week. Also, during the delivery of RIT parental involvement could not be monitored such that some parents wanted to watch the therapy delivery while some did not. This could have had possible confounding effects with some parents motivated to implement components of RIT at home while others did not. Therefore, the number of hours of RIT and behaviours reinforced as part of RIT may have differed for different children based on parent motivation.

Thus, external factors, beyond the control of researcher, could have influenced results. Previous research has shown that there is a direct link between number of hours and outcome (Granpeesheh et al., 2009). Also, a report by National Research Council, USA (2001) recommended a minimum of 25 hours of intervention (National Research Council, 2001). Therefore, the results around elicited imitation and neural social and non-social processing

may not be a comparable reflection of the impact of RIT due to the fewer intervention delivery hours in the present study. Conversely, with this knowledge it can be recommended that lower number of intervention hours may not be feasible for having broad-range effects on imitation skills and other early social skills through RIT and a minimum of 30 hours should be the recommended practice in RIT delivery until further evaluations have been completed.

At the same time, even with 20 hours of intervention children in the RIT group were able to demonstrate an increase in spontaneous, social imitation, especially object imitation, suggesting that RIT is a powerful early intervention program for producing changes in spontaneous, social imitation functioning. Fewer hours of intervention were able to produce changes generalisable to different people (blind assessor) and settings (different therapy and assessment room) suggesting that interactions involving social reciprocity, modelling, prompting and praise (during RIT sessions) can have a significant impact on imitation in a social context and help increase spontaneity in social setting.

6.4.3   Limitations of Measures Used

The studies described in this thesis utilized various behavioural and neurophysiological measures to study change through intervention. Each measure had its strengths and limitations.

In Chapter 3, two behavioural change measures were described. The Structured Imitation Assessment (SIA) was an adaptation of a standardised imitation measure, the Preschool Imitation and Praxis Scale (PIPS; Vanvuchelen et al., 2011b). As the PIPS is currently in Dutch and has only been standardised for a Dutch sample for typically developing children and ASD children, an adaptation was used. Although the measure evaluated various kinds of imitation skills, such as single bodily actions, goal-directed procedural actions,

sequential imitation and non-goal directed procedural actions, it was found to be imbalanced in the progression of complexity across items. For example, only three items were included in the sequential bodily imitation subscale and started with five-step imitation sequences (Appendix E). The complexity of tasks included in the scale may have influenced behavioural results on the scale. Also, the PIPS and subsequently the adapted SIA, was biased towards a greater number of items evaluating gestural imitation skills (See Appendix E) and therefore not a balanced measure while evaluating imitation skills holistically for children with autism where clear deficits were evident. Thus, even though the children may have gained in elicited imitation skills, owing to the complexity of the measure used gains may not have been reflected in the results. Using a concurrent elicited imitation measure with wider range of tasks may have been more appropriate for the current sample.

In Chapter 4 and 5, EEG/ERP measures were used to examine brain activity differences in children with autism. Although EEG/ERPs have very good temporal resolution, they do not have good spatial resolution (Luck, 2014). EEG/ERPs measure brain activity over the scalp making it difficult to draw conclusions regarding the area of the brain that might be producing the EEG activity. Inferences about the results obtained in the present studies were drawn from previous research, which used source localisation procedures or fMRI techniques. From the studies reported in the thesis it is difficult to draw firm conclusions regarding specific areas of the brain. Use of source localisation techniques in future studies would help identify the underlying brain areas and draw precise conclusions regarding which areas of the social brain network RIT may be influencing.

Finally, the social and non-social processing paradigm used in Chapter 5 was found to be a coarse measure of social processing. Issues with novelty of non-social videos and differences in visuo-physical features of the two videos may have influenced results.

Conversely, it has been highlighted previously that while evaluating social processing, differences in EEG activity may be observed during naturalistic interactions versus still photographs. Therefore, videos of adults reading nursery rhymes were found to reflect the natural interaction a young child may have and were used to ascertain brain activity differences. Thus, broadly the measure did capture social and non-social qualities that were of interest and at a general level was an acceptable paradigm to appraise social and non-social processing. Furthermore, experimental manipulation of participants ensured that all participants were carefully matched on various domains and all viewed the same stimuli adding to the reliability of results obtained from this paradigm.

6.4.4   Limitations due to Bias

Administration and scoring of behavioural assessments was highly well controlled. A blind assessor administered all behavioural change measures (UIA and SIA) at both T1 and T2. Blind scorers, blinded to group allocation, scored all behavioural measures. Thus, the double blinding procedure used ensured minimum bias in administration and scoring of behavioural assessments.

RIT was delivered by the author and other trained therapists. Biases associated with the involvement of the author during therapy delivery could not be controlled. The author was aware of group allocation of each child, even though other therapists were kept blind to this. The author's unintentional motivation to improve imitation skills in the children receiving RIT may have influenced results. The ERP and EEG data was cleaned by the author and other trained research assistants, blinded to treatment allocation. Due to the process of cleaning EEG/ERP data, biases in processing are highly unlikely. However, the involvement of the author in analysis may have impacted some results.

6.4.5 Limitations to Generalisability

There is substantial variability observed in ASDs in which heterogeneity is observed in symptoms and in other factors such as intelligence, genetics and gender. In order to constrain heterogeneity various exclusion criteria were employed but children were not excluded based on intellectual ability or gender (Chapter 2 section 2.2.1). Although no criteria for intellectual ability were set, most children (22 out of 24) were found to have verbal and non-verbal mental age below 29 months while having a chronological age of 29 months and above (22 out of 24 children). Thus, most of the sample was intellectually disabled and this may restrict generalisation of results at both behavioural and neural level. Furthermore, children with autism were observed to show a wide range of autism symptomatology and seven females with autism were also recruited in the present sample. Each of these factors may have influenced the results. However, due to small sample sizes of the groups recruited for the studies sophisticated analyses for any differences were not possible. Thus, it remains unclear whether results on gesture imitation, elicited imitation and social processing differences were influenced by any of the factors discussed above.

6.4.6 Lack of Follow-up

In order for an intervention to be accepted as evidence-based, long-term follow-up has been recognised as an important component in order to evaluate the long-term value of the intervention (Sullivan et al., 2014; Wallace & Rogers, 2010). Due to lack of resources and time constraints, none of the studies described in the thesis included follow-up measures. Thus, it is difficult to conclude from the present results whether the skills acquired by children in the RIT group will be maintained long-term. Although brain activity changes were observed post intervention, it is possible for focused short-term interventions to not have

lasting results and therefore addition of follow-up measures in future studies would be important.

6.5 STRENGTHS OF THE RESEARCH

6.5.1 Use of Randomised Controlled Trial Design

There are many strengths associated with the design and methods used in this thesis. As discussed in Chapter 2 although there are significant difficulties with implementing randomised controlled trials (RCT), the experimental design produces the most robust findings. In the present thesis, procedures of stratified randomisation resulted in highly comparable groups at many different levels. As the groups were randomised, the impact of confounding factors such as intellectual ability, gender and autism severity was minimised for some studies. Including blinding procedures at various levels of administration and scoring of behavioural measures ensured that results obtained were reliable.

6.5.2 Use of Neurophysiological Tools to study Intervention-related Changes

The use of neurological tools to evaluate interventions is still fairly new in the field of autism, although there is growing recognition that this is an important dimension that can be added to intervention studies (Dawson, 2008; Sullivan et al., 2014; Zwaigenbaum et al., 2015). The studies described in this thesis are some of the first in the field to utilise neurological tools to study intervention effects on brain activity in children with autism. Chapter 4 included an auditory perceptual processing paradigm and this is the first study in the field evaluating the effect of a social behaviour-based early intervention program on

auditory perceptual action processing in children with autism. The study described in Chapter 5 is the first in the field to employ a naturalistic social paradigm to understand EEG oscillation differences in children with autism.

There is growing support for EEG being an effective methodology to evaluate biomarkers for ASD (Goldani et al., 2014; Ahmadlou & Adeli, 2014). A reliable biomarker would not only help diagnose and potentially explain the disorder but also predict response to treatment (Ruggeri, Sarkans, Schumann, & Persico, 2014). Thus, the use of EEG/ERPs in intervention studies is crucial in order to understand if proposed neurological deficits in autism are impacted by behavioural intervention practices, giving reliable markers of deficits observed in ASD. The present study was able to show initial evidence that ERP responses to action processing, an area found to be impaired in autism, can be modulated by a social-communication intervention. These results also add support to the social motivation theory of autism, which suggests that early deficits in social motivation may impact imitation skills (Van Etten & Carver, 2015; Vivanti & Hamilton, 2014). The present results provide initial evidence that by increasing social reciprocity and motivation through RIT, a positive impact may be observed at a behavioural and neural level.

6.5.3 Delivery of the Intervention and the Application of Neurological Tools to a sample with co-morbid Intellectual Disability

As mentioned in Section 6.4.3 the present sample included children with autism and intellectual delays and disability. Many intervention studies, and studies evaluating neural mechanisms, exclude children with autism with intellectual disability in order to reduce heterogeneity in the sample. However, one limitation of the exclusion is that 31% - 75% individuals with autism are diagnosed with co-morbid intellectual disability (Centre for

Disease Control and Prevention, 2014; Charman, Jones, Pickles, Simonoff, et al., 2010; Fombonne, 2005). Therefore, understanding of the breadth of autism impairments as well as intervention success is limited. The studies described in this thesis produce promising results for children with autism and intellectual disability suggesting that RIT can have a significant impact in this population. The study in Chapter 3 demonstrated that RIT can have an impact at a behavioural level in this sample. The studies in Chapter 4 and 5 were able to demonstrate the successful use of EEG/ERP methodologies in this sample to evaluate brain activity differences. Thus, overall the empirical work demonstrated that RIT may be effective in improving social imitation skills in a broad sample of children with autism.

6.6   IMPLICATIONS AND FUTURE DIRECTIONS

6.6.1   Child Characteristics

Child characteristics was recognised to be an important factor influencing outcome of treatment. Previous intervention studies have also observed that not all children in the sample benefit from intervention (Howlin et al., 2009; Vivanti et al., 2014). In the studies described in this thesis, participant profiles were defined carefully and when group-level analyses were not possible, individual data were analysed descriptively. However, sophisticated analyses of participant characteristics was not possible due to the small sample size and assessments conducted only at two time points, but correlational analyses were conducted in order to identify possible associations that may account for variability in the effects of the intervention. Significant correlations between autism symptoms and intervention success were observed suggesting that certain child characteristics may limit development of skill through RIT, given the delivery model. Individual data was analysed for reliable behavioural change,

and trends were found in child profiles regarding who may benefit more from RIT. Specifically it was found that children with low self-stimulatory behaviours may be showing greater response to RIT compared with other. Additionally, EEG and ERP individual data showed that there were some children in the sample who showed different/reversal patterns over time compared to the group at large. Having knowledge of such patterns, future research must focus on more in-depth analyses of responders and non-responders, and questions regarding the impact of social communication interventions on non-social symptoms of autism such as repetitive behaviours, would be important to address in the light of present results.

6.6.2   Active Ingredients

Many interventions use similar techniques to teach a particular skill leading to considerable overlap in what the intervention looks like. Active ingredients or key teaching techniques are the procedures that facilitate teaching or the new behaviour/learning (Warren, Fey, & Yoder, 2007). Although manualised, with each key technique clearly defined in RIT, there are many components that RIT shares with other intervention approaches. For example, RIT shares the similar component of 'creating joint routines' with other NDBIs (such as ESDM, PRT and JASPER) and developmental interventions. However, the technique of contingent imitation throughout the sessions is unique to RIT. Therefore, understanding components of an intervention that may be unique to the intervention and those that might overlap may provide clues for differential success observed in early intervention practices and help in refinement of models to better target skills and functioning in children.

Additionally, Warren, Fey and Yoder (2007) argue that the time the therapists are spending focusing on the active ingredients may be a major factor differentiating success of

some interventions as compared with others as well as a reason for success of intervention in some studies and not others (Warren, Fey & Yoder, 2007). This highlights the role of the therapist in delivery of intervention. Therapist-based factors, such as previous training and experience, knowledge in the field, interpersonal characteristics (e.g. timing sensitivity) and personal characteristics (such as creativity), may play an important role during delivery of the intervention (Elliott, 2015). Future research therefore must focus on evaluating techniques as well as therapist factors associated with the delivery of an intervention in order to improve treatment effectiveness.

6.6.3   Moving towards Biomarkers for Autism Spectrum Disorders

A key aim of the empirical work was to evaluate neural functioning in children with autism to explore neurological correlates of behaviour change. There is greater effort in the field to move towards reliable biomarkers in order to screen and diagnose autism early in life. The present screening and diagnostic procedures rely on parental report solely and behavioural observations made by the clinician (Camarata, 2014). Furthermore, even though sensitivity in screening and diagnosing children as young as two years may be high, specificity of symptoms observed for autism has been poor (Camarata, 2014). Therefore, biological signatures of autism early in life could prove important, as reliable and valid instruments that inform diagnosis (Dawson, 2008). The studies described in Chapter 4 and 5 used EEG and ERP techniques and social paradigms to understand differences in autism and the impact of intervention. EEG theta and alpha oscillations and time-course analyses using ERPs suggested differential processing between groups. Overall, these findings add to the growing body of support for EEG generating reliable markers differentiating processing styles and intervention changes. Furthermore, low costs, ease of application to various populations,

portability and non-invasive nature, all make it a compelling tool for use in diagnostic protocols.

However, there are many gaps in the EEG literature making it difficult for use as a diagnostic measure. In order to be clinically useful, a biomarker must be consistently observed in the population showing pathology and should be able to reliably distinguish the population from typical controls. Further, developmentally the biomarker must be observable throughout development. At present, understanding of biomarkers for pathological populations is compromised because of lack of reliable developmental models in typical population. EEG studies do not yet have stable developmental models of changes in EEG and ERP activity across age groups. There is conflicting evidence regarding EEG oscillation rhythms for which theta and alpha bands are yet to be defined reliably at younger ages (Stroganova & Orekhova, 2007). Thus, future studies of EEG techniques could focus on creating developmental models of EEG activity to better understand developmental changes in EEG oscillations. Also, currently there is limited knowledge about how different types of EEG measurements (ERP, quantitative EEG etc.) contribute to understanding of similar cortical areas and phenomena. Thus, future studies need to focus on potential contributions of different EEG methods evaluating the same behaviour as well as understand activation of similar brain areas in order to have reliable models of brain activity across neurophysiological tools.

6.6.4   Use of Different Study Designs, Larger Samples and Other Measures

Limitations in the studies described in the thesis included small samples and lack of a range of measures. The use of a large sample, which ensures truly random assignment of participants, and the use of other measures of evaluation are highly recommended for future

studies. Having larger samples will aid in better interpretation of results, and is therefore the most important next step for RIT studies. Dyspraxia was not assessed in the current study, and praxis issues are associated with imitation difficulties and ASD population (MacNeil & Mostofsky, 2012; Bodison, 2015). Including measures of dyspraxia will be important in studying effect of imitation interventions to understand pathways that the intervention may be impacting, that is, motor or social. Including a broader range of imitation measures has also been discussed previously. EEG measures that are not task-based would be beneficial to include in future studies. They are easy to collect data on, and have a higher likelihood of translation to practice rather than task-based neurological methods. The use of creative designs (such as Sequential Multiple Assignment Randomised Trial, SMART) would be more constructive in answering fine-grained questions such as responders versus non-responders, effect of RIT alone versus effect of RIT and another focused intervention, etc. Sequential designs also help in evaluating intervention techniques, and would be recommended for use in future trials.

6.6.5   Reciprocal Imitation Training as a Potential Community Intervention

The studies reported in this thesis focused on RIT delivered in a laboratory setting. Using multiple baseline designs a few previous studies have translated the delivery of RIT to community setting involving siblings (Walton & Ingersoll, 2012) and parents (Ingersoll & Gergans, 2007; Wainer & Ingersoll, 2013a; Wainer & Ingersoll, 2015). However, like most interventions for autism, systematic trials of effectiveness are lacking. As results have been consistently positive, suggesting RIT has a significant impact on children with autism, future studies should focus on effectiveness trials examining translation of RIT into community setting. Most often therapist training and delivery styles are more fluid in community settings

(Kasari, 2002) and therefore translating RIT for community clinicians may need additional training in order to amalgamate RIT-specific techniques with other interventions. Thus, translation into community settings would require additional refinement, and is a possible next step in RIT research.

6.7   CONCLUDING REMARKS

A pilot quasi-Randomised Controlled Trial was conducted to evaluate the effects of Reciprocal Imitation Training (RIT) on behaviour and brain activity of children with autism. In this way evidence was generated for possible impact of RIT on social imitation skills. The strength of the evidence generated comes from both behavioural and neurological data suggesting a probable impact of RIT on social imitation skills at multiple levels. Although the impact of RIT on broader social functioning remains questionable, the studies were able to demonstrate that RIT can have an impact on spontaneous functioning and possibly neural mechanisms of imitation. Therefore, through the use of a rigorous experimental design, a replication trial examining neural correlates of behavioural changes was successfully undertaken and has generated some evidence for RIT as an early intervention for children with autism.

APPENDIX A

ETHICS APPROVAL & PROTOCOLS

A.1: ETHICS APPROVAL BY ETHICAL REVIEW COMMITTEE, UNIVERSITY OF BIRMINGHAM
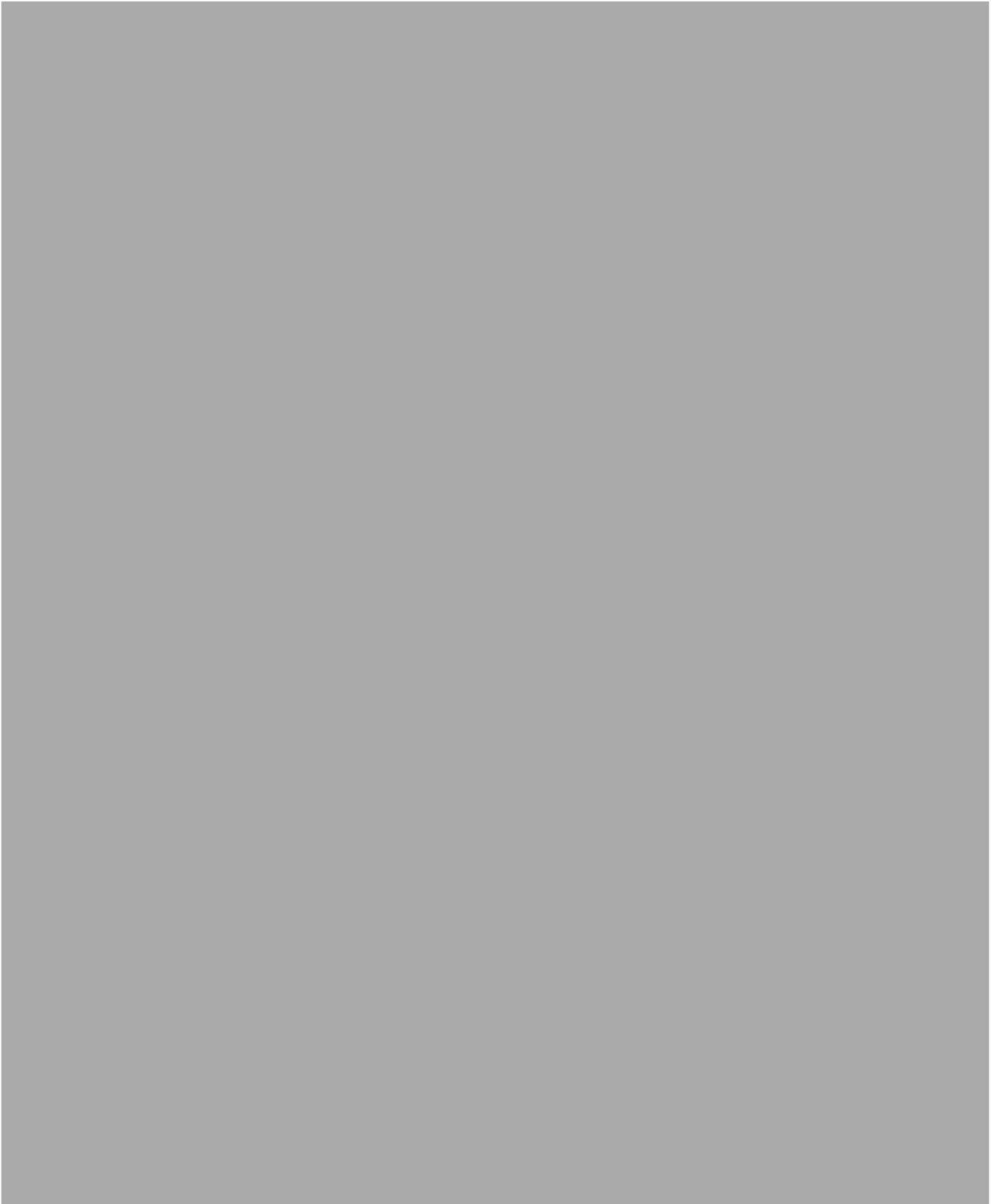
A.2: ETHICAL CONSIDERATIONS

A.2.1. Sources of Materials

Sample population for the current study included two to six year old children with autism spectrum disorders. As the sample population involved very young children with autism, informed consent was obtained from a primary caregiver. Specifically, parents/caregivers were asked to sign a study consent form (Appendix B.1.) describing the details of the study including travel compensation, along with a separate video consent form (Appendix B.3.) to gain consent for recording all assessment and treatment sessions, both approved by the Internal Review Board at the University of Birmingham. Only when consent forms were signed by a primary caregiver, was the child enrolled onto the study database and assessed at T1.

All consent forms, developmental histories, and study data (behavioural, parent interview, brain activity and treatment session videos) were stored on password-protected computers or a locked cabinet in the locked laboratory of the Cerebra Centre for Neurodevelopmental Disorders, based in the School of Psychology at the University of Birmingham. Only the principal investigators and research assistants working directly on the project had access to this data. All participants were given unique identification numbers which were used on all collected data including video files and EEG/ERP data. As the study involved a large number of postgraduate and undergraduate students working with children in different capacities, all were asked to first submit approved Disclosure and Barring Services (DBS) checks before coming into contact with any research participant or data. All were also required to review the Society for Research in Child Development's Ethical Standards of Research with Children, as well as study-specific ethical procedures outlined in the initial study proposal. Participant

histories and information were protected whereby only the particular, limited information necessary for the therapist or research assistant knowledge was disclosed.

No participant individual identification has been/will be used in the PhD or in any future publications. Parents/caregivers of children who participated in the study will be provided with copies of all official publications from this research.

A.2.2. Protection Against Risks

Potential risks to children were minimised by ensuring good lab conditions, regular safety checks, and by using child-friendly materials and techniques. Parents/caregivers were made aware that they could withdraw from the study at any time and this would have no adverse repercussions for the family or child. At any point during test administration or treatment if the experimenter saw extreme child distress the testing/therapy session was discontinued. Special care was taken when working with children with challenging behaviours. During test administration a parent/caregiver was always present in the room and during intervention the parent/caregiver was asked to watch the treatment sessions from a video recording room. All therapists were trained in behavioural management techniques by the researcher in order to minimise child distress in treatment sessions and effectively work with each child. Child safety procedures were also discussed with every therapist as part of their training, and toys used in the sessions were chosen based on age and safety standards.

During EEG recordings, the utmost care was taken to make the experience a pleasant one for the child and the family. However, some children did not like the sensor net placed on their head or to have a stranger touch their head. There were various priming and behavioural desensitisation procedures that were set in place to help familiarise the child with both the net and the experimenter, which were included in the review and approval of the University

ethics board. The EEG recordings were always scheduled post behavioural testing to ensure that some rapport was established between the child and the experimenters. In addition, the researcher played with a variety of hats with the child including encouraging him/her to wear the hat in a playroom prior to the EEG testing. As soon as the child became comfortable with the process, the EEG Sensor Net was introduced in a child-friendly manner. Many sensory and music toys were also used during net application, in an effort to distract the child from the net application and keep them engaged and happy. If at any point the testing caused significant distress to the child, testing was discontinued. Some families were invited for up to three EEG recording sessions in an effort to help to slowly desensitise the child to the EEG setting and net application.

A.2.3. Potential Benefits of the Proposed Research

The proposed study had potential for direct benefits to all of the participating children with autism, as every child in the research received treatment. However, it was clarified at the outset that they were agreeing to participate in a research study where the effects of treatment were in question. Therefore, parents/caregivers were informed clearly that the researcher or the therapists could not guarantee child gains or improvements, and that participation in the study would produce data that had potential to inform and improve services for future ASD population. Typically developing control participants in the EEG study had no direct benefits.

APPENDIX B

INFORMED CONSENT FORMS

B.1: INFORMED CONSENT FORM FOR CHILDREN WITH AUTISM PARTICIPATING IN THE PILOT RANDOMISED CONTROLLED TRIAL EXAMINING EFFECTIVENESS OF RECIPROCAL IMITATION TRAINING.

**University of Birmingham Infant and Child Laboratory Research Study
"Effects of Imitation Training on Brain Activity in Children with Autism or Suspected Autism"**

Why is this research study being conducted? What is its purpose?

The purpose of this study is to determine whether or not gesture imitation training has an effect on the brain activity of young children with autism as they process videos and sounds made by people (e.g., hand clapping) versus videos and sounds made by things (e.g., helicopter). We will also measure the children's imitation skills and other abilities.

Who is conducting this research study, and where is it being conducted?

Prof. Chris Oliver, ClinPsychol, PhD; Joseph McCleery, PhD; Supriya Malik, MSc; and their colleagues, are conducting this study in the University of Birmingham Infant and Child Laboratory.

How are individuals selected for this research study? How many will participate?

You are being asked to participate because your child is between the ages of 2- and 6-years and has been diagnosed with Autistic Disorder, Asperger's Syndrome, or Pervasive Developmental Disorder – Not Otherwise Specified (PDD – NOS), or is currently being evaluated for one of these disorders or syndromes. There will be approximately 30 participants in this study.

What do I have to do if I am in this research study?

If you agree to participate in this study, you will be asked to bring your child to our laboratory approximately 2 times per week for approximately 14 weeks, and the following will happen:

Pre-Training Assessment Visits (3 Visits, 1.5 Weeks):
Behavioral assessments (two 1.5-hour visits): We will administer behavioural assessments of your child's developmental and language abilities, his/her communication and social skills, as well as his/her imitation skills. . These will include

the Mullen Scales of Early Learning, which measures cognitive/motor developmental level in five areas: gross motor, fine motor, visual reception, receptive language, and expressive language. We will also administer the Autism Diagnostic Observation Schedule (ADOS), which measures your child's social and communication skills. Finally, we will administer two brief assessments of your child's imitation skills. During your child's behavioural assessments, you will be also asked to complete simple, short questionnaires that include questions related to your child's social and communication skills.

Electrophysiological Assessments (one 1-hour visit): We will measure your child's brain activity using a sensor net that has electrodes sewn into it. The electrodes measure the electricity that your child's brain generates. The electrodes will not hurt. We will place the net on your child's head, and squirt a salt-water solution onto sponges that touch your child's head. The salt-water solution is not toxic or dangerous. Your child will sit next to you or on your lap in a quiet, dimly lit room while she or he watches a silent video while sounds made by people and sounds made by things are played in the background. We will also show your child short videos of people talking to him or her, and of things moving around and making bouncing and other sounds.

<u>***Training Visits (20 Visits, 10 to 12 Weeks):***</u>
Imitation Training: You will be asked to bring your child to our laboratory for two to three 1-hour visits per week and your child will be filmed interacting with an experimenter for 20-minutes across three sessions (1 hour in total per visit). Your child's participation in the training will take between approximately 10 and 12 weeks.

<u>***Post-Training Assessment Visits (1 Visits):***</u>
Electrophysiological and Behavioural Assessments: After the training is completed, you will be asked to bring your child to the laboratory for one 2-hour visit, in order to complete the post-training EEG assessments (1 hour) as well as the brief behavioural assessments of imitation skills. These are the same assessments described above.
As part of this project, video recordings and/or photographs will be taken of your child and/or you during your participation in the research. This is completely voluntary and up to you. In any use of these images, your name will not be identified. You may request to stop taping at any time and review any or all portions. All video recordings are kept on password protected computers and / or in a locked cabinet in the lab, and they are identified by the participants' ID numbers. A separate consent form related to the use of recorded images will be also given to you to sign. You may request to have your child's data and/or video recordings removed from the study at any time.

Are there any risks associated with participating in this study?

There are no known risks associated with the brainwave recordings. However, your child may not be interested in watching the video and listening to the sounds or they may get tired or bored during the behavioural assessments. Your child also may not

like to have people put things on her/his head. You are free to withdraw from the study at any time, including if your child becomes upset or unhappy.

Your child may also become bored during one or more of the training sessions. The training sessions also sometimes involve the experimenter gently physically prompting your child to imitate her or his actions, which may result in mild frustration in some children. The experiments are aware of this, and they will use positive behaviour management procedures in an effort to reduce any frustration that your child may experience. You are encouraged to communicate with the experimenters, including Dr. McCleery, at any time during or after your participation about these things. You are also free to withdraw from the study at any time, including if your child becomes upset or unhappy.

What are the benefits of this research study?

There may not be any direct benefit to you or your child from participating in this study. Although previous research suggests that the training procedures utilised in this study is effective for teaching some children new imitation skills, you should know that not all children learn new skills as a result of the training procedures.

You should also know that this is a research laboratory and that the researchers are not clinical psychologists. Therefore, we will not be able to provide you with a diagnosis in the case that your child does show signs or symptoms of autism or another disorder based on the results of the assessments. Despite this limitation, at your request, we will provide you with a brief report that includes your child's scores on the assessments and general guidelines for interpreting these scores. You are free to share with clinicians and service providers in an effort to provide them with information that may assist her or him in determining whether or not your child warrants further assessments.

You should know that the EEG procedure is not the same as your child might receive in a hospital, and that the experimenters are not trained to interpret EEGs in the way clinical technicians are. Therefore, we will not have information about any implications of the test for your child's health.

If you are concerned about your child's development, other services are available. These include clinical and educational assessment and treatment services through the National Health Service (NHS). Please remember that we are not a clinic; we are a basic research facility.

Participation in this research is entirely voluntary. You may refuse to participate or withdraw at any time. Also, if we perceive that your child is getting upset, the study may be discontinued.

What will happen with the information obtained as part of this research study?

The records of this study will be kept private. Your child's name and the other personal details you provide will be stored. However, research data will only be identified by participant number. Computer files will be stored on password-secured computers in the School of Psychology at the University of Birmingham. Paper copies as well as copies of videotaped assessment and training sessions will be stored in locked filing cabinets in the Infant and Child Laboratory and/or in the office of Dr. McCleery. Only researchers directly involved in this study will have access to the information collected. In any sort of study we might publish, we will not include any information that will make it possible to identify a participant. Research data obtained from this study will be held indefinitely for use in potential follow up publications as well as in other associated studies.

Will I receive any payments?

You will be paid £8.00 per visit for each of the visits for your child's participation in this study, to help with the costs of travelling to the laboratory. These £8.00 payments will be provided to you each time you visit the laboratory. The researcher will arrange for free parking in front of the laboratory during your visit. Your child will also receive a small toy for his/her participation in the study.

Agreement to Participate

I have been satisfactorily informed of the above-described procedures with its possible risks and benefits. I understand that participation in this study is voluntary. If I refuse to participate or choose to drop out of the study at any time, I understand there will be no penalty, and that this decision will not affect my relationship with the University of Birmingham. I am signing this consent form before participating in any research activities. I give permission for my/my child's participation in this study.

_____   _____

Date   Name of Child

_____   _____

Name of Parent or Guardian   Signature of Parent or Guardian

_____   _____

Name of Researcher/Witness   Signature of Researcher/Witness

B.2: INFORMED CONSENT FORM FOR TYPICALLY DEVELOPING CHILDREN

PARTICIPATING IN STUDY 1 DESCRIBED IN CHAPTER 5.

University of Birmingham Infant and Child Laboratory Research Study
"Children's Brain Processing of Sounds" – Consent for Control Child

Why is this research study being conducted? What is its purpose?

The purpose of this study is to help us understand how normal children process sounds made by people (e.g., hand clapping) and sounds made by things (e.g., helicopter). Your child will be a control participant for children diagnosed with autism and other developmental disorders.

Who is conducting this research study, and where is it being conducted?

Prof. Chris Oliver, PhD, CPsychol.,Joseph McCleery, PhD, Supriya Malik, MSc, and their colleagues, are conducting this study in the University of Birmingham Infant and Child Laboratory.

How are individuals selected for this research study? How many will participate?

You are being asked for your child to participate in this study because she or he is developing normally and is between 2-months and 6-years old. There will be approximately 100 participants in this study.

What do I have to do if I am in this research study?

If you agree to participate in this study, you will be asked to bring your child to our laboratory for 2 visits over the course of a five week period and the following will happen:

Electrophysiological assessment (one 1-hour visit): We will measure your child's brain activity using a sensor net that has electrodes sewn into it. The electrodes measure the electricity that your child's brain generates. The electrodes will not hurt. We will place the net on your child's head, and squirt a salt-water solution onto sponges that touch your child's head. The salt-water solution is not toxic or dangerous. Your child will sit next to you or on your lap in a quiet, dimly lit room while she or he watches a silent video while sounds made by people and sounds made by things are played in the background.

Behavioural assessments (one 1-hour visit): We will administer behavioural assessments of your child's developmental and language abilities. These will be

videotaped, so that the experimenter can re-examine the child's responses, and they will include tasks, such as naming objects in pictures, using coloured blocks to create patterns and answering simple questions. During your child's behavioural assessment, you will be also asked to complete a simple, short questionnaire, which will be related to your child's social and communication skills.

As part of this project, a video recording and/or photograph will be taken of your child and/or you during your participation in this research project. This is completely voluntary and up to you. In any use of these images, your name will not be identified. You may request to stop taping at any time and review any or all portions. All video recordings are kept on password protected computers and / or in a locked cabinet in the lab, and they are identified by the participants' ID numbers. A separate consent form related to the use of recorded images will be also given to you to sign.

Are there any risks associated with participating in this study?

There are no known risks associated with the brainwave recordings. However, your child may not be interested in watching the video and listening to the sounds or they may get tired or bored during the behavioural assessments. Your child also may not like to have people put things on her/his head. You are free to withdraw from the study at any time, including if your child becomes upset or unhappy.

What are the benefits of this research study?

There will not be any benefit to your child from participating in this study. You should know that the EEG procedure is not the same as your child might receive in a hospital, and that the experimenters are not trained to interpret EEGs in the way clinical technicians are. Therefore, we will not have information about any implications of the test for your child's health. The investigators, however, will learn more about how children process sounds made by people and sounds made by objects.

What will happen with the information obtained as part of this research study?

The records of this study will be kept private. Your child's name and the other personal details you provide will be stored. However, research data will only be identified by participant number. Computer files will be stored on password-secured computers in the School of Psychology at the University of Birmingham. Paper copies will be stored in locked filing cabinets in the Infant and Child Laboratory and/or in the office of Dr. McCleery. Only researchers directly involved in this study will have access to the information collected. In any sort of study we might publish, we will not include any information that will make it possible to identify a participant. Research data obtained from this study will be held indefinitely for use in potential follow up publications as well as in other associated studies.

Will I receive any payments?

You will be paid **£10.00**for your child's participation in this study, to help with the costs of traveling to the laboratory. Your child will also receive a small toy for his/her participation in the study. The researcher will arrange for free parking in front of the laboratory during your visit.

Agreement to Participate

I have been satisfactorily informed of the above-described procedures with its possible risks and benefits. I understand that participation in this study is voluntary. If I refuse to participate or choose to drop out of the study at any time, I understand there will be no penalty, and that this decision will not affect my relationship with the University of Birmingham. I am signing this consent form before participating in any research activities. I give permission for my/my child's participation in this study.

_____   _____
Date   Name of Child

_____   _____
Name of Parent or Guardian   Signature of Parent or Guardian

_____   _____
Name of Researcher/Witness   Signature of Researcher/Witness

B.3: VIDEO CONSENT FORM

<u>University of Birmingham, School of Psychology</u>

<u>Image and Video Release Consent Form</u>

As part of this project, a video recording and/or photograph will be taken of your child and/or you during your participation in this research project. Please indicate below the uses of these recorded images to which you are willing to consent. This is completely voluntary and up to you. In any use of these images, your name will not be identified. You may request to stop taping at any time and review any or all portions. All video recordings are kept on password protected computers and / or in a locked cabinet in the lab, and they are identified by the participants' ID numbers.

1. The research team may record images to be used in the study. _____
   Initials

2. The images may be posted on the researcher's website. _____
   Initials

3. The images may be shown to participants in other experiments. _____
   Initials

4. The images may be used for scientific publications. _____
   Initials

5. The images may be shown at scientific meetings or conferences. _____
   Initials

6. The images may be shown in classrooms to students. _____
   Initials

7. The images may be shown in public presentations to non-scientific groups.
   _____
   Initials

8. The images/recordings may be used on television and radio. _____
   Initials

9. The images/recordings may be shown to experienced professionals from other academic / research institutes for training purposes, which may include the mailing of images/recordings through the postal service.

   _____
   Initials

You have the right to request that taping be stopped or erased at any time.

You have read the above description and give your consent for the use of recorded images as indicated above.

_____   _____
Signature   Date   Witness   Date

APPENDIX C

QUESTIONNAIRES FOR PARENTS

C1: QUESTIONNAIRE FOR PARENTS OF CHILDREN WITH AUTISM.

<u>**Questionnaire for parents**</u>   **I.D. _____ (for office use)**

Thank you very much for agreeing to take part in our study in the Infant and Child Laboratory. We would appreciate if you could complete the following questions carefully. Your answers are strictly confidential, so please be honest in responding.

1. **Please indicate your child's day, month and year of birth? _____**

2. **Please indicate the gender of your child:**

   male ☐   female ☐

3. **Did you experience any birth complications?**

   _____

4. **Please indicate your child's formal diagnosis:**

   Autistic Disorder ☐   Asperger's Disorder ☐

   Pervasive Developmental Disorder - Not Otherwise Specified ☐

   If other, please indicate: _____

5. **Has your child experienced any other neurological problems (e.g. epilepsy)?**

   Yes ☐   No ☐

   If yes, please indicate: _____

6. **Has your child experienced any medical problems?**

   _____

7. **Has your child experienced any primary sensory impairments (e.g. hearing problems)**

   _____

8. **Is your child taking any medication? (please tick)**

   Yes ☐   No ☐

   If yes, please indicate: _____

9. **Is your child bilingual? (please tick)**   Yes ☐   No ☐

C2: QUESTIONNAIRE FOR PARENTS OF TYPICALLY DEVELOPING CHILDREN.

<u>Questionnaire for parents</u>   **I.D. _____ (for office use)**

Thank you very much for agreeing to take part in our study in the Infant and Child Laboratory. We would appreciate if you could complete the following questions carefully. Your answers are strictly confidential, so please be completely honest in responding.

1. **Please indicate your child's day, month and year of birth? _____**

2. **Please indicate the gender of your child:**

   male ☐   female ☐

3. **Did you experience any birth complications?**
   _____

4. **Has your child experienced any medical problems?**
   _____

5. **Has your child experienced any developmental delays? (physical or neurological)**
   _____

6. **Has your child experienced any primary sensory impairments (e.g. hearing problems)**
   _____

7. **Is there any history of developmental (e.g.Autism), neurological (e.g. epilepsy) or severe psychiatric (e.g. schizophrenia) disorders in your family?**

   Yes ☐   No ☐

If yes, please indicate: _____

8. **Is your child taking any medication? (please tick)**

   Yes ☐   No ☐

   If yes, please indicate: _____

9. **Is your child bilingual? (please tick)**   Yes ☐   No ☐

C3: BIOLOGICAL HISTORY QUESTIONNAIRE FOR PARTICIPANT.

Enrolled Participant's History

Name of Participant Enrolled in Study: _____

Child's DOB: _____

Today's Date: _____

1. What language(s) is/are spoken in this child's home?
   _____

   If exposed to language(s)other than English, how many hours per week?
   _____

2. How would you describe this sibling's ethnicity?

   White/Caucasian Black/Black British Asian/Asian British Chinese
        Mixed

   Other_____(please specify)

3. Does your baby have a diagnosed disorder of any kind?

     If so, what is the diagnosis?

     When was the diagnosis given?

     Who provided the diagnosis?

4. In the chart below, please list all the organised daycare/playgroups/schools that your child has been involved in, including location and dates of enrolment:

Daycare/Group/School	Location	Month/Year Begun	Month/Year Ended

5. Please indicate which, if any, of the following your child has experienced or been diagnosed with. Circle either yes, no, or I don't know (D/K):

Birth Trauma   YES   NO   D/K

Birth Asphyxia   YES   NO   D/K

PKU   YES   NO   D/K

Congenital Rubella   YES   NO   D/K

Neurofibromatosis (NF1 or 2)   YES   NO   D/K

Tuberous Sclerosis   YES   NO   D/K

Fragile X Syndrome   YES   NO   D/K

Other Chromosomal Abnormality   YES   NO   D/K

                                                                What? _____

Metabolic Disorder   YES   NO   D/K

                                                                What? _____

Progressive Neurological Disorder   YES   NO   D/K

                                                                What? _____

Visual Developmental Delay, e.g. blindness YES   NO   D/K

                                                                What? _____

Auditory Developmental Delay, e.g. deafness YES NO   D/K

                                                                What? _____

Motor Developmental Delay   YES   NO   D/K

                                                                What? _____

6. Has your child received childhood vaccinations?   YES   NO

6a. If yes, did these vaccinations include the MMR vaccine? YES   NO

7. Did your child have any abnormal reaction to a vaccination?   YES   NO

7a. If yes, please describe this reaction and any medical attention received:

   _____

   _____

8. Does your child have a history of gastrointestinal problems?   YES
      NO

8a. If yes, please describe problems, and WHEN they began: _____

9. Did you breastfeed this child at all?   YES   NO

   If YES:

9a. For how long did you only breastfeed? (no formula) _____

9b. At any point, did you supplement breastmilk with formula?   YES
   NO

If yes, how often and how much? _____

If yes, what brand of formula was used? _____

9c. At what age, if ever, did you fully shift from breastfeeding to using formula? (in months) _____

If NO:
   9d. What brand of formula did you use? _____

10. Do you have any current concerns about your child's development (including colds, ear infections, or common health concerns)? If so, please describe in detail below.

_____
_____
_____

Thank you for your support and participation!

C4: BIOLOGICAL HISTORY QUESTIONNAIRE FOR PARTICIPANT'S MOTHER.

Biological History Questionnaires

Biological Parent's History
Please circle one answer for each item

BIOLOGICAL MOTHER
Your Name: _____

Your DOB: _____ Today's date: _____

Baby enrolled in this study: _____ Baby's DOB: _____

1. Please indicate the highest level of education you have completed:

   GCSE's   A-Levels   Bachelor's   Master's   Doctorate

   Other_____

2. In the chart below, please list all past and current occupations, starting/ending dates, and locations:

Occupation title	Location (City)	Month/Year Begun	Month/Year Ended

3. What is your primary (first) language?
   _____

   What language(s) is/are spoken in your home?
   _____

4. How would you describe your ethnicity?

White/Caucasian   Black/Black British   Asian/Asian British   Chinese
            Mixed

Other_____(please specify)

5. How would you rate your school achievement as a child (through year 9)?

a. Arithmetic: Impaired   Below Average   Average   Above Average
            Superior

b. Writing/composition: Impaired   Below Average   Average
                    Above Average   Superior

c. Reading: Impaired   Below Average   Average   Above Average
            Superior

6. Were you ever in a remedial class or did you ever receive special help with academic
    problems in the following subjects?

a. Arithmetic: Yes   No
b. Writing: Yes   No
c. Reading: Yes   No

7. Were you kept back a year in school?   Yes   No

    If yes, which year? _____

8. Did you ever fail a class or subject?   Yes   No

    If yes, was it because of poor performance in: (circle all that apply)

                    Reading   In what grades? _____

                    Writing   In what grades? _____

                    Arithmetic   In what grades? _____

                    Other (specify)   _____
                    In what grades? _____

9. How would you rate your language development when you were a child?

Impaired   Below Average   Average   Above Average   Superior

10. Did you receive speech and/or language therapy?   Yes   No

   If yes, what speech and/or language problems were treated? _____

   For how long? _____

11. Did your mother have a speech, language, or reading problem?   Yes   No
   Don't know

   If yes, what was the nature of the problem? _____

12. Did your father have a speech, language, or reading problem?   Yes   No
   Don't know

   If yes, what was the nature of the problem? _____

13. How many sisters do you have? _____

14. How many sisters have had difficulty with language, reading, or spelling?
   _____

15. How many brothers do you have? _____

16. How many brothers have had difficulty with language, reading or spelling?
   _____

17. To your knowledge, do any family members on your side have diagnoses of autism,
   language disorders, or other developmental delays?
   _____

18. To your knowledge, do any family members on your side have diagnoses of anxiety,
   depression, schizophrenia, or another psychiatric disorder?
   _____

If yes, please list the problem and the relationship of each person to YOU. Please exclude family members with whom you are only related through marriage. For relatives that can be on either the maternal or paternal side (e.g. an aunt), please specify. (If you listed any above, you need not repeat them here.)

Problem: _____

Relationship:_____

Problem: _____

Relationship:_____

Problem: _____

Relationship:_____

C5: BIOLOGICAL HISTORY QUESTIONNAIRE FOR PARTICIPANT'S FATHER.

Biological Parent's History
Please circle one answer for each item

BIOLOGICAL FATHER:
Your Name: _____

Your DOB: _____ Today's date: _____

Baby enrolled in this study: _____
Baby's DOB:_____

19. Please indicate the highest level of education you have completed:

GCSE's   A-Levels   Bachelor's   Master's   Doctorate

Other_____

20. In the chart below, please list all past and current occupations, starting/ending dates, and locations:

Occupation title	Location (City)	Month/Year Begun	Month/Year Ended

21. What is your primary (first) language?
    _____

    What language(s) is/are spoken in your home?
    _____

22. How would you describe your ethnicity?

White/Caucasian   Black/Black British   Asian/Asian British   Chinese
                Mixed

Other_____(please specify)

23. How would you rate your school achievement as a child (through year 9)?

a. Arithmetic: Impaired   Below Average   Average

                           Above Average   Superior

b. Writing/composition: Impaired   Below Average   Average

                           Above Average   Superior

c. Reading: Impaired   Below Average   Average

                           Above Average   Superior

24. Were you ever in a remedial class or did you ever receive special help with academic
    problems in the following subjects?

a. Arithmetic: Yes   No
b. Writing: Yes   No
c. Reading: Yes   No

25. Were you kept back a year in school?   Yes   No

    If yes, which year? _____

26. Did you ever fail a class or subject?   Yes   No

    If yes, was it because of poor performance in: (circle all that apply)
                Reading   In what grades? _____

                Writing   In what grades? _____

                Arithmetic   In what grades? _____

                Other (specify)   _____
                In what grades? _____

27. How would you rate your language development when you were a child?

    Impaired   Below Average   Average   Above Average   Superior

28. Did you receive speech and/or language therapy?   Yes   No

        If yes, what speech and/or language problems were treated? _____

        For how long? _____

29. Did your mother have a speech, language, or reading problem?   Yes   No
        Don't know

        If yes, what was the nature of the problem? _____

30. Did your father have a speech, language, or reading problem?   Yes   No
        Don't know

        If yes, what was the nature of the problem? _____

31. How many sisters do you have? _____

32. How many sisters have had difficulty with language, reading, or spelling?
    _____

33. How many brothers do you have? _____

34. How many brothers have had difficulty with language, reading or spelling?
    _____

35. To your knowledge, do any family members on your side have diagnoses of autism,
    language disorders, or other developmental delays? _____

36. To your knowledge, do any family members on your side have diagnoses of anxiety,
    depression, schizophrenia, or another psychiatric disorder?
        _____

If yes, please list the problem and the relationship of each person to YOU. Please exclude family members with whom you are only related through marriage. For relatives that can be on either the maternal or paternal side (e.g. an aunt), please specify. (If you listed any above, you need not repeat them here.)

       Problem: _____
Relationship:_____

       Problem: _____
Relationship:_____

       Problem: _____
Relationship:_____

       Problem: _____
Relationship:_____

C6: BIOLOGICAL HISTORY QUESTIONNAIRE FOR PARTICIPANT'S SIBLING.

Biological Sibling's History

Participant enrolled in the study: _____ Participant's DOB: _____

FOR EACH FULL OR HALF SIBLING OF THE BABY ENROLLED IN THE STUDY, please list his/her name, birth date, mother's name, and father's name. Then check and describe all illnesses or developmental problems that the child has had. Any other problems, even if you think they may not be important, should also be added. Please use the other side of the page, if necessary.

Name of Sibling: _____   Full Sibling/Half Sibling

Sex: Male   Female

Sibling's DOB: _____

Today's date: _____

Biological Mother: _____

Biological Father: _____

1. What is this sibling's primary (first) language? _____

   What language(s) is/are spoken in his/her home? _____

2. How would you describe this sibling's ethnicity?

   White/Caucasian   Black/Black British   Asian/Asian British   Chinese
            Mixed

   Other_____(please specify)

3. Does this sibling have a diagnosed disorder of any kind?

        If so, what is the diagnosis?

        When was the diagnosis given?

Who provided the diagnosis?

4. In the chart below, please list all the organised daycare/playgroups/schools that this sibling has been involved in, including location and dates of enrolment:

Daycare/Group/ School	Location	Month/Year Begun	Month/Year Ended

5. Please indicate whether this sibling has a history of the following developmental problems or illnesses:

Y   N

__   __   Articulation
_____

__   __   Stuttering
_____

__   __   Language
_____

__   __   Reading
_____

__   __   Writing
_____

__   __   Maths
_____

__   __   Attention Deficit Disorder
_____

__   __   Learning Disability

_____

__   __   Medical

_____

__   __   Recurrent Health Problems

_____

(e.g. allergies, chronic ear infections, seizures, hyperactivity)

__   __   Social/Emotional

_____

6. If you did not previously answer these questions over the phone, please indicate which, if any, of the following this sibling has experienced or been diagnosed with. Circle either yes, no, or I don't know (D/K):

Birth Trauma	YES	NO	D/K
Birth Asphyxia	YES	NO	D/K
PKU	YES	NO	D/K
Congenital Rubella	YES	NO	D/K
Neurofibromatosis (NF1 or 2)	YES	NO	D/K
Tuberous Sclerosis	YES	NO	D/K
Fragile X Syndrome	YES	NO	D/K
Other Chromosonal Abnormality	YES	NO	D/K

What? _____

Metabolic Disorder	YES	NO	D/K

What? _____

Progressive Neurological Disorder	YES	NO	D/K

What? _____

Visual Developmental Delay, e.g. blindness	YES	NO	D/K

What? _____

Auditory Developmental Delay, e.g. deafness YES   NO   D/K

What? _____

Motor Developmental Delay   YES   NO   D/K

What? _____

7. Has this sibling received childhood vaccinations?   YES   NO

7a. If yes, did these vaccinations include the MMR vaccine?   YES   NO

8. Did your child have any abnormal reaction to a vaccination?   YES   NO

8a. If yes, please describe this reaction and any medical attention received:
_____
_____

9. Does this sibling have a history of gastrointestinal problems?   YES
NO

9a. If yes, please describe problems, and WHEN they began:
_____

10. Was this child breastfed at all?   YES   NO

If YES:
11a. For how long were they breastfed? (no formula) _____

11b. At any point, was breastmilk supplemented with formula?   YES
NO

If yes, how often and how much? _____

If yes, what brand of formula was used? _____

11c.At what age, if ever, did you fully shift from breastfeeding to using formula? (in months)
_____

If NO:
11d. What brand of formula was used? _____

265

11. Do you have any current concerns about this sibling's development? If so, please describe in detail below.

_____
_____
_____
_____
_____
_____
_____

APPENDIX D

INTERVENTION RECORD FORM

D.1: INTERVENTION RECORD FORM.

<div align="center">

Intervention Record Form

</div>

Date: _____   Child ID: _____

Please answer the following questions regarding the therapies/interventions your child may be CURRENTLY enrolled in:

1. Is your child currently receiving any intervention (other than Reciprocal Imitation Training/RIT)?

    Yes   No

2. Is your child currently receiving any behavioural interventions (e.g. ABA, Floortime, RDI, PECS, SonRise)?

    Yes   No

3. Is your child currently receiving Speech Therapy?

    Yes   No

4. Is your child currently receiving Occupational Therapy?

    Yes   No

5. Is your child currently receiving any early childhood special education (e.g. TEACCH, STAR curriculum, Early Bird Programme, PACT, Discrete Trail Training, General special ed. Etc.)

    Yes   No

6. Is your child currently following any dietary/biomedical interventions (GFCF, Chelation, Megavitamins etc.)?

    Yes   No

7. Does your child have a Statement of Special Educational Needs (SEN)?

    Yes   No

8. Does your child have an Individual Education Plan?

Yes   No

9. Please list all interventions your child is enrolled in and rate how satisfied you were with these:

Name of Intervention	Number of hours/week	Group/ Individual	Therapy centre/home	Please rate your level of satisfaction with the intervention service				
				1 2 3 4 5 Not satisfied Highly at all satisfied				
				1 2 3 4 5 Not satisfied Highly at all satisfied				
				1 2 3 4 5 Not satisfied Highly at all satisfied				
				1 2 3 4 5 Not satisfied Highly at all satisfied				
				1 2 3 4 5 Not satisfied Highly at all satisfied				

Please answer the following questions regarding the therapies/interventions your child may have been PREVIOUSLY enrolled in:
1. Has your child *ever* received any intervention?

   Yes   No

2. Has your child *ever* received any behavioural interventions (e.g. ABA, Floortime, RDI, PECS, SonRise)?

   Yes   No

3. Has your child *ever* received Speech Therapy?

   Yes   No

4. Has your child *ever* received Occupational Therapy?

   Yes   No

5. Has your child *ever* received any early childhood special education (e.g. TEACCH, STAR curriculum, Early Bird Programme, PACT, Discrete Trail Training, General special ed. Etc.)

   Yes   No

6. Has your child *ever* followed any dietary/biomedical interventions (GFCF, Chelation, Megavitamins etc.)?   Yes   No

7. Please list all interventions your child has *ever* been enrolled in and rate how satisfied you were with these:

Name of Intervention	Date started & ended	Number of hours/week	Group/ Individual	Therapy centre/home	Please rate your level of satisfaction with the intervention service
					1 2 3 4 5 Not satisfied Highly at all satisfied
					1 2 3 4 5 Not satisfied Highly at all satisfied
					1 2 3 4 5 Not satisfied Highly at all satisfied
					1 2 3 4 5 Not satisfied Highly at all satisfied
					1 2 3 4 5 Not satisfied Highly at all satisfied

APPENDIX E

IMITATION ASSESSMENTS

E.1: UNSTRUCTURED IMITATION ASSESSMENT.

Unstructured Imitation Scale
Object Imitation Assessment

E.2: STRUCTURED IMITATION ASSESSMENT.

SIA Scoring Sheet

Child ID: _____   **Scorer: _____**   **Date: _____**

Examiner: _____   **Primary/Reliability**
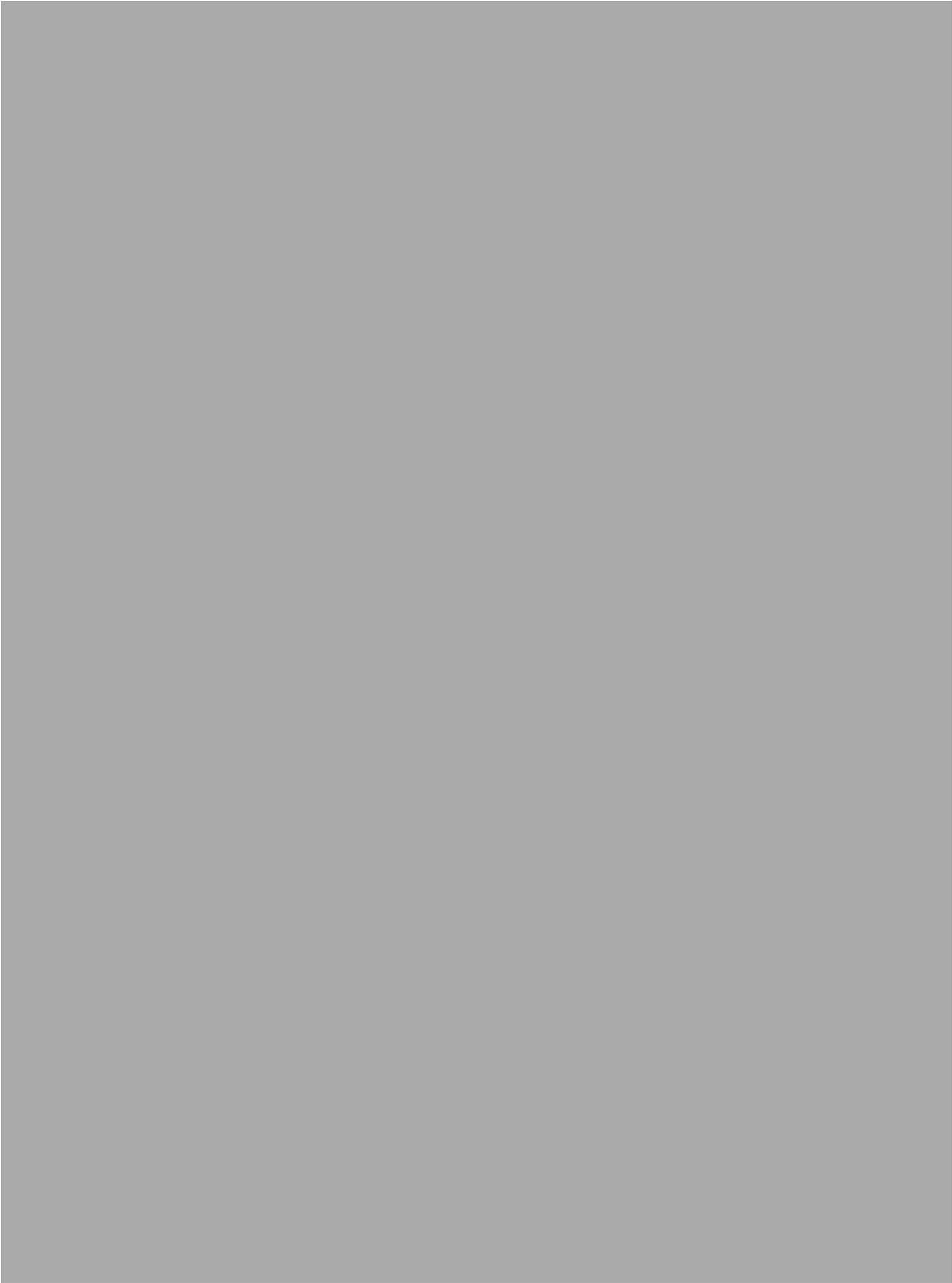
Scoring Guidelines for Structured Imitation Assessment
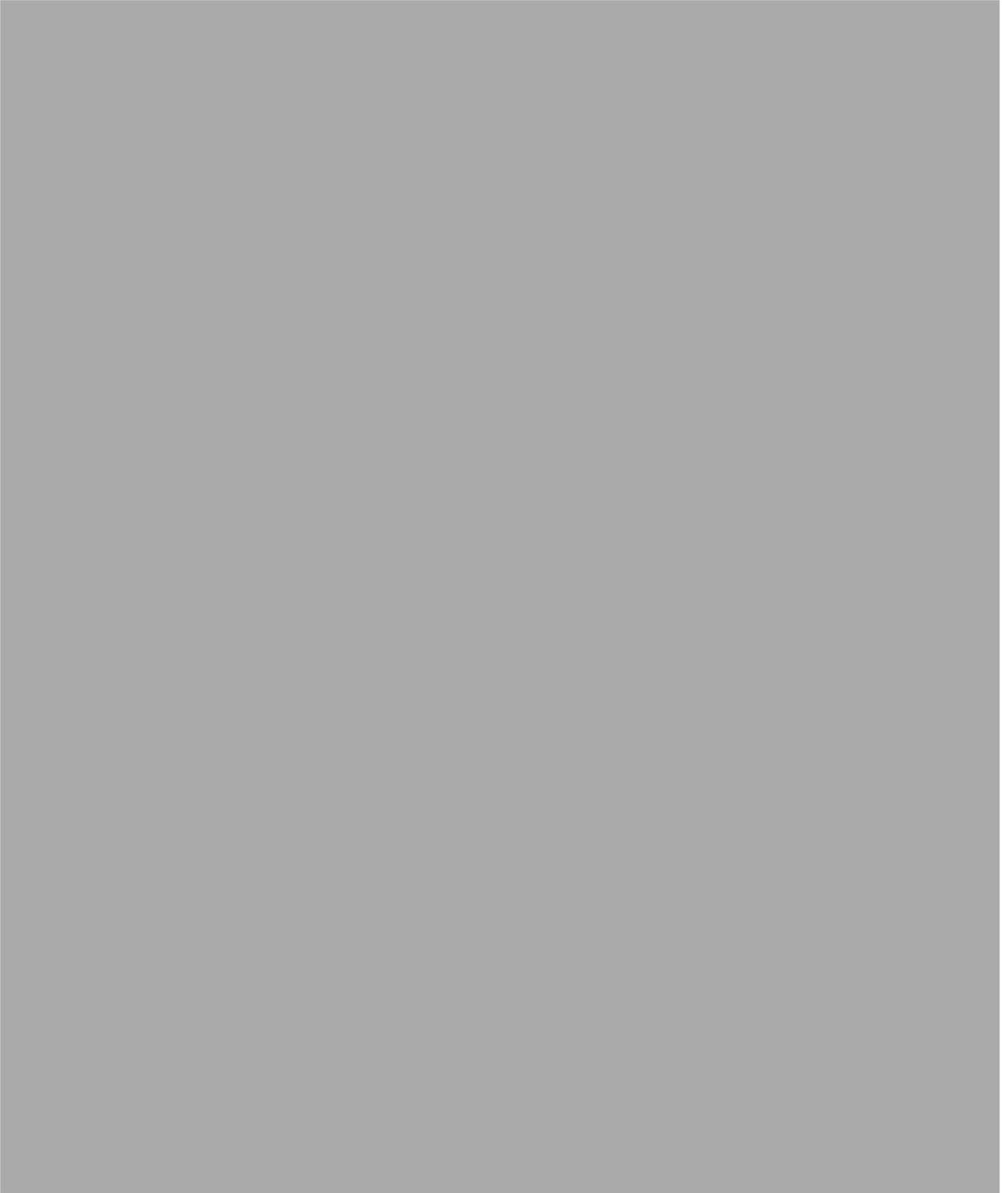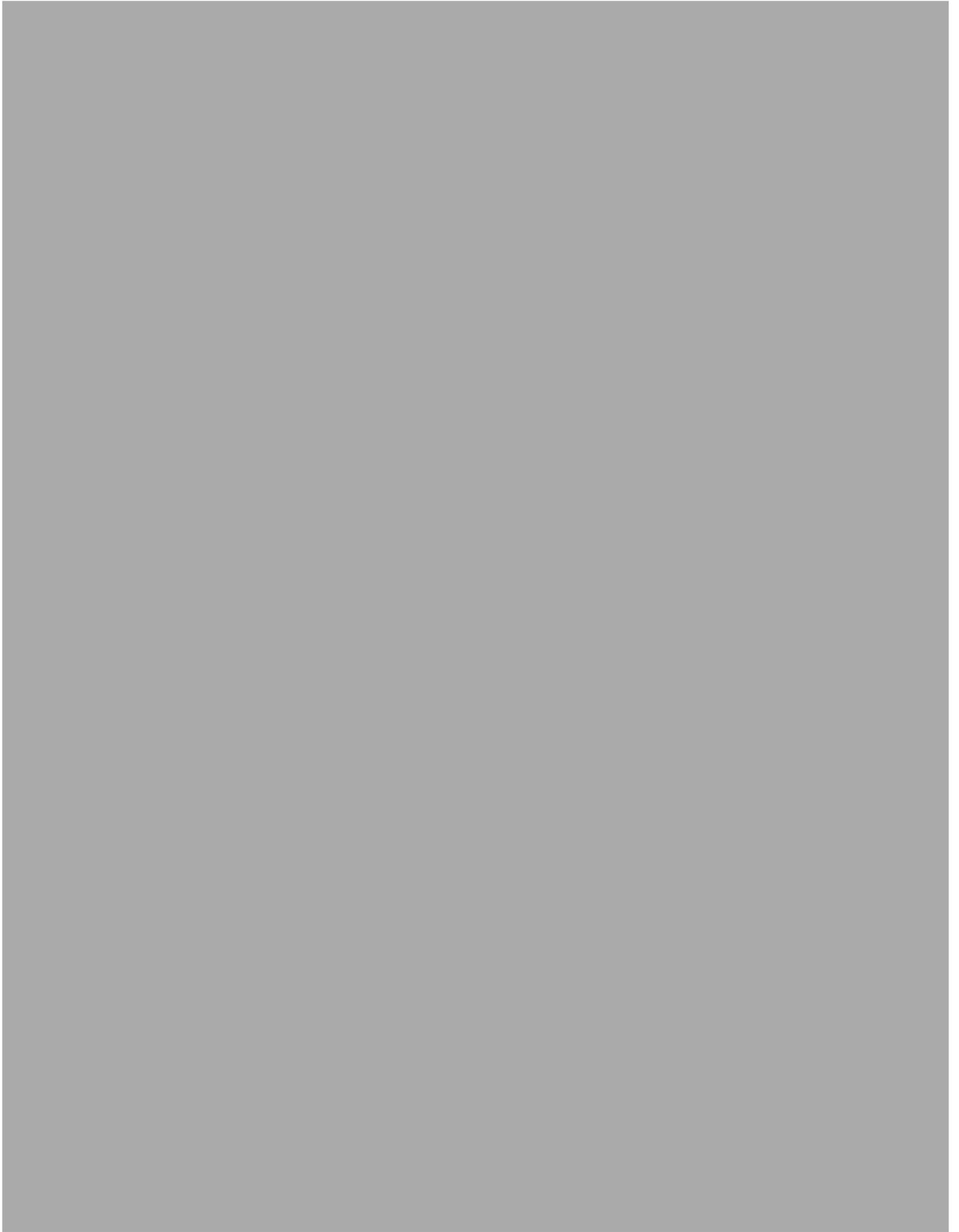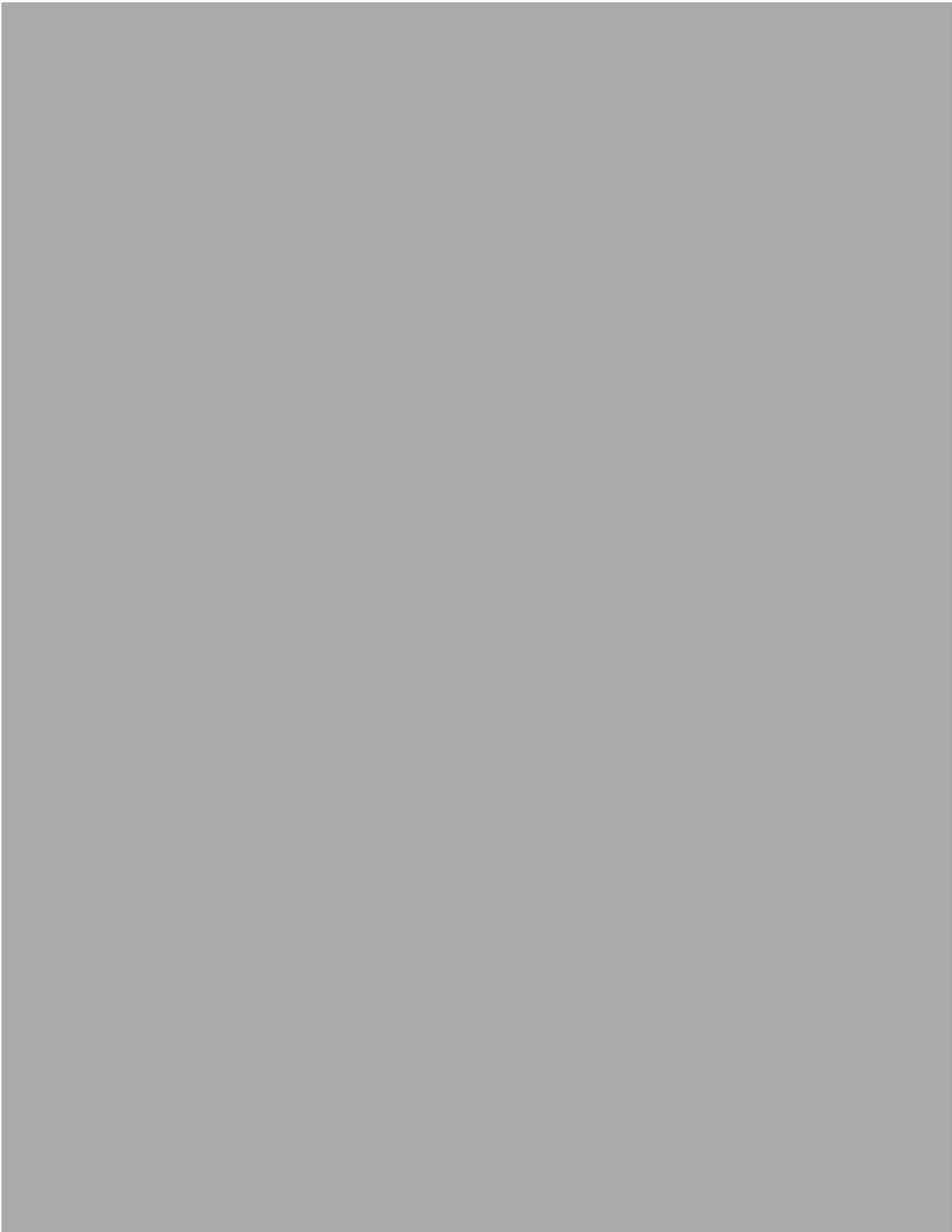
APPENDIX F

STUDY DESIGN: THREATS TO VALIDITY

F.1: COMMON THREATS TO VALIDITY IN AN RCT AND SOLUTIONS TAKEN IN THE PRESENT STUDY TO MINIMISE THESE THREATS.

Table F.1: Common threats to validity in an RCT.

Threat	Meaning	Resolution
1. Internal Validity	The extent to which one can confidently conclude that a given treatment had a given effect on behaviour.	
Temporal Precedence	To establish a causal relationship the treatment must occur before the outcome.	Only children with difficulties in spontaneous imitation were included in the sample, that is, children who reached ceiling on the spontaneous imitation scale were excluded.
Selection	The existence of significant differences between the treatment and control groups in the RCT before treatment.	Strict inclusion and exclusion criteria were laid out (Section 2.2.1). Given the well-documented high degree of variability in verbal skills in the ASD population, a stratified randomisation procedure was also used. Statistical analyses were conducted on pre-treatment characteristics in order to confirm that there were no significant group differences.
History	An event occurring in or out of the study that may provide for an alternative explanation of the results.	Any other treatment the child may be enrolled in before and during the trial was identified and monitored using an Intervention Record Form (Appendix E). Number of hours spent in other interventions by each participant group was also statistically analysed.
Maturation	Any natural growth or deterioration factors that may occur over time.	The control group in our study was well matched on age, non-verbal and verbal mental age. Also, the wait-list control design controls for change over time that result from normal

		maturation, because both groups are maturing to the same extent.
Regression to Mean	The tendency of a participant to receive an extreme score on a measure at a given time in testing and on re-test to receive a less extreme score. Random allocation of subjects, use of statistical analysis such as ANCOVA, avoiding self-report measures and using tests with high test-retest reliability are ways to reduce this threat.	Groups were randomly allocated and well matched. Repeated-measures ANOVA were used for statistical analysis as it was thought to be more appropriate for the sample and the research questions. No self-report measures were included in the study and all tests used had high test-retest reliability.
Attrition	The significant loss of participants over time.	Attrition rate was not seen to be very high. Seven participants dropped out before random allocation to groups and only one child dropped out after random allocation.
Testing and instrumentation	Impact of repeated test administration.	Double blinding procedures were used. This problem was particularly kept in mind with tests such as the ADOS that rely heavily on administrators' observation and scoring skills. All ADOS administrators attended regular reliability meetings and videos were cross-scored by ADOS-trained lab members to ensure accuracy. Furthermore, the potential for rater-drift in coding protocols was addressed while training blind coders and ad-hoc 'drift-checks' were performed by comparing all observers' scorings. If the inter-rater agreement fell below kappa of 0.6, 'revised training' sessions were conducted.
External Validity	This refers to generalisability of the results beyond the specific population and conditions.	
Sample Characteristics	The ability to generalise from the sample in the trial to the general population.	All children in the sample met criteria for autism however they were not excluded on the basis of gender, intellectual capacity, or autism

		symptom severity. Also, children with co-occurring seizures, primary sensory impairments, or a known genetic disorder, were excluded in order to maintain homogeneity of the sample and, therefore, allow us to reasonably draw conclusions regarding generalization of any observed effects to the larger population of children with autism.
Setting Characteristics	The inability to generalise intervention effects to settings beyond the study setting.	Generalisability across settings (such as the home) was not addressed, and was beyond the scope of the current project. Although the current RCT was a laboratory-based treatment trial, generalisability across people was tested by having the experimental change measures administered by experimentally blinded examiners who were not involved in treatment. Also, the room in which all tests were administered was different from the treatment room, in order to minimise confounders related to setting characteristics.
Testing effects	Relates to actual timing of the testing, knowing that one is being tested, and pre-test sensitisation.	Using child friendly, play-based assessments which were administered only once at T1 and T2. The timing of testing was matched across the two groups; that is, length of time between T1 and T2 assessments was monitored and closely matched across participants in the two groups.
Construct Validity	This focuses on the ability of the study to test the constructs as intended (West & Spring, 2007).	
Inadequate explication of constructs	Ill-defined, inadequately operationalised constructs of interest.	Spontaneous social use of imitation was the main construct and RIT is an intervention specifically designed to improve the construct

		in question. Clear definitions regarding imitation and its techniques are also laid out in the intervention manual.
Confounding constructs	Confusing two constructs	An in-depth literature review was carried out on the construct of imitation and the two constructs of spontaneous imitation and social imitation were clearly defined (refer to Chapter 1 for detailed discussion) therefore minimising any confounders due to constructs being measured.
Singular definitions	Threats can come from 'mono-operation bias' as well as 'monomethod bias'. Having various methods when defining and implementing a construct. The use of multiple therapists in delivery of treatment and multiple measures to look at the same construct are two ways of overcoming this challenge.	Multiple therapists delivered the intervention, therefore conclusions regarding therapist generalisability of treatment could be drawn.
Participant reactivity	This involves different ways in which a participant may react to aspects of the RCT which are unintended and not included in the actual investigation.	As participants were young children unaware of the research design, such threats were minimal. On the contrary, participants' reactions to new test administrators were considered such that administrators were given some initial time to develop a rapport with the child. Secondly, various needs of the children were also taken into consideration when administering tests (short attention spans, challenging behaviours, etc.) and individualised strategies were used in order to help children complete the assessments.
Experimenter expectancies	Unintentional biases that come from the experimenter.	Double blinding procedures for both administration and scoring were followed and protocols for therapist included blinding the therapist to group status.

Treatment diffusion	When various components of the treatment in question may be inadvertently provided to the control group.	RIT is an intervention that uses techniques embedded in both behavioural and developmental theories. Therefore there may be some overlap in techniques used for the treatment group and the techniques used in the therapies availed by the control group. On the other hand, RIT is a n NDBI and, as such, is unlikely to be similar to most interventions in the UK – which are either developmental or behavioural (Salomone et al., 2015), and it is this unique combination of techniques that makes RIT a successful intervention programme that was aimed to be tested. Additionally, as enrolment in other treatments was not an exclusion criterion, *our specific research question was to look at efficacy of RIT in children with autism over and above treatment-as-usual, which may include various other treatments as well as no treatment.*
Statistical Conclusion Validity	Validity of the conclusions reached through statistical methods about the variables in question.	
Low Statistical power	Statistical power is the ability to detect an effect when it does truly exist, i.e. reject the null hypothesis when it is false.	Sample size was determined through two ways. As this study was based on the previous pilot-RCT, sample size was kept similar. Further, power was also determined using the online statistical software, G*power.
Family-wise error	Conducting multiple statistical analyses.	Planned analyses as well as use of Bonferonni/Holm-Boneferonni correction ensured minimising this threat.
Unreliable measures	The use of unreliable assessment procedures and tests.	All tests used in this study were either standardized tests for children or tests devised and used in multiple previously published

		academic research articles designed to answer questions regarding imitation in children with autism spectrum disorders. All tests used in the current study have high test-retest reliabilities.
Unreliability of treatment implementation	Variability in treatment across subjects.	Regular fidelity of implementation checks. As the PhD researcher is a trained trainer for RIT, all therapists trained were regularly, on an ad-hoc basis, scored for fidelity of implementation to minimise therapist biases as well as control for treatment variability due to the subject. Also, therapists evaluated and discussed each other's therapy delivery to best ensure that understanding of treatment techniques was the same across all therapists.
Subject heterogeneity	Increased heterogeneity in participants can lead to unwanted variability and increased standard deviations for study measures.	Although this was kept in control through strict inclusion and exclusion criteria, some effects of this were seen as there was a mix of children with very low intellectual abilities as well as high functioning children in the study which led to higher standard deviations. At the same time, it was important to keep a balance between controlling for this threat and having a sample representative of the ASD population. Independent samples t-test showed that the groups were well matched on pre-treatment characteristics and thus threat to validity was minimised.

APPENDIX G

SCATTER PLOTS FOR CORRELATIONS

(ADDITIONAL RESULTS CHAPTER 3)

G.1: Scatter Plots Showing Correlation Between Spontaneous Imitation Change Scores And Reciprocal Social Interaction Skills
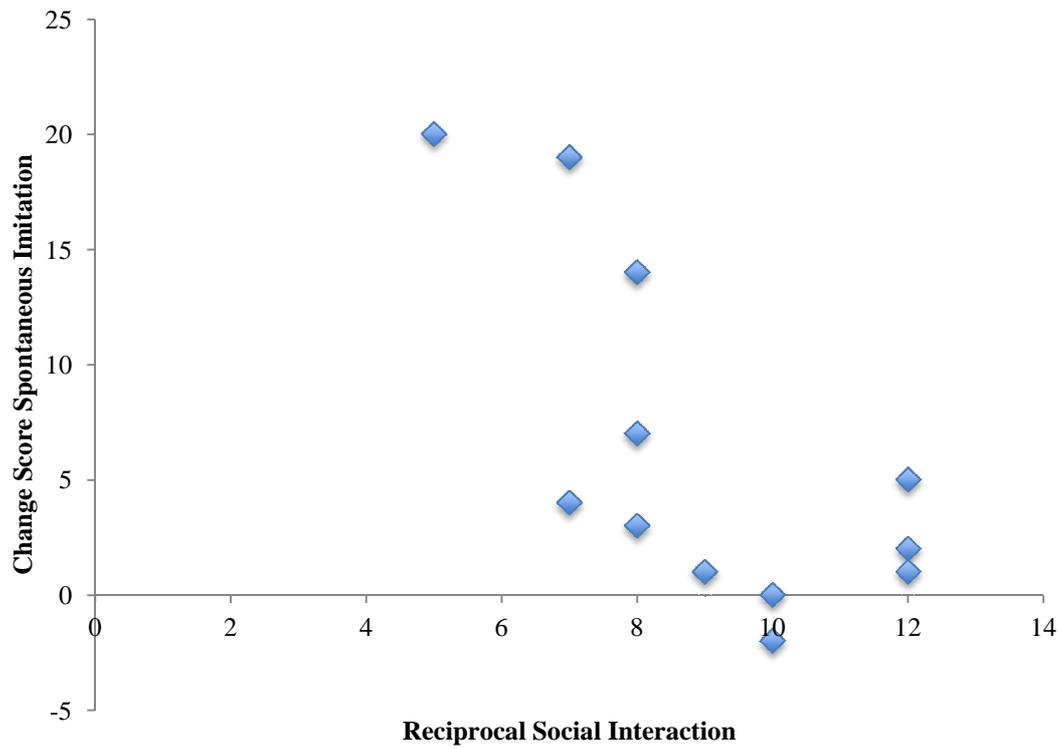
Figure G.1: Correlation between Spontaneous Imitation change score and Reciprocal Social Interaction skills as measured on the ADOS.
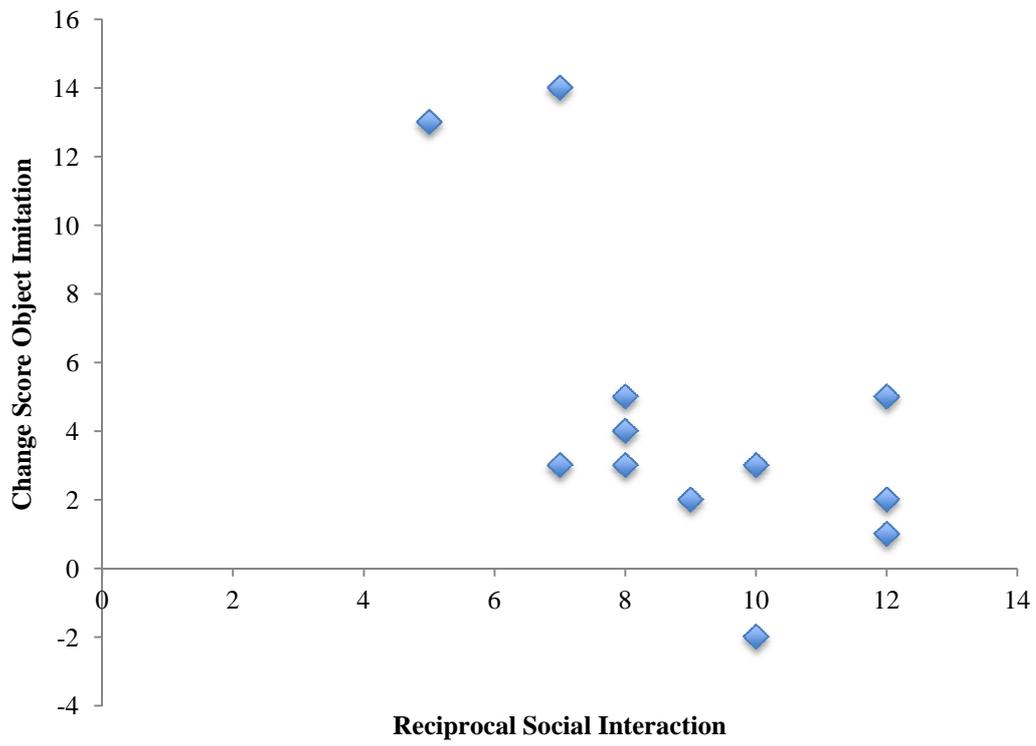
Figure G.2: Correlation between Object Imitation change score and Reciprocal Social Interaction skills as measured on the ADOS.
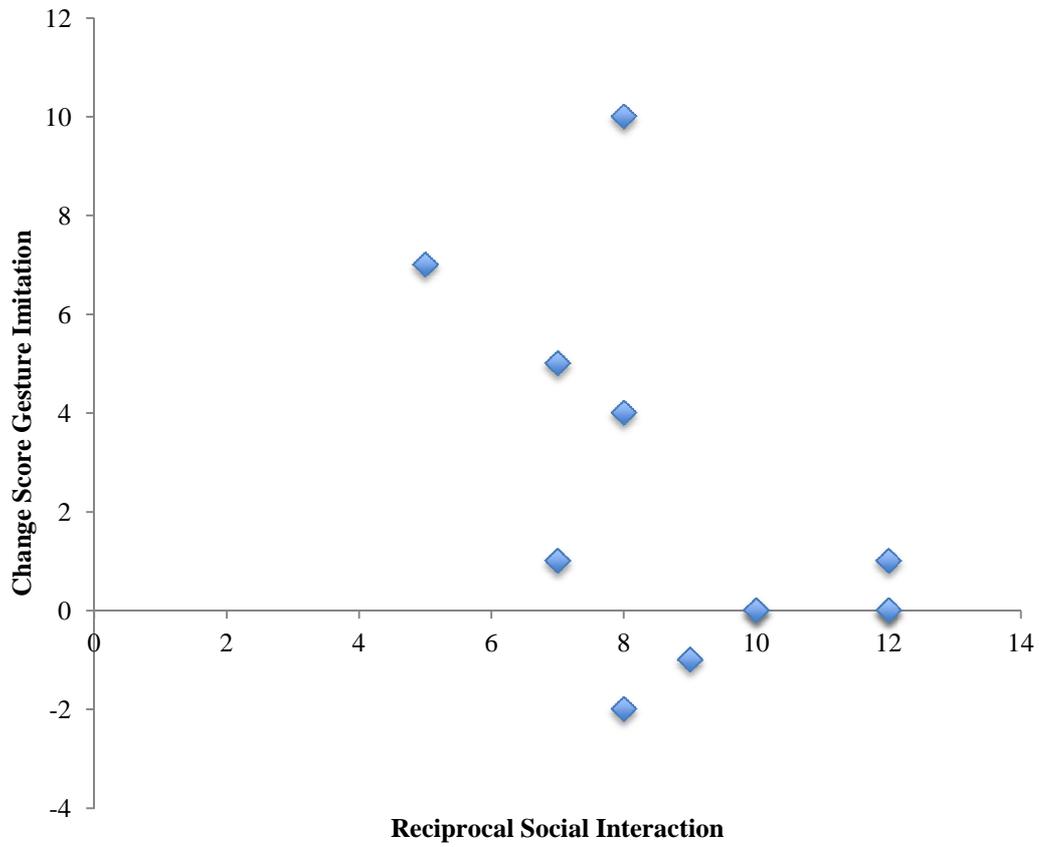
Figure G.3: Correlation between Gesture Imitation change score and Reciprocal Social Interaction skills as measured on the ADOS.

G.2: Scatter Plot Showing Correlation Between Spontaneous Imitation Change Scores And Stereotyped Behaviours And Restricted Interests
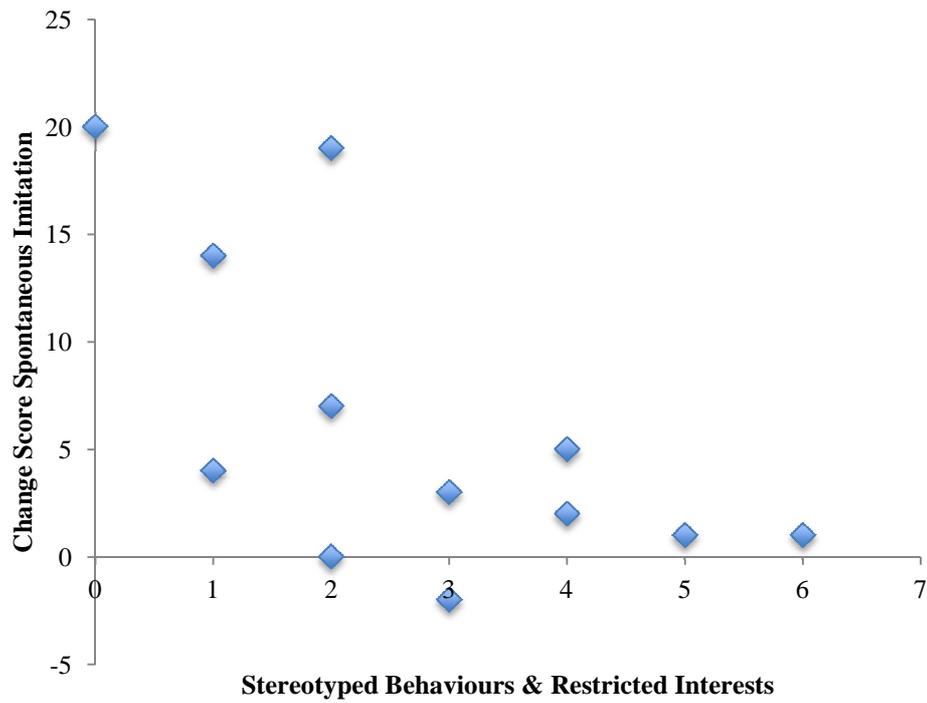
Figure G.4: Correlation between Spontaneous Imitation change score and Stereotyped Behaviours and Restricted Interests as measured on the ADOS.
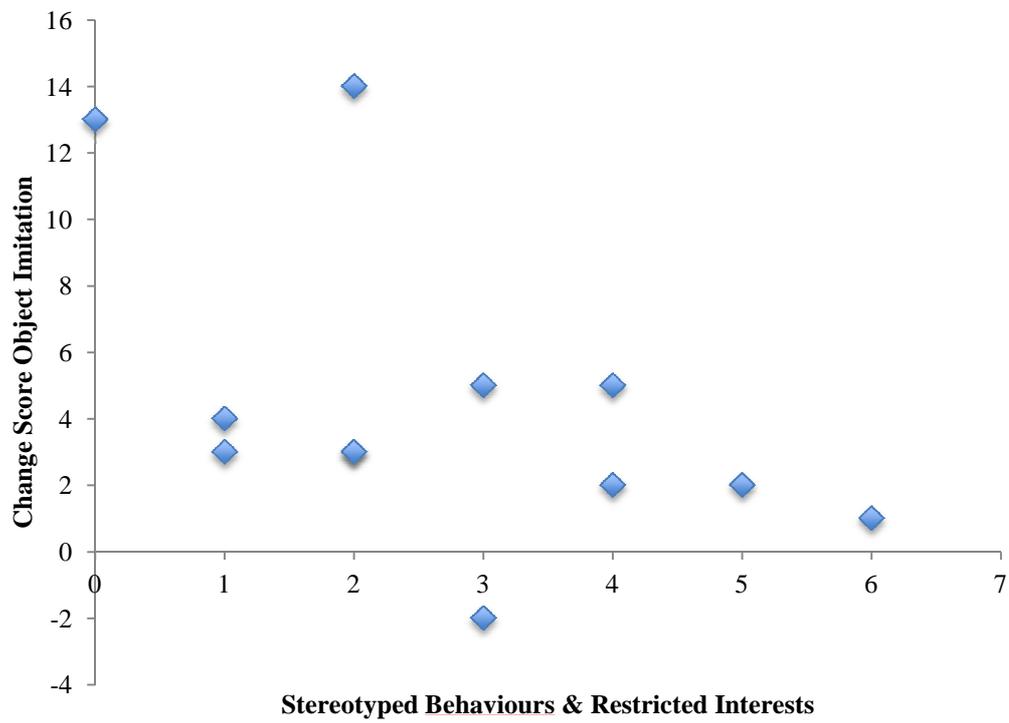
Figure G.5: Correlation between Object Imitation change score and Stereotyped Behaviours and Restricted Interests as measured on the ADOS.
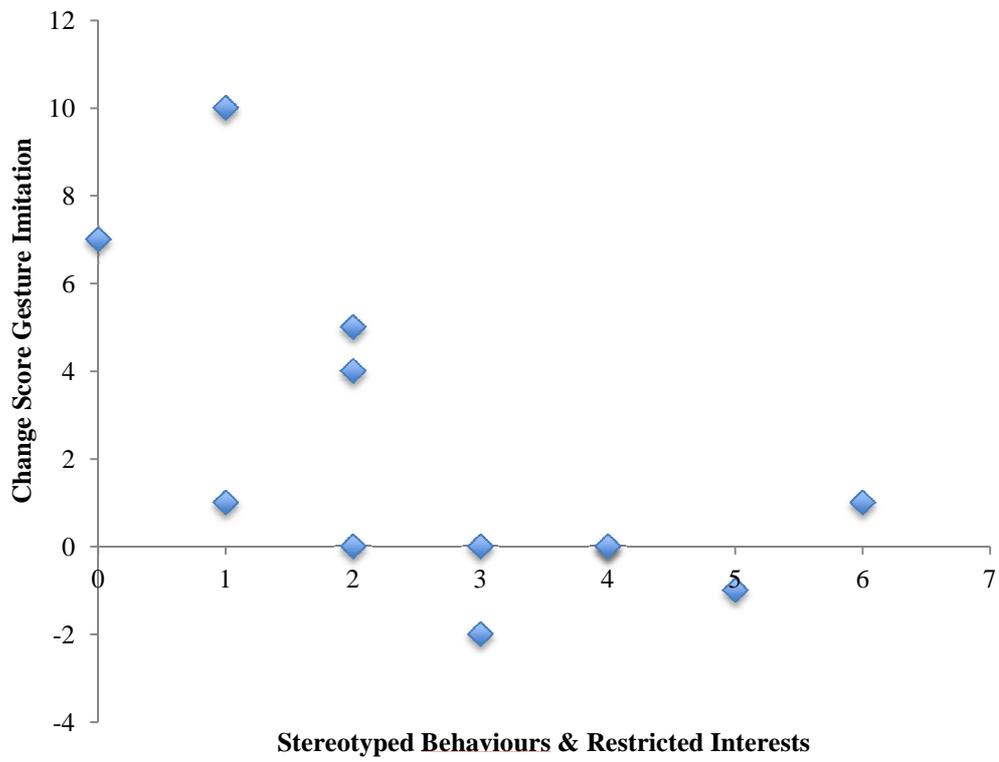
Figure G.6: Correlation between Gesture Imitation change score and Stereotyped Behaviours and Restricted Interests as measured on the ADOS.

APPENDIX H

ADDITIONAL RESULTS CHAPTER 4

H.1: HUMAN ACTION SOUNDS

Table H.1: Summary of two-way ANOVA for P1 mean amplitude and peak latency human action sounds in match and mismatch conditions at T2 for the Treatment and Wait-List Control groups in the Central channels.

	Mean Amplitude			Latency		
	$F (1,13)$	p	η_p^2	$F (1,13)$	p	η_p^2
Condition	0.003	0.96	0.00	0.00	0.99	0.00
C x G	0.79	0.39	0.06	0.10	0.76	0.01

Table H.2: Summary of three-way ANOVA for P1/N1 mean amplitude human action sounds in match and mismatch conditions at T2 for the Treatment and Wait-List Control groups in the Frontal and Parietal channels.

	Frontal (P1)			Parietal (N1)		
	$F (1,13)$	p	η_p^2	$F (1,13)$	p	η_p^2
Condition	1.44	0.25	0.10	1.61	0.23	0.11
Hemisphere	3.50	0.06	0.21	5.63	0.01*	0.30
C x G	0.02	0.90	0.00	1.99	0.18	0.13
H x G	0.50	0.56	0.04	1.50	0.25	0.10
C x H	2.59	0.11	0.17	0.54	0.55	0.04
C x H x G	0.39	0.64	0.03	1.49	0.25	0.10

**F-statistic significant at p<0.01.

All values shaded grey were significant at p <0.05. C = Condition, H = Hemisphere, G = Group.

Table H.3: Summary of three-way ANOVA for P1/N1 peak latency human action sounds in match and mismatch conditions at T2 for the Treatment and Wait-List Control groups in the Frontal and Parietal channels.

	Frontal (P1)			Parietal (N1)		
	F (1,13)	*p*	η_p^2	*F (1,13)*	*p*	η_p^2
Condition	0.60	0.45	0.04	0.44	0.52	0.03
Hemisphere	0.48	0.61	0.04	3.57	0.04*	0.22
C x G	0.09	0.77	0.01	0.21	0.65	0.02
H x G	0.22	0.78	0.02	1.19	0.32	0.08
C x H	1.80	0.19	0.12	0.79	0.46	0.06
C x H x G	1.09	0.34	0.08	1.02	0.37	0.07

**F-statistic significant at p<0.01.

All values shaded grey were significant at p <0.05. C = Condition, H = Hemisphere, G = Group.

Table H.4: Summary of four-way ANOVA for human action sounds in match and mismatch conditions for the four time windows (180-310ms, 310-440ms, 440-570ms, 570-700ms) at T2 for the Treatment and Wait-List Control groups in the Frontal channels.

	Frontal		
	F (1,13)	*p*	$\eta_p{}^2$
Condition	1.93	0.19	0.13
Hemisphere	0.95	0.37	0.07
Timing Window	2.54	0.10	0.16
C x G	3.35	0.09	0.21
H x G	0.73	0.44	0.05
T x G	0.13	0.88	0.01
C x H	1.39	0.27	0.10
C x T	0.24	0.83	0.02
H x T	1.34	0.28	0.09
C x H x G	0.62	0.49	0.05
C x T x G	0.70	0.53	0.05
H x T x G	1.33	0.28	0.09
C x H x T	2.30	0.11	0.15
C x H x T x G	0.40	0.71	0.03

**F-statistic significant at p<0.01.

All values shaded grey were significant at p <0.05. T = Timing window, C = Condition, H = Hemisphere, G = Group.

H.1.1. Mismatch effect comparison at T1 for human action sounds

In section 4.3.1.2 mismatch effect (mismatch – match trials) was calculated and compared for individual participant and group data at T1 and T2 to evaluate change through treatment. Visual inspection of group data means at T1 showed a marginal difference between Treatment and Wait-List Control group. Independent samples t-test however did not show any difference over the central and parietal channels (Table H.5).

Table H.5: Mean (S.E.) of human-action mismatch effect for Treatment and Wait-List Control group.

Mismatch Effect	Treatment (*n=5*)	Wait-List Control (*n=5*)	*t(8)*	*p-value*
Central	0.46 (0.7)	-0.21 (0.3)	0.48	0.64
Parietal Left	-0.73 (0.7)	0.81 (1.1)	-1.17	0.28
Parietal Middle	-1.17 (1.1)	1.68 (1.2)	-1.79	0.11
Parietal Right	-0.61 (1.1)	1.78 (1.5)	-1.29	0.23

H.1.2. Group Data Analysis: T1 And T2 Comparison for Human Action Sounds

Between subjects repeated measures ANOVAs were conducted for the Central and Parietal channels to compare change in ERP responses from T1 to T. As group by condition interactions were significant for both the regions, the mean of four timing windows (180-310ms, 310-440ms, 440-570ms, 570-700ms) was calculated for each human action trial, that is, match and mismatch trials. Independent samples t-test were carried out for data at T1. No significant difference was found between the Treatment and Wait-List Control group on match and mismatch trials at T1 for the central channels; however, a significant difference was observed between the Treatment and Wait-List Control groups for the match trials at T1 in the middle parietal region (Table H.6).

Table H.6: Mean (S.E.) of human-action match and mismatch conditions for Treatment and Wait-List Control group T1.

Condition	Treatment (*n*=5)	Wait-list Control (*n*=5)	*t (8)*	*p-value*
Match Sounds				
Central	0.35 (0.7)	0.39 (0.3)	-0.06	0.95
Parietal Left	-0.78 (0.4)	-0.74 (0.9)	-0.04	0.97
Parietal Middle	0.31 (0.4)	-2.94 (1.2)	2.54	0.05*
Parietal Right	-0.41 (0.8)	-1.62 (1.1)	0.89	0.40
Mismatch Sounds				
Central	0.81 (1.1)	0.18 (0.6)	0.51	0.63
Parietal Left	-1.50 (0.8)	0.07 (0.6)	-1.55	0.16
Parietal Middle	-0.86 (0.9)	-1.26 (0.7)	0.35	0.74
Parietal Right	-1.01 (0.6)	0.16 (1.1)	-0.91	0.39

<u>*Central*</u>: A between-subjects repeated measures ANOVA with condition (match, mismatch) and time (T1, T2) as within-subjects factors and group (Treatment, Wait-List Control) as between-subjects factor was conducted (Table H.7).

Table H.7: Summary of three-way ANOVA for human action sounds in match and mismatch conditions at T1 and T2 for the Treatment and Wait-List Control groups for the Central channels.

	Central		
	F (1,8)	*p*	η_p^2
Condition	0.005	0.94	0.001
Time	0.20	0.66	0.03
C x G	4.73	0.61	0.37
T x G	0.36	0.56	0.04
C x T x G	14.34	**	0.64

**F-statistic significant at p<0.01.

All values shaded grey were significant at p <0.05. C = condition, T = time, G = group.

Post-hoc analysis using pairwise comparisons with Bonferroni correction for the condition x time x group interaction found no difference in activity between Treatment and Wait-List control group at T1 or T2 in the match and mistmatch conditions. Within group differences were found for the Wait-List Control group, where at T2 there was a significant difference in ERP responses between match trials (*M* = 2.01μV, *S.E.* = 0.9) and mismatch trials (*M* = -0.68μV, *S.E.* = 1.0, *p* = 0.03), showing a larger positive response to match trials compared to mismatch trials which showed a larger negative response. In the Treatment group there was a trend towards significance for greater mismatch response (*M* = 1.8μV, *S.E.* = 0.96) compared to match trials (*M* = -0.46μV, *S.E.* = 0.9) at T2 (*p* = 0.056).

Parietal: A between-subjects repeated measures ANOVA with condition (match, mismatch), hemisphere (left, middle, right) and time (T1, T2) as within-subjects factors and group (Treatment, Wait-List Control) as between-subjects factor was carried out (Table H.8).

Table H.8: Summary of four-way ANOVA for human action sounds in match and mismatch conditions at T1 and T2 for the Treatment and Wait-List Control groups for the Parietal channels.

	Parietal		
	F (1,8)	*p*	η_p^2
Time	0.00	0.99	0.00
Condition	0.04	0.84	0.005
Hemisphere	2.20	0.15	0.21
T x G	0.29	0.61	0.04
C x G	0.002	0.97	0.00
H x G	1.93	0.19	0.20
T x C	0.18	0.69	0.02
C x H	0.36	0.67	0.04
T x H	3.83	0.06	0.32
T x C x G	6.82	0.03*	0.46
T x H x G	1.09	0.35	0.12
C x H x G	1.15	0.34	0.13
T x C x H	2.70	0.12	0.25
T x C x H x G	7.34	0.01*	0.48

**F-statistic significant at p<0.01. * F-statistic significant at p<0.05.

All values shaded grey were significant at p <0.05. C = condition, T = time, H = hemisphere, G = group.

Pairwise comparisons using Bonferroni correction were conducted for the two significant interactions. In the Group x Time x Condition interaction, a significant difference between ERP activity at T1 (M = -0.29μV, S.E. = 0.7) and T2 (M = -1.51μV, S.E. = 0.7) was found for the Treatment group during match trials (p = 0.05). A significant difference between activity at T1 (M = -1.77μV, S.E. = 0.7) and T2 (M = -0.20μV, S.E. = 0.7) was also found for the Wait-List Control group during match trials (p = 0.02). No other comparisons were significant for this interaction.

Post-hoc analysis for the Group x Time x Hemisphere x Condition interaction revealed a significant difference in the middle parietal ERP response between Treatment (M =

0.31μV, S.E. = 0.9) and Wait-List Control group (M = -2.91μV, S.E. = 0.9) at T1 during match trials (p = 0.04), suggesting a larger negative-going response for the Wait-List group and a small positive-going ERP response for the Treatment group. Further, in the Treatment group a larger negative response was observed in the middle parietal region for match trials at T2 (M = -1.82μV, S.E. = 1.2) compared to T1 (M = 0.31μV, S.E. = 0.9, p = 0.04), whereas in the Wait-List Control group a larger negative response was observed for match trials in the mid-parietal region at T1 (M = -2.91μV, S.E. = 0.9) compared to T2 (M = 0.59μV, S.E. = 1.2, p <0.01). Thus a different pattern of activity was observed in the Treatment and Wait-List Control group at both T1 and T2 in the middle parietal region for match trials.

Also, the Wait-List Control group showed a significant difference between the match and mismatch trials in the middle parietal region at T2 (p = 0.05).

H.1.3. Correlation Analysis:

Table H.9: Correlations between age, ADOS domain scores and total scores and mean amplitude difference for human-action sounds (n=15).

	Central	Parietal Left	Parietal Middle	Parietal Right
Chronological Age	-0.18	0.17	-0.24	-0.37
Reciprocal Social Interaction	-0.29	-0.22	-0.14	-0.08
Communication	-0.19	-0.04	-0.06	-0.11
Play	-0.13	-0.29	-0.07	0.03
Stereotyped Behaviors & Restricted Interests	-0.08	-0.20	0.06	-0.25
ADOS Total Score	-0.26	-0.15	-0.11	-0.10

H.2: NON-HUMAN ACTION SOUNDS

Table H.10: Summary of two-way ANOVA for P1 mean amplitude and peak latency non-human action sounds in match and mismatch conditions at T2 for the Treatment and Wait-List Control groups over the Central channels.

	Mean Amplitude			Latency		
	$F\,(1,13)$	p	η_p^2	$F\,(1,13)$	p	η_p^2
Condition	0.012	0.73	0.01	0.20	0.66	0.02
C x G	0.31	0.59	0.02	1.14	0.31	0.08

Table H.11: Summary of three-way ANOVA for P1/N1 mean amplitude non-human action sounds in match and mismatch conditions at T2 for the Treatment and Wait-List Control groups for the Frontal and Parietal channels.

	Frontal (P1)			Parietal (N1)		
	$F\,(1,13)$	p	η_p^2	$F\,(1,13)$	p	η_p^2
Condition	0.39	0.54	0.03	0.14	0.72	0.01
Hemisphere	0.34	0.65	0.03	0.09	0.89	0.01
C x G	5.75	0.03*	0.30	0.47	0.50	0.04
H x G	1.45	0.26	0.10	0.15	0.83	0.01
C x H	0.97	0.37	0.07	1.77	0.20	0.12
C x H x G	0.76	0.44	0.06	1.57	0.23	0.11

*F-statistic significant at p<0.05.

All values shaded grey were significant at p <0.05. C = Condition, H = Hemisphere, G = Group.

Table H.12: Summary of three-way ANOVA for P1/N1 peak latency non-human action sounds in match and mismatch conditions at T2 for the Treatment and Wait-List Control groups in the Frontal and Parietal channels.

	Frontal (P1)			Parietal (N1)		
	$F (1,13)$	p	η_p^2	$F (1,13)$	p	η_p^2
Condition	0.14	0.71	0.01	0.21	0.65	0.02
Hemisphere	1.39	0.27	0.10	0.41	0.63	0.03
C x G	0.06	0.81	0.00	1.28	0.28	0.09
H x G	0.06	0.92	0.01	0.27	0.72	0.02
C x H	1.15	0.33	0.08	1.79	0.19	0.12
C x H x G	1.18	0.32	0.08	3.21	0.06	0.20

C = Condition, H = Hemisphere, G = Group.

Table H.13: Summary of four-way ANOVA for non-human action sounds in match and mismatch conditions for the four time windows (180-310ms, 310-440ms, 440-570ms, 570-700ms) at T2 for the Treatment and Wait-List Control groups in the Central channels.

	$F (1,13)$	p	η_p^2
Condition	0.25	0.63	0.02
Time	1.01	0.38	0.07
C x G	0.13	0.73	0.01
T x G	0.62	0.54	0.05
C x T	1.42	0.26	0.10
C x T x G	0.28	0.79	0.02

C = Condition, T = time window, G = Group.

H.2.1. Group Data Analysis: T1 And T2 Comparison for Non-Human Action Sounds.

Groups were analysed for differences in the Frontal and Parietal regions in the non-human action sounds condition and as time x group effects were found previously mean of hemispheric ERP responses were calculated for the four timing windows. Independent samples t-test were carried out for data at T1. No significant difference was found between the Treatment and Wait-List Control group on match and mismatch trials at T1 for the frontal or parietal channels (Table H.15).

A between-subjects repeated measures ANOVA with condition (match, mismatch), timing windows (180-310ms, 310-440ms, 440-570ms, 570-700ms) and time (T1, T2) as within-subjects factors and group (Treatment, Wait-List Control) as between-subjects factor was carried out for both Frontal and Parietal channels (Table H.16).

Table H.15: Mean (S.E.) of non-human action match and mismatch conditions for Treatment

and Wait-List Control group.

Condition	Treatment (*n*=5)	Wait-list Control (*n*=5)	*t (8)*	*p-value*
Match Sounds				
Frontal TW1	-0.83 (1.2)	0.83 (0.7)	-1.18	0.27
Frontal TW2	-1.43 (0.9)	-0.18 (0.8)	-1.08	0.31
Frontal TW3	-1.16 (0.8)	-0.58 (1.1)	-0.43	0.69
Frontal TW4	-0.89 (0.6)	-0.68 (1.1)	-0.17	0.87
Parietal TW1	0.28 (0.5)	-0.77 (0.9)	1.07	0.32
Parietal TW2	-0.18 (0.6)	-1.20 (0.6)	1.20	0.26
Parietal TW3	-0.48 (0.3)	-0.59 (0.8)	0.12	0.91
Parietal TW4	-0.51 (0.7)	-1.20 (0.7)	0.68	0.52
Mismatch Sounds				
Frontal TW1	0.74 (0.4)	0.35 (0.6)	0.52	0.62
Frontal TW2	0.68 (0.7)	0.23 (0.9)	0.41	0.70
Frontal TW3	-0.20 (0.8)	-0.40 (0.8)	0.17	0.87
Frontal TW4	-0.81 (0.7)	-1.18 (1.3)	0.25	0.81
Parietal TW1	-1.53 (0.9)	0.58 (1.0)	-1.58	0.15
Parietal TW2	-2.00 (0.8)	0.29 (0.7)	-2.08	0.07
Parietal TW3	-1.42 (0.9)	0.57 (0.7)	-1.70	0.13
Parietal TW4	-0.38 (0.8)	1.20 (0.4)	-1.83	0.11

TW = Time Window; TW 1= 180-310ms, TW2 = 310-440ms, TW3 = 440-570ms, TW4 = 570-700ms.

Table H.16: Summary of four-way ANOVA for non-human action sounds in match and mismatch conditions at T1 and T2 for the Treatment and Wait-List Control groups in the Parietal channels.

	Frontal			Parietal		
	F (1,8)	*p*	η_p^2	*F (1,8)*	*p*	η_p^2
Time	5.30	0.05*	0.40	0.03	0.88	0.00
Condition	0.22	0.65	0.03	0.52	0.49	0.06
TW	1.93	0.15	0.19	4.29	0.04*	0.35
T x G	0.05	0.83	0.01	0.01	0.93	0.00
C x G	0.35	0.57	0.04	1.04	0.34	0.12
TW x G	1.60	0.23	0.17	2.91	0.09	0.27
T x C	1.40	0.27	0.15	0.40	0.54	0.05
C x TW	7.83	**	0.50	4.52	0.03	0.36
T x TW	4.16	0.03	0.34	0.05	0.95	0.01
T x C x G	0.10	0.80	0.01	1.76	0.22	0.18
T x TW x G	9.93	**	0.55	1.59	0.24	0.17
C x TW x G	2.62	0.11	0.25	0.27	0.77	0.03
T x C x TW	0.83	0.43	0.09	0.34	0.75	0.04
T x C x TW x G	0.66	0.50	0.08	0.77	0.50	0.09

**F-statistic significant at p<0.01. * F-statistic significant at p<0.05.

All values shaded grey were significant at p <0.05. C = condition, T = time, TW = Time Windows, G = group.

<u>*Frontal*</u>: Post-hoc analysis using Bonferroni correction for the Condition x Time Window interaction effect did not reveal any significant differences.

Pairwise comparisons using Bonferroni correction for Group x Time x Time Window interaction revealed that a significant difference in the Wait-List control group for time window 3 (440-570ms) between T1 (*M* = -0.49µV, *S.E.* = 0.7) and T2 (*M* = 1.64µV, *S.E.* = 0.5), *p* =0.02; and time window 4 (570-700ms) between T1 (*M* = -0.93µV, *S.E.* = 0.8) and T2 (*M* = 1.13µV, *S.E.* = 0.4), *p* =0.05.

Parietal: Post-hoc analysis using pairwise comparisons using Bonferroni correction for the Condition x Time Window interaction did not show any significant did not reveal any differences in processing of match and mismatch trials for any time window.

H.2.2. Correlations Analyses:

Table H.17: Correlations between age, ADOS domain scores and total scores and mean amplitude difference for non-human action sounds (n=15).

	Frontal Left	Frontal Middle	Frontal Right	Parietal Left	Parietal Middle	Parietal Right
Chronological Age	0.03	-0.25	-0.41	-0.02	-0.04	-0.31
Reciprocal Social Interaction	-0.28	-0.22	-0.01	-0.17	-0.27	0.11
Communication	-0.39	-0.36	0.03	-0.07	-0.06	0.27
Play	-0.06	0.083	0.44	0.03	-0.02	0.08
Stereotyped Behaviors & Restricted Interests	0.12	-0.07	0.16	-0.12	-0.27	-0.01
ADOS Total Score	-0.35	-0.30	0.01	-0.13	-0.19	0.19

Table H.18: Correlations between spontaneous imitation change scores and mean amplitude difference for human-action sounds (n=15).

	Frontal Left	Frontal Middle	Frontal Right	Parietal Left	Parietal Middle	Parietal Right
Spontaneous Imitation Total	-0.10	-0.08	0.13	0.08	0.38	0.27
Object Imitation	0.03	0.02	0.16	0.08	0.22	0.10
Gesture Imitation	-0.22	-0.17	0.02	0.03	0.41	0.40

APPENDIX I

ADDITIONAL RESULTS CHAPTER 5

I.1. CORRELATION: ASD SAMPLE & EEG THETA, LOWER ALPHA & UPPER ALPHA ACTIVITY ($N = 12$)

Pearson correlations were conducted to investigate relationship between social and non-social processing in the three EEG frequency bands and autism symptomatology as measured on the ADOS: reciprocal social interaction, communication, stereotyped behaviours and restricted interests and play, in the ASD group. Non-social and social theta, lower alpha and upper alpha activity was calculated by calculating the mean of hemispheric activity. Holm-Bonferroni sequential correction was used to correct for Type 1 error due to the large number of analyses conducted (Gaetano, 2013; Holm, 1979). Corrected values revealed no significant correlations between EEG activity and ADOS domain or total scores.[11]

---

[11] The tables are presented based on region only for aesthetic purposes and increase ease of reader.

	Non-Social			Social		
	Theta	Lower Alpha	Theta	Lower Alpha	Theta	Lower Alpha
Communication	0.16	0.29	-0.04	0.05	0.09	-0.03
Reciprocal Social Interaction	0.35	0.31	-0.25	0.31	0.37	-0.20
ADOS Total Score	0.28	0.31	-0.16	0.20	0.25	-0.13
Play	0.33	0.40	-0.24	0.30	0.54	-0.27
Stereotyped Interests and Repetitive Behaviours	0.37	0.43	0.06	0.30	0.44	0.02

All p-values corrected using Holm-Bonferrioni correction. No significant correlations were found.

Table I.2: *Correlation between pre-treatment child characteristics of autism severity as measured on the ADOS-G and social and non-social processing measured on EEG oscillations of theta, lower alpha and upper alpha frequency bands over the Temporal-Parietal Junction (TPJ) region.*

	Non-Social			Social		
	Theta	Lower Alpha	Theta	Lower Alpha	Theta	Lower Alpha
Communication	-0.08	0.07	-0.24	-0.25	-0.30	-0.28
Reciprocal Social Interaction	0.13	0.09	-0.44	0.05	0.07	-0.35
ADOS Total Score	0.04	0.08	-0.36	-0.09	-0.11	-0.33
Play	-0.02	0.13	-0.46	-0.10	0.22	-0.41
Stereotyped Interests and Repetitive Behaviours	0.06	0.11	-0.29	-0.10	0.00	-0.26

All p-values corrected using Holm-Bonferrioni correction. No significant correlations were found.

Table I.3: *Correlation between pre-treatment child characteristics of autism severity as measured on the ADOS-G and social and non-social processing measured on EEG oscillations of theta, lower alpha and upper alpha frequency bands over the Orbitofrontal Cortex (OFC) region.*

	Non-Social			Social		
	Theta	Lower Alpha	Theta	Lower Alpha	Theta	Lower Alpha
Communication	0.23	0.46	0.13	0.21	0.39	0.18
Reciprocal Social Interaction	0.32	0.38	-0.07	0.38	0.50	-0.02
ADOS Total Score	0.29	0.44	0.02	0.31	0.47	0.08
Play	0.26	0.39	-0.16	0.35	0.53	-0.10
Stereotyped Interests and Repetitive Behaviours	0.31	0.47	0.09	0.39	0.59	0.14

All p-values corrected using Holm-Bonferrioni correction. No significant correlations were found.

Table I.4: *Correlation between pre-treatment child characteristics of autism severity as measured on the ADOS-G and social and non-social processing measured on EEG oscillations of theta, lower alpha and upper alpha frequency bands over the Dorsolateral Prefrontal Cortex (dlPFC) region.*

	Non-Social			Social		
	Theta	Lower Alpha	Theta	Lower Alpha	Theta	Lower Alpha
Communication	0.30	0.48	0.12	0.21	0.31	0.09
Reciprocal Social Interaction	0.35	0.39	-0.09	0.37	0.46	-0.06
ADOS Total Score	0.35	0.45	0.01	0.31	0.41	0.01
Play	0.29	0.40	-0.14	0.39	0.56	-0.01
Stereotyped Interests and Repetitive Behaviours	0.36	0.49	0.11	0.47	0.62	0.22

All p-values corrected using Holm-Bonferrioni correction. No significant correlations were found.

I.2: CORRELATION: TREATMENT & WAIT-LIST CONTROL GROUPS (*N*=14).

To examine association between changes in imitation and EEG activity, theta, lower alpha and upper alpha activity for social and non-social condition in the four regions of Central, TPJ, OFC and dlPFC were compared with change scores on Unstructured Imitation Assessment (UIA) using Pearson correlations. Corrected values using Holm-Bonferroni correction did not reveal any significant correlations.

Table I.5: Correlation between change in spontaneous imitation, object imitation and gesture imitation scores and social and non-social processing measured on EEG oscillations of theta, lower alpha and upper alpha frequency bands over the Central channels.

	Non-Social			Social		
	Theta	Lower Alpha	Upper Alpha	Theta	Lower Alpha	Upper Alpha
Spontaneous Imitation Total	-0.02	0.21	0.19	-0.04	0.12	0.08
Object Imitation	-0.04	0.24	0.08	0.00	0.17	0.04
Gesture Imitation	0.02	0.06	0.23	-0.08	-0.02	0.08

All p-values corrected using Holm-Bonferrioni correction. No significant correlations were found.

Table I.6: Correlation between change in spontaneous imitation, object imitation and gesture imitation scores and social and non-social processing measured on EEG oscillations of theta, lower alpha and upper alpha frequency bands over the Temporal-Parietal Junction region.

	Non-Social			Social		
	Theta	Lower Alpha	Upper Alpha	Theta	Lower Alpha	Upper Alpha
Spontaneous Imitation Total	-0.07	0.09	0.15	-0.10	0.03	-0.001
Object Imitation	-0.12	0.13	0.03	-0.11	0.07	-0.05
Gesture Imitation	0.04	-0.01	0.23	-0.04	-0.05	0.07

All p-values corrected using Holm-Bonferrioni correction. No significant correlations were found.

Table I.7: Correlation between change in spontaneous imitation, object imitation and gesture imitation scores and social and non-social processing measured on EEG oscillations of theta, lower alpha and upper alpha frequency bands over the Orbitofrontal Cortex (OFC) region.

	Non-Social			Social		
	Theta	Lower Alpha	Upper Alpha	Theta	Lower Alpha	Upper Alpha
Spontaneous Imitation Total	0.02	0.28	0.25	-0.01	0.28	0.22
Object Imitation	-0.14	0.24	0.08	-0.01	0.26	0.08
Gesture Imitation	0.23	0.18	0.33	0.001	0.15	0.30

All p-values corrected using Holm-Bonferrioni correction. No significant correlations were found.

Table I.8: Correlation between change in spontaneous imitation, object imitation and gesture imitation scores and social and non-social processing measured on EEG oscillations of theta, lower alpha and upper alpha frequency bands over the Dorsolateral Prefrontal Cortex (dlPFC) region.

	Non-Social			Social		
	Theta	Lower Alpha	Upper Alpha	Theta	Lower Alpha	Upper Alpha
Spontaneous Imitation Total	-0.01	0.27	0.19	0.05	0.28	0.21
Object Imitation	-0.14	0.23	0.03	0.02	0.25	0.07
Gesture Imitation	0.17	0.17	0.29	0.07	0.16	0.28

All p-values corrected using Holm-Bonferrioni correction. No significant correlations were found.

APPENDIX J

POWER CALCULATION

J.1: POWER CALCULATION

In order to ascertain the minimum number of participants required to have a study with sufficient power, power analysis was conducted using G*Power. Eta-square from the previous pilot RCT (Ingersoll, 2010b) was used to calculate the minimum effect size. Analysis revealed a minimum sample of 24 to be able to observe an effect at 0.80.

Figure J.1: Graph showing minimum number of participants needed, 24, for the study to have sufficient statistical power calculated at an effect size of $\eta_p^2 = 0.29$ (as reported in the previous RCT; Ingersoll, 2010b).
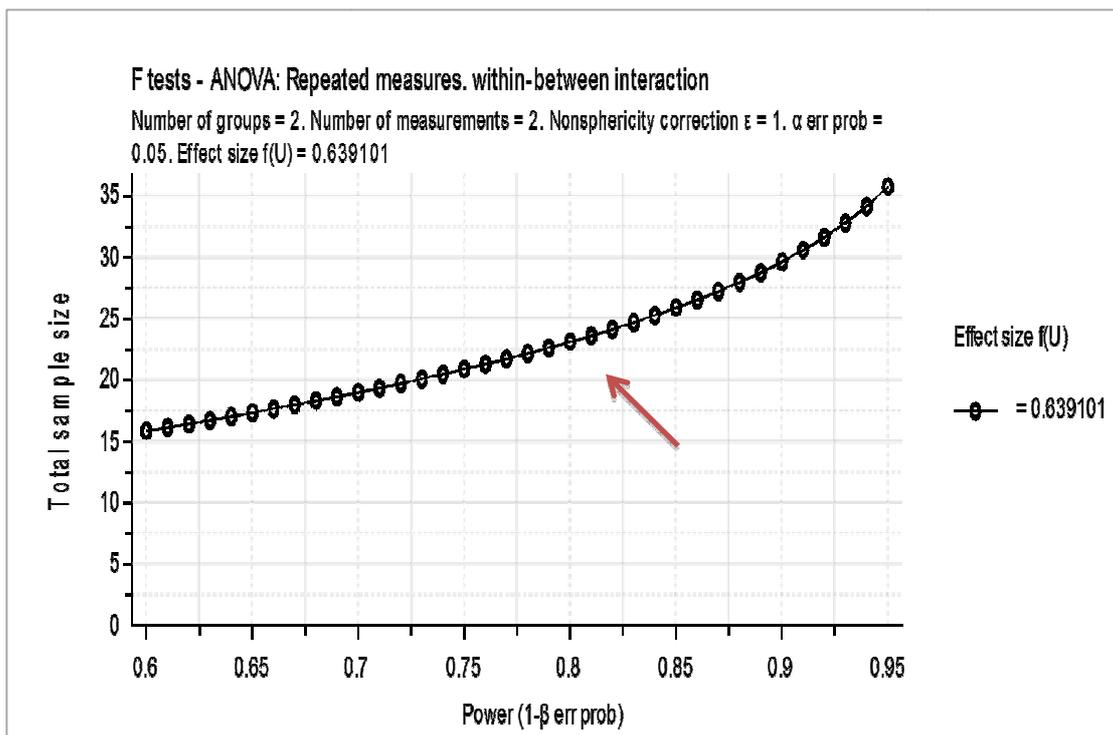
REFERENCES

Adolphs, R. (2009). The social brain: Neural basis of social knowledge. *Annual Review of Psychology, 60*, 693-716.

Ahmadlou, M., & Adeli, H. (2014). Electroencephalograms in diagnosis of autism. In V. B. Patel, V. R. Preedy, & C. R. Martin, (Eds.) *Comprehensive Guide to Autism* (pp. 327-343). New York: Springer.

Akshoomoff, N. (2006). Use of the Mullen Scales of Early Learning for the assessment of young children with autism spectrum disorders. *Child Neuropsychology, 12*, 269-277.

Aldred, C., Green J., & Adams, C. (2004). A new social communication intervention for children with autism: A pilot randomised controlled treatment study suggesting effectiveness. *Journal of Child Psychology & Psychiatry*, *45*, 1420–1430.

Allen, C., Silove, N., Williams, K., & Hutchins, P. (2007). Validity of the social communication questionnaire in assessing risk of autism in preschool children with developmental problems. *Journal of Autism and Developmental Disorders, 37*, 1272-1278.

Allison, C., Baron-Cohen, S., Wheelwright, S., Charman, T., Richler, J., Pasco, G., & Brayne, C. (2008). The Q-CHAT (Quantitative CHecklist for Autism in Toddlers): A normally distributed quantitative measure of autistic traits at 18–24 months of age: Preliminary report. *Journal of Autism and Developmental Disorders, 38*, 1414-1425.

Alpert, C. L., & Kaiser, A. P. (1992). Training parents as milieu language teachers. *Journal of Early intervention*, *16*, 31-52.

American Psychiatric Association. (2013). Diagnostic and statistical manual of mental disorders: DSM-5. Washington, D.C.: American Psychiatric Association.

Amodio, D. M., & Frith, C. D. (2006). Meeting of minds: The medial frontal cortex and social cognition. *Nature Reviews Neuroscience, 7*, 268-277.

Aoki, Y., Cortese, S., & Tansella, M. (2015). Neural bases of atypical emotional face processing in autism: A meta-analysis of fMRI studies. *The World Journal of Biological Psychiatry*, *16,* 1-10.

Baron-Cohen, S., Ring, H. A., Bullmore, E. T., Wheelwright, S., Ashwin, C., & Williams, S. (2000). The amygdala theory of autism. *Neuroscience & Biobehavioral Reviews, 24*, 355-364.

Baron-Cohen, S., Ring, H. A., Wheelwright, S., Bullmore, E. T., Brammer, M. J., Simmons, A., & Williams, S. C. (1999). Social intelligence in the normal and autistic brain: an fMRI study. *European Journal of Neuroscience, 11*, 1891-1898.

Bastiaansen, J. A., Thioux, M., Nanetti, L., van der Gaag, C., Ketelaars, C., Minderaa, R., & Keysers, C. (2011). Age-related increase in inferior frontal gyrus activity and social functioning in autism spectrum disorder. *Biological Psychiatry, 69*, 832-838.

Bates, E., & Dick, F. (2002). Language, gesture, and the developing brain. *Developmental Psychobiology, 40*, 293-310.

Bekkedal, M. Y., Rossi, J., & Panksepp, J. (2011). Human brain EEG indices of emotions: Delineating responses to affective vocalizations by measuring frontal theta event-related synchronization. *Neuroscience & Biobehavioral Reviews, 35*, 1959-1970.

Bekkering, H., Wohlschlager, A., & Gattis, M. (2000). Imitation of gestures in children is goal-directed. *The Quarterly Journal of Experimental Psychology: Section A, 53*, 153-164.

Belger, A., Carpenter, K. L., Yucel, G. H., Cleary, K. M., & Donkers, F. C. (2011). The neural circuitry of autism. *Neurotoxicity Research, 20*, 201-214.

Ben-Sasson, A., Hen, L., Fluss, R., Cermak, S. A., Engel-Yeger, B., & Gal, E. (2009). A meta-analysis of sensory modulation symptoms in individuals with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *39*, 1-11.

Bernier, R., Aaronson, B., & McPartland, J. (2013). The role of imitation in the observed heterogeneity in EEG mu rhythm in autism and typical development. *Brain and Cognition, 82*, 69-75.

Bernier, R., Dawson, G., Webb, S., & Murias, M. (2007). EEG mu rhythm and imitation impairments in individuals with autism spectrum disorder. *Brain and Cognition, 64*, 228-237.

Billeci, L., Sicca, F., Maharatna, K., Apicella, F., Narzisi, A., Campatelli, G., . . . Muratori, F. (2013). On the application of quantitative EEG for characterizing autistic brain: a systematic review. *Frontiers in Human Neuroscience, 5*:442. doi:10.3389/fnhum.2013.00442

Bird, G., Leighton, J., Press, C., & Heyes, C. (2007). Intact automatic imitation of human and robot actions in autism spectrum disorders. *Proceedings of the Royal Society of London B: Biological Sciences, 274*, 3027-3031.

Bishop, S. L., Guthrie, W., Coffing, M., & Lord, C. (2011). Convergent validity of the Mullen Scales of Early Learning and the Differential Ability Scales in children with autism spectrum disorders. *American Journal on Intellectual and Developmental Disabilities, 116*, 331-343.

Bishop, S. L., Richler, J., & Lord, C. (2006). Association between restricted and repetitive behaviors and nonverbal IQ in children with autism spectrum disorders. *Child Neuropsychology, 12*, 247-267.

Bloom, L., Hood, L., & Lightbown, P. (1974). Imitation in language development: If, when, and why. *Cognitive Psychology, 6*, 380-420.

Blumberg, S. J., Bramlett, M. D., Kogan, M. D., Schieve, L. A., Jones, J. R., & Lu, M. C. (2013). Changes in prevalence of parent-reported autism spectrum disorder in school-aged US children: 2007 to 2011–2012. *National Health Statistics Reports, 65*, 1-7.

Bodison, S. C. (2015). Developmental dyspraxia and the play skills of children with autism. *American Journal of Occupational Therapy*, *69*(5), 6905185060p1-6905185060p6.

Braadbaart, L., Williams, J. H., & Waiter, G. D. (2013). Do mirror neuron areas mediate mu rhythm suppression during imitation and action observation? *International Journal of Psychophysiology, 89*, 99-105.

Burgess, A. P., & Gruzelier, J. H. (1997). Short duration synchronization of human theta rhythm during recognition memory. *Neuroreport*, *8*(4), 1039-1042.

Butterworth, G. (1999). Neonatal imitation: Existence, mechanisms and motives. In J. Nadel & G. Butterworth (Ed.), *Imitation in infancy* (pp. 63-88). New York, NY: Cambridge University Press.

Byrne, R. W., & Russon, A. E. (1998). Learning by imitation: a hierarchical approach. *Behavioral and Brain Sciences, 21*, 667-684.

Camarata, S. (2014). Early identification and early intervention in autism spectrum disorders: Accurate and effective? *International Journal of Speech-Language Pathology*, *16*, 1-10.

Campatelli, G., Federico, R., Apicella, F., Sicca, F., & Muratori, F. (2013). Face processing in children with ASD: Literature review. *Research in Autism Spectrum Disorders, 7*, 444-454.

Cardon, T. A., & Wilcox, M. J. (2011). Promoting imitation in young children with autism: A comparison of reciprocal imitation training and video modeling. *Journal of Autism and Developmental Disorders, 41*, 654-666.

Carpenter, M., Nagell, K., Tomasello, M., Butterworth, G., & Moore, C. (1998). Social Cognition, Joint Attention, and Communicative Competence from 9 to 15 Months of Age. *Monographs of the Society for Research in Child Development, 63*, 1-174.

Carpenter, M., Pennington, B. F., & Rogers, S. J. (2001). Understanding of others' intentions in children with autism. *Journal of Autism and Developmental Disorders, 31*, 589-599.

Carpenter, M., Pennington, B. F., & Rogers, S. J. (2002). Interrelations among social-cognitive skills in young children with autism. *Journal of Autism and Developmental Disorders, 32*, 91-106.

Carroll, K.M. & Rounsaville, B. J. (2008). Efficacy and effectiveness in developing treatment manuals. In A.M. Nezu & C.M. Nezu, *Evidence-based Outcome Research: A practical guide to conducting Randomized Controlled Trials for psychosocial interventions* (pp. 219-243), New York: Oxford University Press.

Carter, A. S., Messinger, D. S., Stone, W. L., Celimli, S., Nahmias, A. S., & Yoder, P. (2011). A randomized controlled trial of Hanen's 'More than Words' in toddlers with early autism symptoms. *Journal of Child Psychology and Psychiatry*, *52*, 741–752.

Casenhiser, D. M., Shanker, S. G., & Stieben, J. (2013). Learning through interaction in children with autism: preliminary data from a social-communication-based intervention. *Autism, 17*, 220-241.

Centers for Disease Control and Prevention (2014) Prevalence of autism spectrum disorder among children aged 8 years - Autism and developmental disabilities monitoring network, 11 sites, United States, 2010. *MMWR,* 63(SS02): 1–21.

Čeponienė, R., Lepistö, T., Shestakova, A., Vanhala, R., Alku, P., Näätänen, R., & Yaguchi, K. (2003). Speech–sound-selective auditory impairment in children with autism: they can perceive but do not attend. *Proceedings of the National Academy of Sciences, 100*, 5567-5572.

Charman, T. (2006). Imitation and the development of language. In S.J. Rogers & J.H.G. Williams (Eds.), *Imitation and the social mind: Autism and typical development* (pp. 96-117). New York: The Guilford Press.

Charman, T., Baron-Cohen, S., Swettenham, J., Baird, G., Cox, A., & Drew, A. (2000). Testing joint attention, imitation, and play as infancy precursors to language and theory of mind. *Cognitive Development, 15*, 481-498.

Charman, T., Pickles, A., Simonoff, E., Chandler, S., Loucas, T., & Baird, G. (2011). IQ in children with autism spectrum disorders: data from the Special Needs and Autism Project (SNAP). *Psychological medicine*, *41*(03), 619-627.

Charman, T., Swettenham, J., Baron-Cohen, S., Cox, A., Baird, G., & Drew, A. (1997). Infants with autism: An investigation of empathy, pretend play, joint attention, and imitation. *Developmental Psychology, 33*, 781.

Chevallier, C., Kohls, G., Troiani, V., Brodkin, E. S., & Schultz, R. T. (2012). The social motivation theory of autism. *Trends in Cognitive Sciences, 16*, 231-239.

Chiang, H. M., & Carter, M. (2008). Spontaneity of communication in individuals with autism. *Journal of Autism and Developmental Disorders*, *38*, 693-705.

Christou, A. I., Endo, S., Wallis, Y., Bair, H., Zeegers, M. P., & McCleery, J. P. (2015). Variation in serotonin transporter linked polymorphic region (5-HTTLPR) short/long genotype modulates resting frontal electroencephalography asymmetries in children. *Development and Psychopathology*, 1-12.

Cicchetti, D. V. (1994). Guidelines, criteria, and rules of thumb for evaluating normed and standardized assessment instruments in psychology. *Psychological Assessment*, *6*, 284.

Coan, J. A., & Allen, J. J. (2003a). The state and trait nature of frontal EEG asymmetry in emotion. In K. Hugdahl & R.J. Davidson (Eds.) *The Asymmetrical Brain* (pp. 565–615). Cambridge, MA: MIT Press.

Coan, J.A., & Allen., J. J. (2003b). Frontal EEG asymmetry and the behavioral activation and inhibition systems. *Psychophysiology, 40*, 106-114.

Coan, J. A., & Allen, J. J. (2004). Frontal EEG asymmetry as a moderator and mediator of emotion. *Biological Psychology, 67*, 7-50.

Coben, R., Clarke, A. R., Hudspeth, W., & Barry, R. J. (2008). EEG power and coherence in autistic spectrum disorder. *Clinical Neurophysiology, 119*, 1002-1009.

Concato, J., Shah, N., & Horwitz, R. I. (2000). Randomized, controlled trials, observational studies, and the hierarchy of research designs. *New England Journal of Medicine, 342*, 1887-1892.

Cook, R., Bird, G., Catmur, C., Press, C., & Heyes, C. (2014). Mirror neurons: From origin to function. *Behavioral and Brain Sciences, 37*, 177-192.

Corbett, B. A., Swain, D. M., Coke, C., Simon, D., Newsom, C., Houchins Juarez, N., ... & Song, Y. (2014). Improvement in social deficits in autism spectrum disorders using a theatre based, peer mediated intervention. *Autism Research*, *7*, 4-16.

Crano, W. D., & Lac, A. (2012). The evolution of research methodologies in social psychology: A historical analysis. In A. W. Kruglanski, & W. Stroebe, (Eds.). *Handbook of The History of Social Psychology* (pp. 159-174). New York: Psychology Press.

Dapretto, M., Davies, M. S., Pfeifer, J. H., Scott, A. A., Sigman, M., Bookheimer, S. Y., & Iacoboni, M. (2005). Understanding emotions in others: Mirror neuron dysfunction in children with autism spectrum disorders. *Nature Neuroscience, 9*, 28-30.

Davidson, R. J. (1988). EEG measures of cerebral asymmetry: Conceptual and methodological issues. *International Journal of Neuroscience, 39*, 71-89.

Davidson, R. J. (1992). Anterior cerebral asymmetry and the nature of emotion. *Brain and Cognition, 20*, 125-151.

Davidson, R. J. (2004). What does the prefrontal cortex "do" in affect: perspectives on frontal EEG asymmetry research. *Biological Psychology, 67*, 219-234.

Dawson, G. (2008). Early behavioral intervention, brain plasticity, and the prevention of autism spectrum disorder. *Development and Psychopathology, 20*, 775-803.

Dawson, G., & Adams, A. (1984). Imitation and social responsiveness in autistic children. *Journal of Abnormal Child Psychology, 12*, 209-226.

Dawson, G., & Burner, K. (2011). Behavioral interventions in children and adolescents with autism spectrum disorder: a review of recent findings. *Current Opinion in Pediatrics*, *23*, 616-620.

Dawson, G., Carver, L., Meltzoff, A. N., Panagiotides, H., McPartland, J., & Webb, S. J. (2002). Neural correlates of face and object recognition in young children with autism spectrum disorder, developmental delay, and typical development. *Child Development, 7*, 700-717.

Dawson, G., Finley, C., Phillips, S., Galpert, L., & Lewy, A. (1988). Reduced P3 amplitude of the event-related brain potential: Its relationship to language ability in austism. *Journal of Autism and Developmental Disorders*, *18*, 493-504.

Dawson, G., Jones, E. J., Merkle, K., Venema, K., Lowy, R., Faja, S., . . . Winter, J. (2012). Early behavioral intervention is associated with normalized brain activity in young children with autism. *Journal of the American Academy of Child & Adolescent Psychiatry, 51*, 1150-1159.

Dawson, G., Klinger, L. G., Panagiotides, H., Lewy, A., & Castelloe, P. (1995). Subgroups of autistic children based on social behavior display distinct patterns of brain activity. *Journal of Abnormal Child Psychology, 23*, 569-583.

Dawson, G., Rogers, S., Munson, J., Smith, M., Winter, J., Greenson, J., et al. (2010). Randomized, controlled trial of an intervention for toddlers with autism: The Early Start Denver Model. *Pediatrics*, *125*, 17-23.

Dawson, G., Webb, S. J., & McPartland, J. (2005). Understanding the nature of face processing impairment in autism: insights from behavioral and electrophysiological studies. *Developmental Neuropsychology, 27*, 403-424.

Dawson, G., Webb, S. J., Wijsman, E., Schellenberg, G., Estes, A., Munson, J., & Faja, S. (2005). Neurocognitive and electrophysiological evidence of altered face processing in parents of children with autism: Implications for a model of abnormal development of social brain circuitry in autism. *Development and Psychopathology, 17*, 679-697.

DeBoer, T., Scott, L. S., & Nelson, C. A. (2007). Methods for acquiring and analyzing infant event-related potentials. In M. De Haan (Ed.). *Infant EEG and event-related potentials* (pp. 5-37) East Sussex: Psychology Press.

De Haan, M. (Ed.). (2007). *Infant EEG and Event-Related Potentials*. East Sussex:Psychology Press.

De Haan, M., & Nelson, C. A. (1999). Brain activity differentiates face and object processing in 6-month-old infants. *Developmental Psychology, 35*, 1113-1121.

DeMyer, M. K., Alpern, G. D., Barton, S., DeMyer, W. E., Churchill, D. W., Hingtgen, J. N., . . . Kimberlin, C. (1972). Imitation in autistic, early schizophrenic, and non-psychotic subnormal children. *Journal of Autism and Childhood Schizophrenia, 2*, 264-287.

DeMeyer, M.K., Hingtgen, J.N., & Jackson, R.K. (1981). Infantile autism reviewed: A decade of research. *Schizophrenia Bulletin, 7*, 388-451.

Di Martino, A., Ross, K., Uddin, L. Q., Sklar, A. B., Castellanos, F. X., & Milham, M. P. (2009). Functional brain correlates of social and nonsocial processes in autism spectrum disorders: An activation likelihood estimation meta-analysis. *Biological Psychiatry, 65*, 63-74.

Eckerman, C. O., & Didow, S. M. (1996). Nonverbal imitation and toddlers' mastery of verbal means of achieving coordinated action. *Developmental Psychology, 32*, 141-152.

Edwards, L. A. (2014). A meta analysis of imitation abilities in individuals with autism spectrum disorders. *Autism Research, 7*, 363-380.

Elliot, N. A., (2015). *Effective Interventions for Children and Adolescents with Autism Spectrum Disorders and Other Special Educational Needs.* Doctoral dissertation, University of Birmingham.

Elsabbagh, M., Divan, G., Koh, Y. J., Kim, Y. S., Kauchali, S., Marcín, C., ... & Yasamy, M. T. (2012). Global prevalence of autism and other pervasive developmental disorders. *Autism Research*, *5*, 160-179.

Enticott, P. G., Kennedy, H. A., Rinehart, N. J., Tonge, B. J., Bradshaw, J. L., Taffe, J. R., . . . Fitzgerald, P. B. (2012). Mirror neuron activity associated with social impairments but not age in autism spectrum disorder. *Biological Psychiatry, 71*, 427-433.

Estes, A., Munson, J., Rogers, S. J., Greenson, J., Winter, J., & Dawson, G. (2015). Long-term outcomes of early intervention in 6-year-old children with autism spectrum disorder. *Journal of the American Academy of Child & Adolescent Psychiatry, 54*, 580-587.

Faja, S., Webb, S. J., Jones, E., Merkle, K., Kamara, D., Bavaro, J., ... & Dawson, G. (2012). The effects of face expertise training on the behavioral performance and brain activity of adults with high functioning autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *42*, 278-293.

Fan, Y. T., Decety, J., Yang, C. Y., Liu, J. L., & Cheng, Y. (2010). Unbroken mirror neurons in autism spectrum disorders. *Journal of Child Psychology and Psychiatry, 51*, 981-988.

Farroni, T., Johnson, M. H., & Csibra, G. (2004). Mechanisms of eye gaze perception during infancy. *Journal of Cognitive Neuroscience, 16*, 1320-1326.

Fishman, I., Datko, M., Cabrera, Y., Carper, R. A., & Müller, R. A. (2015). Reduced integration and differentiation of the imitation network in autism: A combined functional connectivity magnetic resonance imaging and diffusion weighted imaging study. *Annals of Neurology, 78*, 958-969.

Fombonne, E. (2005). The changing epidemiology of autism. *Journal of Applied Research in Intellectual Disabilities*, *18*, 281-294.

Foxx, M.R. (1996). Twenty years of applied behavior analysis in treating the most severe problem behavior: Lessons learned. *The Behavior Analyst. 19*, 225 – 235.

Frith, U. (1991). *Autism and Asperger syndrome*. Cambridge, UK: Cambridge

University Press.

Frith, U., & Frith, C. (2010). The social brain: allowing humans to boldly go where no other species has been. *Philosophical Transactions of the Royal Society of London B: Biological Sciences*, *365*, 165-176.

Gabard-Durnam, L., Tierney, A. L., Vogel-Farley, V., Tager-Flusberg, H., & Nelson, C. A. (2013). Alpha asymmetry in infants at risk for autism spectrum disorders. *Journal of Autism and Developmental Disorders, 45*, 473-480.

Gaetano J. (2013). Holm-Bonferroni sequential correction: An EXCEL calculator (1.2) [Microsoft Excel workbook]. Retrieved from https://www.researchgate.net/publication/242331583_Holm-Bonferroni_Sequential_Correction_An_EXCEL_Calculator_-_Ver._1.2.

Galati, G., Committeri, G., Spitoni, G., Aprile, T., Di Russo, F., Pitzalis, S., & Pizzamiglio, L. (2008). A selective representation of the meaning of actions in the auditory mirror system. *Neuroimage, 40*, 1274-1286.

García-Primo, P., Hellendoorn, A., Charman, T., Roeyers, H., Dereu, M., Roge, B., . . Van Daalen, E. (2014). Screening for autism spectrum disorders: State of the art in Europe. *European Child & Adolescent Psychiatry, 23*, 1005-1021.

Gasser, T., Verleger, R., Bächer, P., & Sroka, L. (1988). Development of the EEG of school-age children and adolescents. I. Analysis of band power. *Electroencephalography and Clinical Neurophysiology, 69*, 91-99.

Geangu, E., Quadrelli, E., Lewis, J. W., Cassia, V. M., & Turati, C. (2015). By the sound of it. An ERP investigation of human action sound processing in 7 month-old infants. *Developmental Cognitive Neuroscience*, *12*, 134-144.

Gerson, S. A., Bekkering, H., & Hunnius, S. (2015). Short-term motor training, but not observational training, alters neurocognitive mechanisms of action processing in infancy. *Journal of Cognitive Neuroscience*, 27, 1207-1214.

Gervais, H., Belin, P., Boddaert, N., Leboyer, M., Coez, A., Sfaello, I., . . . Zilbovicius, M. (2004). Abnormal cortical voice processing in autism. *Nature Neuroscience, 7*, 801-802.

Gevins, A., Smith, M. E., McEvoy, L., & Yu, D. (1997). High-resolution EEG mapping of cortical activation related to working memory: effects of task difficulty, type of processing, and practice. *Cerebral Cortex, 7*, 374-385.

Giusti, M., Bozzacchi, C., Pizzamiglio, L., & Di Russo, F. (2010). Sight and sound of actions share a common neural network. *European Journal of Neuroscience, 32*, 1754-1764.

Gliga, T., Jones, E. J., Bedford, R., Charman, T., & Johnson, M. H. (2014). From early markers to neuro-developmental mechanisms of autism. *Developmental Review, 34*, 189-207.

Gopnik, A., & Meltzoff, A. N. (1994). Minds, bodies, and persons: Young children's understanding of the self and others as reflected in imitation and theory of mind research. In S. T. Parker, R. W. Mitchell & M. L. Boccia (Eds.) *Self-awareness in animals and humans: Developmental perspectives* (pp. 161). New York: Cambridge University Press.

Graham, K. A. (2014). *Social processing, frontal asymmetries and the effect of emotion based disorders upon brain functioning and behaviour in infancy.* Doctoral dissertation, University of Birmingham.

Granpeesheh, D., Dixon, D. R., Tarbox, J., Kaplan, A. M., & Wilke, A. E. (2009). The effects of age and treatment intensity on behavioral intervention outcomes for children with autism spectrum disorders. *Research in Autism Spectrum Disorders*, *3*, 1014-1022.

Green, J., Charman, T., McConachie, H., Aldred, C., Slonims, V., Howlin, P., . . . Pickles, A. (2010). Parent-mediated communication-focused treatment in children with autism (PACT): A randomised controlled trial. *Lancet, 375*, 2152-2160.

Gresham, F. M., & MacMillan, D. L. (1998). Early intervention project: can its claims be substantiated and its effects replicated? *Journal of Autism and Developmental Disorders, 28*, 5-13.

Grice, S. J., Halit, H., Farroni, T., Baron-Cohen, S., Bolton, P., & Johnson, M. H. (2005). Neural correlates of eye-gaze detection in young children with autism. *Cortex, 41*, 342-353.

Groen, W. B., Zwiers, M. P., van der Gaag, R.-J., & Buitelaar, J. K. (2008). The phenotype and neural correlates of language in autism: An integrative review. *Neuroscience & Biobehavioral Reviews, 32*, 1416-1425.

Grossmann, T., & Johnson, M. H. (2007). The development of the social brain in human infancy. *European Journal of Neuroscience, 25*, 909-919.

Grossmann, T., Striano, T., & Friederici, A. D. (2005). Infants' electric brain responses to emotional prosody. *Neuroreport, 16*, 1825-1828.

Grossmann, T., Striano, T., & Friederici, A. D. (2006). Crossmodal integration of emotional information from face and voice in the infant brain. *Developmental Science, 9*, 309-315.

Goldani, A. A., Downs, S. R., Widjaja, F., Lawton, B., & Hendren, R. L. (2014). Biomarkers in autism. *Frontiers in Psychiatry*, *5*.

Golding, R. (2009). *Early developmental history questionnaire.* National Health Service, UK.

Gonsiorowski, A., Williamson, R. A., & Robins, D. L. (2015). Brief Report: Imitation of Object-Directed Acts in Young Children with Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders*, *46,* 691-697.

Gutstein, S. E., & Sheely, R. K. (2002). Relationship development intervention with young children. London: Jessica Kingsley.

Hadjikhani, N., Joseph, R. M., Snyder, J., & Tager-Flusberg, H. (2006). Anatomical differences in the mirror neuron system and social cognition network in autism. *Cerebral Cortex, 16*, 1276-1282.

Halit, H., De Haan, M., & Johnson, M. (2003). Cortical specialisation for face processing: face-sensitive event-related potential components in 3-and 12-month-old infants. *Neuroimage, 19*, 1180-1193.

Hallgren, K. A. (2012). Computing inter-rater reliability for observational data: An overview and tutorial. *Tutorials in Quantitative Methods for Psychology*, *8*, 23-34.

Hamilton, A. F. D. C. (2013). Reflecting on the mirror neuron system in autism: A systematic review of current theories. *Developmental Cognitive Neuroscience, 3*, 91-105.

Hamilton, A. F. D. C., Brindley, R. M., & Frith, U. (2007). Imitation and action understanding in autistic spectrum disorders: How valid is the hypothesis of a deficit in the mirror neuron system? *Neuropsychologia, 45*, 1859-1868.

Hanson, E., Cerban, B. M., Slater, C. M., Caccamo, L. M., Bacic, J., & Chan, E. (2013). Brief report: Prevalence of attention deficit/hyperactivity disorder among individuals with an autism spectrum disorder. *Journal of Autism and Developmental Disorders, 43*, 1459-1464.

Hari, R., Henriksson, L., Malinen, S., & Parkkonen, L. (2015). Centrality of social interaction in human brain function. *Neuron, 88*, 181-193.

Harris, S. L., & Handleman, J. S. (2000). Age and IQ at intake as predictors of placement for young children with autism: A four-to six-year follow-up. *Journal of Autism and Developmental Disorders*, *30*, 137-142.

Hart, B., & Risley, T. R. (1975). Incidental teaching of language in preschool. *Journal of Applied Behavior Analysis, 8,* 411–420.

Herrington, J. D., Baron-Cohen, S., Wheelwright, S. J., Singh, K. D., Bullmore, E. T., Brammer, M., & Williams, S. C. (2007). The role of MT+/V5 during biological motion perception in Asperger Syndrome: An fMRI study. *Research in Autism Spectrum Disorders, 1*, 14-27.

Heyes, C. (2001). Causes and consequences of imitation. *Trends in Cognitive Sciences*, *5*, 253-261.

Heyes, C. (2010). Where do mirror neurons come from? *Neuroscience & Biobehavioral Reviews, 34*, 575-583.

Heyes, C. (2013). A new approach to mirror neurons: Developmental history, system-level theory and intervention experiments. *Cortex, 49*, 2946-2948.

Hickok, G. (2009). Eight problems for the mirror neuron theory of action understanding in monkeys and humans. *Journal of Cognitive Neuroscience, 21*, 1229-1243.

Hillyard, S. A., Teder-Sälejärvi, W. A., & Münte, T. F. (1998). Temporal dynamics of early perceptual processing. *Current Opinion in Neurobiology*, *8*, 202-210.

Hirai, M., Fukushima, H., & Hiraki, K. (2003). An event-related potentials study of biological motion perception in humans. *Neuroscience Letters, 344*, 41-44.

Hirai, M., Gunji, A., Inoue, Y., Kita, Y., Hayashi, T., Nishimaki, K., . . . Inagaki, M. (2014). Differential electrophysiological responses to biological motion in children and adults

with and without autism spectrum disorders. *Research in Autism Spectrum Disorders, 8*, 1623-1634.

Hirai, M., & Hiraki, K. (2005). An event-related potentials study of biological motion perception in human infants. *Cognitive Brain Research, 22*, 301-304.

Hobson, R. P., & Lee, A. (1999). Imitation and identification in autism. *Journal of Child Psychology and Psychiatry, 40*, 649-659.

Hofmann, S. G., & Smits, J. A. (2008). Cognitive-behavioral therapy for adult anxiety disorders: a meta-analysis of randomized placebo-controlled trials. *The Journal of Clinical Psychiatry, 69*, 621.

Holm, S. (1979). A simple sequential rejective method procedure. *Scandinavian Journal of Statistics, 6*, 65-70.

Honaga, E., Ishii, R., Kurimoto, R., Canuet, L., Ikezawa, K., Takahashi, H., . . . Yoshimine, T. (2010). Post-movement beta rebound abnormality as indicator of mirror neuron system dysfunction in autistic spectrum disorder: an MEG study. *Neuroscience Letters, 478*, 141-145.

Howlin, P., Magiati, I., & Charman, T. (2009). Systematic review of early intensive behavioral interventions for children with autism. *American Journal on Intellectual and Developmental Disabilities*, *114*, 23-41.

Hudson, E., & DeMeyer, M.K. (1968). Food as a reinforcer in educational therapy of autistic children. *Behaviour Research and Therapy, 6,* 37-43.

Hwang, B., & Hughes, C. (2000). The effects of social interactive training on early social communicative skills of children with autism. *Journal of Autism and Developmental Disorders*, *30*, 331-343.

Iacoboni, M. (2005). Neural mechanisms of imitation. *Current Opinion in Neurobiology, 15*, 632-637.

Iacoboni, M. (2009). Neurobiology of imitation. *Current Opinion in Neurobiology, 19*(6), 661-665.

Ingersoll, B. (2008a). The social role of imitation in autism: Implications for the treatment of imitation deficits. *Infants & Young Children, 21*, 107-119.

Ingersoll, B. (2008b). The effect of context on imitation skills in children with autism. *Research in Autism Spectrum Disorders*, 2, 332–340.

Ingersoll, B. (2010a). Teaching social communication: A comparison of naturalistic behavioral and development, social pragmatic approaches for children with autism spectrum disorders. *Journal of Positive Behavior Interventions*, *12*, 33-43.

Ingersoll, B. (2010b). Brief report: Pilot randomized controlled trial of reciprocal imitation training for teaching elicited and spontaneous imitation to children with autism. *Journal of Autism and Developmental Disorders*, *40*, 1154-1160.

Ingersoll, B. (2012). Brief report: Effect of a focused imitation intervention on social functioning in children with autism. *Journal of Autism and Developmental Disorders*, *42*, 1768-1773.

Ingersoll, B., & Gergans, S. (2007). The effect of a parent-implemented imitation intervention on spontaneous imitation skills in young children with autism. *Research in Developmental Disabilities*, *28*, 163-175.

Ingersoll, B., & Lalonde, K. (2010). The impact of object and gesture imitation training on language use in children with autism spectrum disorder. *Journal of Speech, Language, and Hearing Research, 53*, 1040-1051.

Ingersoll, B., Lewis, E., & Kroman, E. (2007). Teaching the imitation and spontaneous use of descriptive gestures in young children with autism using a naturalistic behavioral intervention. *Journal of Autism and Developmental Disorders*, *37*, 1446-1456.

Ingersoll, B., & Meyer, K. (2011). Do object and gesture imitation skills represent independent dimensions in autism?. *Journal of Developmental and Physical Disabilities*, *23*, 421-431.

Ingersoll, B., Meyer, K., Bonter, N., & Jelinek, S. (2012). A comparison of developmental social–pragmatic and naturalistic behavioral interventions on language use and social engagement in children with autism. *Journal of Speech, Language, and Hearing Research, 55*, 1301-1313.

Ingersoll, B., & Schreibman, L. (2006). Teaching reciprocal imitation skills to young children with autism using a naturalistic behavioral approach: Effects on language, pretend play, and joint attention. *Journal of Autism and Developmental Disorders, 36*, 487-505.

Ingersoll, B., Schreibman, L., & Tran, Q. H. (2003). Effect of sensory feedback on immediate object imitation in children with autism. *Journal of Autism and Developmental Disorders, 33*, 673-683.

Ingersoll, B., Walton, K., Carlsen, D., & Hamlin, T. (2013). Social intervention for adolescents with autism and significant intellectual disability: Initial efficacy of Reciprocal Imitation Training. *American Journal on Intellectual and Developmental Disabilities, 118*, 247-261.

Iverson, G. L. (2011). Reliable change index. In *Encyclopedia of clinical neuropsychology* (pp. 2150-2153). Springer New York.

Jeste, S. S., & Nelson, C. A. (2009). Event related potentials in the understanding of autism spectrum disorders: An analytical review. *Journal of Autism and Developmental Disorders, 39*, 495-510.

Jochaut, D., Lehongre, K., Saitovitch, A., Devauchelle, A.-D., Olasagasti, I., Chabane, N., . . . Giraud, A.-L. (2015). Atypical coordination of cortical oscillations in response to speech in autism. *Frontiers in Human Neuroscience, 9*, 171.

Johnson, M. H. (2005). Subcortical face processing. *Nature Reviews Neuroscience, 6*, 766-774.

Jokisch, D., Daum, I., Suchan, B., & Troje, N. F. (2005). Structural encoding and recognition of biological motion: Evidence from event-related potentials and source analysis. *Behavioural Brain Research, 157*, 195-204.

Jones, E. J., Venema, K., Lowy, R., Earl, R. K., & Webb, S. J. (2015). Developmental changes in infant brain activity during naturalistic social experiences. *Developmental Psychobiology, 57*, 842-853.

Kaiser, M. D., Hudac, C. M., Shultz, S., Lee, S. M., Cheung, C., Berken, A. M., . . . Voos, A. C. (2010). Neural signatures of autism. *Proceedings of the National Academy of Sciences, 107*, 21223-21228.

Kanner, L. (1943). 'Autistic distrubances of Affective Contact', *Nervous Child*, 2, 217-250.

Kasari, C. (2002). Assessing change in early intervention programs for children with autism. *Journal of Autism and Developmental Disorders*, *32*, 447-461.

Kasari, C., Freeman, S. F., & Paparella, T. (2006). Joint attention and symbolic play in young children with autism: A randomized controlled intervention study. *Journal of Child Psychology and Psychiatry*, *47,* 611–620.

Kasari, C., Freeman, S., Paparella, T., Wong, C., Kwon, S., & Gulsrud, A. (2005). Early intervention on core deficits in autism. *Clinical Neuropsychiatry*, *2*, 380-388.

Kasari, C., Gulsrud, A., Freeman, S., Paparella, T., & Hellemann, G. (2012). Longitudinal follow-up of children with autism receiving targeted interventions on joint attention and play. *Journal of the American Academy of Child & Adolescent Psychiatry, 51*, 487-495.

Kasari, C., Gulsrud, A. C., Wong, C., Kwon, S., & Locke, J. (2010). Randomized controlled caregiver mediated joint engagement intervention for toddlers with autism. *Journal of Autism and Developmental Disorders, 40,* 1045–1056.

Kasari, C., Kaiser, A., Goods, K., Nietfeld, J., Mathy, P., Landa, R., ... & Almirall, D. (2014). Communication interventions for minimally verbal children with autism: A sequential multiple assignment randomized trial. *Journal of the American Academy of Child & Adolescent Psychiatry*, *53*, 635-646.

Kasari, C., Paparella, T., Freeman, S., & Jahromi, L. B. (2008). Language outcome in autism: randomized comparison of joint attention and play interventions. *Journal of Consulting and Clinical Psychology*, *76*, 125.

Keehn, B., Müller, R. A., & Townsend, J. (2013). Atypical attentional networks and the emergence of autism. *Neuroscience and Biobehavioral Reviews*, *37*, 164-183.

Keenan, M., Dillenburger, K., Doherty, A., Byrne, T., & Gallagher, S. (2010). The experiences of parents during diagnosis and forward planning for children with autism spectrum disorder. *Journal of Applied Research in Intellectual Disabilities, 23*, 390-397.

Klimesch, W. (1999). EEG alpha and theta oscillations reflect cognitive and memory performance: a review and analysis. *Brain Research Reviews, 29*, 169-195.

Klimesch, W. (2012). Alpha-band oscillations, attention, and controlled access to stored information. *Trends In Cognitive Sciences, 16*, 606-617.

Klin, A., Lin, D. J., Gorrindo, P., Ramsay, G., & Jones, W. (2009). Two-year-olds with autism orient to non-social contingencies rather than biological motion. *Nature, 459*, 257-261.

Klinger, L., & Dawson, G. (1992). Facilitating early social and communicative development in children with autism. In S. F. Warren & J. Reichle (Eds.), *Causes and effects in communication and language intervention* (Vol. 1, pp. 157–186). Baltimore, MD: Brookes.

Knyazev, G., Slobodskoj-Plusnin, J., & Bocharov, A. (2009). Event-related delta and theta synchronization during explicit and implicit emotion processing. *Neuroscience, 164*, 1588-1600.

Koegel, R. L., O'Dell, M. C., & Koegel, L. K. (1987). A natural language teaching paradigm for nonverbal autistic children. *Journal of Autism and Developmental Disorders, 17*, 187–200.

Koldewyn, K., Whitney, D., & Rivera, S. M. (2011). Neural correlates of coherent and biological motion perception in autism. *Developmental Science, 14*, 1075-1088.

Krakowski, A. I., Ross, L. A., Snyder, A. C., Sehatpour, P., Kelly, S. P., & Foxe, J. J. (2011). The neurophysiology of human biological motion processing: A high-density electrical mapping study. *Neuroimage, 56*, 373-383.

Kröger, A., Bletsch, A., Krick, C., Siniatchkin, M., Jarczok, T. A., Freitag, C. M., & Bender, S. (2014). Visual event-related potentials to biological motion stimuli in autism spectrum disorders. *Social Cognitive and affective neuroscience*, *9*, 1214-1222.

Kuhl, P., & Rivera-Gaxiola, M. (2008). Neural substrates of language acquisition. *Annual Review of Neuroscience, 31*, 511-534.

Kujala, T., Lepistö, T., & Näätänen, R. (2013). The neural basis of aberrant speech and audition in autism spectrum disorders. *Neuroscience and Biobehavioral Reviews, 37*, 697-704.

Landa, R.J., Holman, K. C., O'Neill, A.H., & Stuart, E. A. (2011). Intervention targeting development of socially synchronous engagement in toddlers with autism spectrum disorder: a randomized controlled trial. *Journal of Child Psychology & Psychiatry, 52*, 13 – 21.

Leekam, S. (2016). Social cognitive impairment and autism: what are we trying to explain? *Philosophical Transactions of The Royal Society B*, *371*(1686), 20150082.

Lepage, J. F., & Théoret, H. (2006). EEG evidence for the presence of an action observation–execution matching system in children. *European Journal of Neuroscience*, *23*, 2505-2510.

Lloyd-Fox, S., Blasi, A., Elwell, C., Charman, T., Murphy, D., & Johnson, M. H. (2013). Reduced neural sensitivity to social stimuli in infants at risk for autism. *Proceedings of the Royal Society of London B: Biological Sciences, 280*(1758), 20123026.

Lombardo, M. V., Chakrabarti, B., Bullmore, E. T., Baron-Cohen, S., & Consortium, M. A. (2011). Specialization of right temporo-parietal junction for mentalizing and its relation to social impairments in autism. *Neuroimage, 56*, 1832-1838.

Loo, S. K., Lenartowicz, A., & Makeig, S. (2016). Research review: Use of EEG biomarkers in child psychiatry research–current state and future directions. *Journal of Child Psychology and Psychiatry, 57*, 4-17.

Lord, C., Risi, S., Lambrecht, L., Cook Jr, E. H., Leventhal, B. L., DiLavore, P. C., ... & Rutter, M. (2000). The Autism Diagnostic Observation Schedule—Generic: A standard measure of social and communication deficits associated with the spectrum of autism. *Journal of autism and developmental disorders*, *30*, 205-223.

Lord, C., Rutter, M., & Le Couteur, A. (1994). Autism Diagnostic Interview-Revised: a revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. *Journal of Autism and Developmental Disorders*, *24*, 659-685.

Lord, C., Wagner, A., Rogers, S., Szatmari, P., Aman, M., Charman, T.,… & Yoder, P. (2005). Challenges in evaluating psychosocial interventions for autistic spectrum disorders. *Journal of Autism and Developmental Disorders*,*35*, 695-708.

Lovaas, O.I. (1987). Behavioral treatment and normal educational and intellectual functioning in young autistic children. *Journal of Consulting and Clinical Psychology, 55*, 3 – 9.

Lovaas, O. I., Freitas, L., Nelson, K., & Whalen, C. (1967). The establishment of imitation and its use for the development of complex behavior in schizophrenic children. *Behaviour Research and Therapy, 5*, 171-181.

Lovaas, O.I., Koegel, R.L., Simmons, J.Q., & Long, J. (1973). Some generalization and follow-up measures on autistic children in behavior therapy. *Journal of Applied Behavior Analysis, 6,* 131-166.

Lovaas, O. I., & Smith, T. (2003). Early and intensive behavioral intervention in autism. In A. E. Kazdin, & J. R. Weisz, (Ed), *Evidence-based psychotherapies for children and adolescents*, (pp. 325-340). New York, NY, US: Guilford Press.

Luck, S. J. (2014). *An introduction to the event-related potential technique*. Massachusetts: MIT press.

Machado, C., Estévez, M., Leisman, G., Melillo, R., Rodríguez, R., DeFina, P., ... & Garófalo, N. (2015). QEEG spectral and coherence assessment of autistic children in three different experimental conditions. *Journal of Autism and Developmental Disorders*, *45*, 406-424.

MacNeil, L. K., & Mostofsky, S. H. (2012). Specificity of dyspraxia in children with autism. *Neuropsychology*, *26*(2), 165.

Mahoney, G., & MacDonald, J. (2005). *Responsive teaching: Parent-mediated developmental intervention*. Cleveland: Case Western Reserve University.

Marsh, L. E., & Hamilton, A. F. D. C. (2011). Dissociation of mirroring and mentalising systems in autism. *Neuroimage, 56*, 1511-1519.

Marsh, L., Pearson, A., Ropar, D., & Hamilton, A. (2013). Children with autism do not overimitate. *Current Biology*, 23, R266–R268.

Marshall, P. J., Bar-Haim, Y., & Fox, N. A. (2002). Development of the EEG from 5 months to 4 years of age. *Clinical Neurophysiology, 113*, 1199-1208.

Marshall, P. J., Bouquet, C. A., Shipley, T. F., & Young, T. (2009). Effects of brief imitative experience on EEG desynchronization during action observation. *Neuropsychologia*, *47*, 2100-2106.

Marshall, P. J., & Meltzoff, A. N. (2011). Neural mirroring systems: Exploring the EEG mu rhythm in human infancy. *Developmental Cognitive Neuroscience*, *1*, 110-123.

Marshall, P. J., Young, T., & Meltzoff, A. N. (2011). Neural correlates of action observation and execution in 14 month old infants: an event related EEG desynchronization study. *Developmental Science*, *14*, 474-480.

Martineau, J., Andersson, F., Barthélémy, C., Cottier, J.-P., & Destrieux, C. (2010). Atypical activation of the mirror neuron system during perception of hand motion in autism. *Brain Research, 1320*, 168-175.

Martineau, J., Cochin, S., Magne, R., & Barthelemy, C. (2008). Impaired cortical activation in autistic children: Is the mirror neuron system involved? *International Journal of Psychophysiology, 68*, 35-40.

Masur, E. F. (2006). Vocal and action imitation by infants and toddlers during dyadic interactions. In S.J. Rogers & J.H.G. Williams (Eds.), *Imitation and the social mind: Autism and typical development* (pp. 27-47). New York: The Guilford Press.

Matson, J. L., Dempsey, T., LoVullo, S. V., & Wilkins, J. (2008). The effects of intellectual functioning on the range of core symptoms of autism spectrum disorders. *Research in Developmental Disabilities, 29*, 341-350.

McCleery, J. P. (2011). Neurodevelopment of social/non-social functioning differences in autism. *European Journal of Neuroscience, 21*, 2575-2585.

McCleery, J. P., Akshoomoff, N., Dobkins, K. R., & Carver, L. J. (2009). Atypical face versus object processing and hemispheric asymmetries in 10-month-old infants at risk for autism. *Biological Psychiatry, 66*, 950-957.

McCleery, J. P., Elliott, N. A., Sampanis, D. S., & Stefanidou, C. A. (2013). Motor development and motor resonance difficulties in autism: relevance to early intervention for language and communication skills. *Frontiers in Integrative Neuroscience, 7.* doi: 10.3389/fnint.2013.00030

McDuffie, A., Turner, L., Stone, W., Yoder, P., Wolery, M., & Ulman, T. (2007). Developmental correlates of different types of motor imitation in young children with

autism spectrum disorders. *Journal of Autism and Developmental Disorders, 37*, 401-412.

McDuffie, A., Yoder, P., & Stone, W. (2005). Prelinguistic predictors of vocabulary in young children with autism spectrum disorders. *Journal of Speech, Language, and Hearing Research, 48*, 1080-1097.

McGee, G. G., Morrier, M. J., & Daly, T. (1999). An incidental teaching approach to early intervention for toddlers with autism. *Journal of the Association for Persons with Severe Handicaps*, 24, 133–146.

McPartland, J., Dawson, G., Webb, S. J., Panagiotides, H., & Carver, L. J. (2004). Event related brain potentials reveal anomalies in temporal processing of faces in autism spectrum disorder. *Journal of Child Psychology and Psychiatry, 45*, 1235-1245.

Meltzoff, A. N., & Decety, J. (2003). What imitation tells us about social cognition: a rapprochement between developmental psychology and cognitive neuroscience. *Philosophical Transactions of the Royal Society of London. Series B: Biological Sciences, 358*, 491-500.

McPartland, J. C., & Jeste, S. S. (2015). Connectivity in context: emphasizing neurodevelopment in autism spectrum disorder. *Biological psychiatry, 77*(9).

Meltzoff, A. N., & Moore, M. K. (1983). Newborn infants imitate adult facial gestures. *Child Development*, 702-709.

Meltzoff, A. N., & Moore, M. K. (1992). Early imitation within a functional framework: The importance of person identity, movement, and development. *Infant Behavior and Development, 15*, 479-505.

Metz, J. R. (1965). Conditioning generalized imitation in autistic children. *Journal of Experimental Child Psychology*, *2*(4), 389-399.

Miyahara, M. (2013). Meta review of systematic and meta analytic reviews on movement differences, effect of movement based interventions, and the underlying neural mechanisms in autism spectrum disorder. *Frontiers in Integrative Neuroscience*, *7*, 16.

Molenberghs, P., Cunnington, R., & Mattingley, J. B. (2009). Is the mirror neuron system involved in imitation? A short review and meta-analysis. *Neuroscience and Biobehavioral Reviews, 33*, 975-980.

Molenberghs, P., Cunnington, R., & Mattingley, J. B. (2012). Brain regions with mirror properties: a meta-analysis of 125 human fMRI studies. *Neuroscience and Biobehavioral Reviews, 36*, 341-349.

Morin, O., & Grezes, J. (2008). What is "mirror" in the premotor cortex? A review. *Neurophysiologie Clinique/Clinical Neurophysiology, 38*, 189-195.

Morley, S., Dowzer, C.N. (2014). Manual for the Leeds Reliable Change Indicator: Simple Excel(tm) applications for the analysis of individual patient and group data. University of Leeds, Leeds, UK.

Mullen, E. (1995). *Mullens Scales of Early Learning (AGS Edition).* Circle Pines: American Guidance Service: Inc.

Muthukumaraswamy, S. D., Johnson, B. W., & McNair, N. A. (2004). Mu rhythm modulation during observation of an object-directed grasp. *Cognitive Brain Research, 19*, 195-201.

Nadel, J., & Butterworth, G. (1999). Introduction: Immediate imitation rehabilitated at last. In J. Nadel & G. Butterworth (Ed.), *Imitation in infancy* (pp. 1-5). New York : Cambridge University Press.

Nadel, J., Guérini, C., Pezé, A., & Rivet, C. (1999). The evolving nature of imitation as a format for communication. In J. Nadel & G. Butterworth (Ed.), *Imitation in infancy* (pp. 209-234). New York, NY, US: Cambridge University Press.

Nadel-Brulfert, J., & Baudonniere, P. (1982). The social function of reciprocal imitation in 2-year-old peers. *International Journal of Behavioral Development, 5*, 95-109.

Nagell, K., Olguin, R. S., & Tomasello, M. (1993). Processes of social learning in the tool use of chimpanzees (Pan troglodytes) and human children (Homo sapiens). *Journal of Comparative Psychology, 107*, 174.

National Research Council (NRC). (2001). *Educating children with autism.* Washington, DC: The National Academies Press.

Nelson, C. A. (2001). The development and neural bases of face recognition. *Infant and Child Development, 10*, 3-18.

Nelson, C. A., & McCleery, J. P. (2008). Use of event-related potentials in the study of typical and atypical development. *Journal of the American Academy of Child & Adolescent Psychiatry*, *47*, 1252-1261.

Nezu, A.M., & Nezu, C.M. (2008). The "Devil Is in The Details": Recognizing and dealing with threats to validity in randomized controlled trials. In A.M. Nezu & C.M. Nezu, *Evidence-based Outcome Research: A practical guide to conducting Randomized Controlled Trials for psychosocial interventions* (pp. 3-24). New York: Oxford University Press.

Nielsen, M., & Dissanayake, C. (2004). Pretend play, mirror self-recognition and imitation: A longitudinal investigation through the second year. *Infant Behavior and Development, 27*, 342-365.

Nielsen, M., Subiaul, F., Galef, B., Zentall, T., & Whiten, A. (2012). Social learning in humans and nonhuman animals: theoretical and empirical dissections. *Journal of Comparative Psychology, 126*, 109.

Nishitani, N., Avikainen, S., & Hari, R. (2004). Abnormal imitation related cortical activation sequences in Asperger's syndrome. *Annals of neurology, 55*, 558-562.

Nock, M.K., Janis, I.B., Wedig, M.M. (2008). Research designs. In A.M. Nezu & C.M. Nezu, *Evidence-based Outcome Research: A practical guide to conducting Randomized Controlled Trials for psychosocial interventions* (pp. 201-218). New York: Oxford University Press.

Oberman, L. M., Hubbard, E. M., McCleery, J. P., Altschuler, E. L., Ramachandran, V. S., & Pineda, J. A. (2005). EEG evidence for mirror neuron dysfunction in autism spectrum disorders. *Cognitive Brain Research, 24*, 190-198.

Oberman, L. M., McCleery, J. P., Hubbard, E. M., Bernier, R., Wiersema, J. R., Raymaekers, R., & Pineda, J. A. (2013). Developmental changes in mu suppression to observed and executed actions in autism spectrum disorders. *Social cognitive and affective neuroscience, 8*, 300-304.

Oberman, L. M., Pineda, J. A., & Ramachandran, V. S. (2007). The human mirror neuron system: A link between action observation and social skills. *Social Cognitive and Affective Neuroscience, 2*, 62-66.

Oberman, L. M., Ramachandran, V. S., & Pineda, J. A. (2008). Modulation of mu suppression in children with autism spectrum disorders in response to familiar or unfamiliar stimuli: the mirror neuron hypothesis. *Neuropsychologia, 46*, 1558-1565.

Odom, S. L., Boyd, B. A., Hall, L. J., & Hume, K. (2010a). Evaluation of comprehensive treatment models for individuals with autism spectrum disorders. *Journal of Autism and Developmental Disorders*, *40*, 425-436.

Odom, S. L., Collet-Klingenberg, L., Rogers, S. J., & Hatton, D. D. (2010b). Evidence-based practices in interventions for children and youth with autism spectrum

disorders. *Preventing school failure: Alternative education for children and youth*, *54*, 275-282.

Orekhova, E. V., Elsabbagh, M., Jones, E., Dawson, G., Charman, T., Johnson, M. H., & Team, B. (2014). EEG hyper-connectivity in high-risk infants is associated with later autism. *Journal of Neurodevelopmental Disorders, 6*, 40-51.

Orekhova, E. V., Stroganova, T. A., Nygren, G., Tsetlin, M. M., Posikera, I. N., Gillberg, C., & Elam, M. (2007). Excess of high frequency electroencephalogram oscillations in boys with autism. *Biological Psychiatry, 62*, 1022-1029.

Orekhova, E. V., Stroganova, T. A., & Posikera, I. N. (1999). Theta synchronization during sustained anticipatory attention in infants over the second half of the first year of life. *International Journal of Psychophysiology, 32*, 151-172.

Orekhova, E. V., Stroganova, T., Posikera, I., & Elam, M. (2006). EEG theta rhythm in infants and preschool children. *Clinical Neurophysiology, 117*, 1047-1062.

Ospina, M. B., Seida, J. K., Clark, B., Karkhaneh, M., Hartling, L., Tjosvold, L., . . . Smith, V. (2008). Behavioural and developmental interventions for autism spectrum disorder: a clinical systematic review. *PloS one, 3*, e3755.

Over, H., & Carpenter, M. (2013). The social side of imitation. *Child Development Perspectives, 7*, 6-11.

Pajareya, K., & Nopmaneejumruslers, K. (2011). A pilot randomized controlled trial of DIR/Floortime™ parent training intervention for pre-school children with autistic spectrum disorders. *Autism, 15*, 563-577.

Pantelis, P. C., Byrge, L., Tyszka, J. M., Adolphs, R., & Kennedy, D. P. (2015). A specific hypoactivation of right temporo-parietal junction/posterior superior temporal sulcus in

response to socially awkward situations in autism. *Social Cognitive and Affective Neuroscience, 10*, 1348-1356.

Paulus, M., Hunnius, S., Van Elk, M., & Bekkering, H. (2012). How learning to shake a rattle affects 8-month-old infants' perception of the rattle's sound: electrophysiological evidence for action-effect binding in infancy. *Developmental Cognitive Neuroscience*, *2*, 90-96.

Pavlova, M. A. (2012). Biological motion processing as a hallmark of social cognition. *Cerebral Cortex*, *22,* 981-995.

Pavlova, M., Lutzenberger, W., Sokolov, A., & Birbaumer, N. (2004). Dissociable cortical processing of recognizable and non-recognizable biological movement: analysing gamma MEG activity. *Cerebral Cortex, 14*, 181-188.

Pelphrey, K. A., Mitchell, T. V., McKeown, M. J., Goldstein, J., Allison, T., & McCarthy, G. (2003). Brain activity evoked by the perception of human walking: controlling for meaningful coherent motion. *The Journal of Neuroscience*, *23*, 6819-6825.

Pelphrey, K. A., Morris, J. P., & McCarthy, G. (2005). Neural basis of eye gaze processing deficits in autism. *Brain, 128*, 1038-1048.

Pelphrey, K. A., Shultz, S., Hudac, C. M., & Vander Wyk, B. C. (2011). Research review: constraining heterogeneity: the social brain and its development in autism spectrum disorder. *Journal of Child Psychology and Psychiatry, 52*, 631-644.

Perry, A., Cummings, A., Geier, J. D., Freeman, N. L., Hughes, S., Managhan, T., ... & Williams, J. (2011). Predictors of outcome for children receiving intensive behavioral intervention in a large, community-based program. *Research in Autism Spectrum Disorders*, *5*, 592-603.

Pineda, J. A. (2005). The functional significance of mu rhythms: translating "seeing" and "hearing" into "doing". *Brain Research Reviews*, *50*, 57-68.

Pineda, J. A. (2008). Sensorimotor cortex as a critical component of an 'extended' mirror neuron system: Does it solve the development, correspondence, and control problems in mirroring?. *Behavioral and Brain Functions*, *4*, 47-64.

Pizzamiglio, L., Aprile, T., Spitoni, G., Pitzalis, S., Bates, E., D'Amico, S., & Di Russo, F. (2005). Separate neural systems for processing action-or non-action-related sounds. *Neuroimage, 24*, 852-861.

Pokorny, J. J., Hatt, N. V., Colombi, C., Vivanti, G., Rogers, S. J., & Rivera, S. M. (2015). The action observation system when observing hand actions in autism and typical development. *Autism Research, 8*, 284-296.

Prizant, B. M., Wetherby, A. M., Rubin, E., & Laurent, A. C. (2003). The SCERTS Model: A family-centered, transactional approach to enhancing communication and socioemotional abilities of young children with ASD. *Infants and Young Children, 16,* 296–316.

Puce, A., & Bertenthal, B. I. (2015). New Frontiers of Investigation in Social Attention. In A. Puce & B. I. Bertenhal (Eds.) *The Many Faces of Social Attention* (pp. 1-19) Switzerland: Springer International.

Raymaekers, R., Wiersema, J. R., & Roeyers, H. (2009). EEG study of the mirror neuron system in children with high functioning autism. *Brain research, 1304*, 113-121.

Reichow, B., Barton, E. E., Boyd, B. A., & Hume, K. (2012). Early intensive behavioral intervention (EIBI) for young children with autism spectrum disorders (ASD). *Cochrane Database Systematic Review, 10*.

Reid, V. M., Csibra, G., Belsky, J., & Johnson, M. H. (2007). Neural correlates of the perception of goal-directed action in infants. *Acta psychologica, 124*, 129-138.

Reid, V., & Dunn, K. (2015). Development of brain mechanisms for social attention in humans. In A. Puce & B. I. Bertenhal (Eds.) *The Many Faces of Social Attention* (pp. 67-91). Switzerland: Springer International.

Reid, V. M., Hoehl, S., & Striano, T. (2006). The perception of biological motion by infants: An event-related potential study. *Neuroscience Letters, 395*, 211-214.

Renty, J., & Roeyers, H. (2006). Satisfaction with formal support and education for children with autism spectrum disorder: The voices of the parents. *Child: Care, Health and Development, 32*, 371-385.

Richard Metz, J. (1965). Conditioning generalized imitation in autistic children. *Journal of Experimental Child Psychology, 2*, 389-399.

Rizzolatti, G., & Fabbri-Destro, M. (2010). Mirror neurons: from discovery to autism. *Experimental Brain Research, 200*, 223-237.

Rizzolatti, G., Fogassi, L., & Gallese, V. (2001). Neurophysiological mechanisms underlying the understanding and imitation of action. *Nature Reviews Neuroscience, 2*, 661-670.

Rogers, S. J. (1996). Brief report: Early intervention in autism. *Journal of Autism and Developmental Disorders*, *26*, 243-246.

Rogers, S. J. (2006). Studies of Imitation in Early Infancy: Findings and Theories. In S.J. Rogers & J.H.G. Williams (Eds.), *Imitation and the social mind: Autism and typical development* (3-26). New York: The Guilford Press.

Rogers, S. J., Bennetto, L., McEvoy, R., & Pennington, B. F. (1996). Imitation and pantomime in high-functioning adolescents with autism spectrum disorders. *Child Development*, *67,* 2060-2073.

Rogers, S. J., & Dawson, G. (2010). *Early Start Denver Model for young children with autism: Promoting language, learning and engagement.* New York: The Guilford Press.

Rogers, S. J., Hepburn, S. L., Stackhouse, T., & Wehner, E. (2003). Imitation performance in toddlers with autism and those with other developmental disorders. *Journal of Child Psychology and Psychiatry, 44*, 763-781.

Rogers, S. J., Herbison, J. M., Lewis, H. C., Pantone, J., & Reis, K. (1986). An approach for enhancing the symbolic, communicative, and interpersonal function for young children with autism or severe emotional handicaps. *Journal of Early Intervention, 10,* 135–148.

Rogers, S. J., & Pennington, B. F. (1991). A theoretical approach to the deficits in infantile autism. *Development and Psychopathology*, *3*, 137-162.

Rogers, S. J., & Williams, J. H. G. (2006). Imitation in autism: Findings and controversies. In S.J. Rogers & J.H.G. Williams (Eds.), *Imitation and the social mind: Autism and typical development* (pp. 277-309). New York: The Guilford Press.

Rogers, S. J., Young, G. S., Cook, I., Giolzetti, A., & Ozonoff, S. (2008). Deferred and immediate imitation in regressive and early onset autism. *Journal of Child Psychology and Psychiatry, 49*, 449-457.

Ruggeri, B., Sarkans, U., Schumann, G., & Persico, A. M. (2014). Biomarkers in autism spectrum disorder: the old and the new. *Psychopharmacology*, *231*, 1201-1216.

Rutter, M., Bailey, A., & Lord, C. (2003). *The social communication questionnaire: Manual*: Western Psychological Services.

Ruysschaert, L., Warreyn, P., Wiersema, J. R., Oostra, A., & Roeyers, H. (2014). Exploring the role of neural mirroring in children with autism spectrum disorder. *Autism Research, 7*, 197-206.

Sabbagh, M. A. (2004). Understanding orbitofrontal contributions to theory-of-mind reasoning: Implications for autism. *Brain and cognition, 55*, 209-219.

Saby, J. N., Meltzoff, A. N., & Marshall, P. J. (2013). Infants' somatotopic neural responses to seeing human actions: I've got you under my skin. *PloS one, 8*, e77905.

Saitovitch, A., Bargiacchi, A., Chabane, N., Brunelle, F., Samson, Y., Boddaert, N., & Zilbovicius, M. (2012). Social cognition and the superior temporal sulcus: implications in autism. *Revue Neurologique, 168*, 762-770.

Salomone, E., Beranová, Š., Bonnet-Brilhault, F., Lauritsen, M. B., Budisteanu, M., Buitelaar, J., . . . Freitag, C. (2016). Use of early intervention for young children with autism spectrum disorder across Europe. *Autism*, *20,* 233-249.

Sallows, G. O., & Graupner, T. D. (2005). Intensive behavioral treatment for children with autism: Four-year outcome and predictors. *American Journal on Mental Retardation*, *110*, 417-438.

Sauseng, P., Klimesch, W., Schabus, M., & Doppelmayr, M. (2005). Fronto-parietal EEG coherence in theta and upper alpha reflect central executive functions of working memory. *International Journal of Psychophysiology, 57*, 97-103.

Schertz, H. H., & Odom, S. L. (2007). Promoting joint attention in toddlers with autism: A parent-mediated approach. *Journal of Autism and Developmental Disorders, 37,* 1562–1575.

Schneider, W., Eschman, A., & Zuccolotto, A. (2002). *E-Prime User's Guide*. Pittsburgh: Psychology Software Tools, Inc.

Schreibman, L. (1997). Theoretical perspectives on behavioral intervention for individuals with autism. In D. J. Cohen & F. R. Volkmar (Eds.) *Handbook of autism and pervasive developmental disorders* (2nd ed., pp. 920–933). New York: Wiley.

Schreibman, L. (2000). Intensive behavioral/psychoeducational treatments for autism: Research needs and future directions. *Journal of Autism and Developmental Disorders*, *30*, 373-378.

Schreibman, L., Dawson, G., Stahmer, A. C., Landa, R., Rogers, S. J., McGee, G. G., . . . Bruinsma, Y. (2015). Naturalistic developmental behavioral interventions: Empirically validated treatments for autism spectrum disorder. *Journal of Autism and Developmental Disorders, 45*, 2411-2428.

Schreibman, L., & Koegel, R. L. (2005). Training for parents of children with autism: Pivotal responses, generalization, and individualization of interventions. In E. D. Hibbs & P. S. Jensen (Eds.) *Psychosocial treatment for child and adolescent disorders: Empirically based strategies for clinical practice* (2nd ed., pp. 605–631). Washington, D. C.: American Psychological Association.

Schultz, R. T. (2005). Developmental deficits in social perception in autism: the role of the amygdala and fusiform face area. *International Journal of Developmental Neuroscience, 23*, 125-141.

Sevlever, M., & Gillis, J. M. (2010). An examination of the state of imitation research in children with autism: Issues of definition and methodology. *Research in Developmental Disabilities, 31*, 976-984.

Shih, P., Shen, M., Öttl, B., Keehn, B., Gaffrey, M. S., & Müller, R.-A. (2010). Atypical network connectivity for imitation in autism spectrum disorder. *Neuropsychologia, 48*, 2931-2939.

Shultz, S., Jones, W., & Klin, A. (2015). Early departures from normative processes of social engagement in infants with autism spectrum disorder. In A. Puce & B. I. Bertenhal

(Eds.) *The Many Faces of Social Attention* (pp. 157-177). Switzerland: Springer International.

Sibbald, B., & Roland, M. (1998). Understanding controlled trials: Why are randomised controlled trials important? *British Medical Journal, 316*, 201.

Simonoff, E., Pickles, A., Charman, T., Chandler, S., Loucas, T., & Baird, G. (2008). Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. *Journal of the American Academy of Child & Adolescent Psychiatry, 47*, 921-929.

Smith, I. M., & Bryson, S. E. (2007). Gesture imitation in autism: II. Symbolic gestures and pantomimed object use. *Cognitive Neuropsychology, 24*, 679-700.

Sparrow, S. S., Balla, D. A., & Cicchetti, D. V. (2005). *Vineland II: Vineland Adaptive Behavior Scales*: American Guidance Service.

Srinivasan, R., Nunez, P.L., Tucker, D.M., Silberstein, R.B., & Cadusch, P.J. (1996). Spatial sampling and filtering of EEG with splinelaplacians to estimate cortical potentials. *Brain Topography, 8*, 355-366.

Stefanidou, C. (2014). *The neurodevelopmental basis of human action sound processing in typically developing children, children with autism spectrum disorders, and toddlers at risk for autism*. Doctoral dissertation, University of Birmingham.

Stefanidou, Cepionenie, McCleery (in review). Humans versus non-human action sound processing in toddlers and young children. Submitted to *Developmental Cognitive Neuroscience*.

Stewart, M. E., Barnard, L., Pearson, J., Hasan, R., & O'Brien, G. (2006). Presentation of depression in autism and Asperger syndrome A review. *Autism, 10*, 103-116.

Stolberg, H. O., Norman, G., & Trop, I. (2004). Randomized controlled trials. *American Journal of Roentgenology, 183*, 1539-1544.

Stone, W. L., Ousley, O. Y., & Littleford, C. D. (1997). Motor imitation in young children with autism: What's the object? *Journal of Abnormal Child Psychology, 25*, 475-485.

Stroganova, T. A., Nygren, G., Tsetlin, M. M., Posikera, I. N., Gillberg, C., Elam, M., & Orekhova, E. V. (2007). Abnormal EEG lateralization in boys with autism. *Clinical Neurophysiology, 118*, 1842-1854.

Stroganova, T. A., & Orekhova, E. V. (2007). EEG and infant states. In M. De Haan (Ed.). *Infant EEG and event-related potentials* (pp. 251-288) East Sussex: Psychology Press.

Sullivan, K., Stone, W. L., & Dawson, G. (2014). Potential neural mechanisms underlying the effectiveness of early intervention for children with autism spectrum disorder. *Research in Developmental Disabilities, 35*, 2921-2932.

Sussman, F. (1999). *More than words.* Toronto: The Hanen Centre.

Sutton, S. K., & Davidson, R. J. (1997). Prefrontal brain asymmetry: A biological substrate of the behavioral approach and inhibition systems. *Psychological Science, 8*, 204-210.

Taylor, M. J., Batty, M., & Itier, R. J. (2004). The faces of development: A review of early face processing over childhood. *Journal of Cognitive Neuroscience, 16*, 1426-1442.

Théoret, H., Halligan, E., Kobayashi, M., Fregni, F., Tager-Flusberg, H., & Pascual-Leone, A. (2005). Impaired motor facilitation during action observation in individuals with autism spectrum disorder. *Current Biology, 15*, R84-R85.

Tierney, A. L., Gabard-Durnam, L., Vogel-Farley, V., Tager-Flusberg, H., & Nelson, C. A. (2012). Developmental trajectories of resting EEG power: An endophenotype of autism spectrum disorder. *PloS one, 7*, e39127.

Tonge, B. J., Bull, K., Brereton, A., & Wilson, R. (2014). A review of evidence-based early intervention for behavioural problems in children with autism spectrum disorder: The core components of effective programs, child-focused interventions and comprehensive treatment models. *Current Opinions in Psychiatry, 27*, 158-165.

Toth, K., Munson, J., Meltzoff, A. N., & Dawson, G. (2006). Early predictors of communication development in young children with autism spectrum disorder: Joint attention, imitation, and toy play. *Journal of Autism and Developmental Disorders, 36*, 993-1005.

Tucker, D. M. (1993). Spatial sampling of head electrical fields: The geodesic sensor net. *Electroencephalography and Clinical Neurophysiology, 87,* 154-163.

Uzgiris, I. C. (1981). Two functions of imitation during infancy. *International Journal of Behavioral Development*, *4*, 1-12.

Uzgiris, I. C. (1990). How does intentional action develop? *Psychological Inquiry, 1*, 269-271.

Uzgiris, I. (1999). Imitation as activity: Its developmental aspects. In J. Nadel & G. Butterworth (Ed.), *Imitation in infancy* (pp. 186-206). New York, NY, US: Cambridge University Press.

Van Etten, H. M., & Carver, L. J. (2015). Does Impaired Social Motivation Drive Imitation Deficits in Children with Autism Spectrum Disorder? *Review Journal of Autism and Developmental Disorders, 2*, 310-319.

Van Hecke, A. V., Stevens, S., Carson, A. M., Karst, J. S., Dolan, B., Schohl, K., . . . Brockman, S. (2013). Measuring the plasticity of social approach: A randomized controlled trial of the effects of the PEERS intervention on EEG asymmetry in

adolescents with autism spectrum disorders. *Journal of Autism and Developmental Disorders, 45*, 316-335.

Van Steensel, F. J., Bögels, S. M., & Perrin, S. (2011). Anxiety disorders in children and adolescents with autistic spectrum disorders: A meta-analysis. *Clinical Child and Family Psychology Review, 14*, 302-317.

Vanvuchelen, M., Roeyers, H., & De Weerdt, W. (2011a). Do imitation problems reflect a core characteristic in autism? Evidence from a literature review. *Research in Autism Spectrum Disorders, 5*, 89-95.

Vanvuchelen, M., Roeyers, H., & De Weerdt, W. (2011b). Development and initial validation of the Preschool Imitation and Praxis Scale (PIPS). *Research in Autism Spectrum Disorders*, *5*, 463-473.

Villalobos, M. E., Mizuno, A., Dahl, B. C., Kemmotsu, N., & Müller, R.-A. (2005). Reduced functional connectivity between V1 and inferior frontal cortex associated with visuomotor performance in autism. *Neuroimage, 25*, 916-925.

Virués-Ortega, J. (2010). Applied behavior analytic intervention for autism in early childhood: Meta-analysis, meta-regression and dose–response meta-analysis of multiple outcomes. *Clinical Psychology Review*, *30*(4), 387-399.

Vismara, L. A., & Rogers, S. J. (2010). Behavioral treatments in autism spectrum disorder: What do we know?. *Annual Review of Clinical Psychology*, *6*, 447-468.

Vivanti, G., & Hamilton, A. (2014). Imitation in autism spectrum disorders. In F.R. Volkmar, S.J. Rogers, R. Paul & K.A. Pelphrey, *Handbook of Autism and Pervasive Developmental Disorders (*4th Edition, 278-301). New Jersey: Wiley & Sons.

Vivanti, G., Prior, M., Williams, K., & Dissanayake, C. (2014). Predictors of outcomes in autism early intervention: why don't we know more?. *New Treatment Perspectives In Autism Spectrum Disorders*, 81.

Volkmar, F. R., & McPartland, J. C. (2014). From Kanner to DSM-5: autism as an evolving diagnostic concept. *Annual Review of Clinical Psychology, 10*, 193-212.

Voos, A. C., Pelphrey, K. A., Tirrell, J., Bolling, D. Z., Vander Wyk, B., Kaiser, M. D., . . . Ventola, P. (2013). Neural mechanisms of improvements in social motivation after pivotal response treatment: two case studies. *Journal of Autism and Developmental Disorders, 43*, 1-10.

Wagner, A. L., Wallace, K. S., & Rogers, S. J. (2014). Developmental approaches to treatment of young children with autism spectrum disorder. In J. Tarbox, D. R. Dixon, P. Sturmey & J. L. Matson (Eds.), *Handbook of Early Intervention for Autism Spectrum Disorders*, Autism and Child Psychopathology Series (pp. 393-427). New York: Springer.

Wainer, A. L., & Ingersoll, B. R. (2013a). Disseminating ASD interventions: A pilot study of a distance learning program for parents and professionals. *Journal of Autism and Developmental Disorders, 43*, 11-24.

Wainer, A., & Ingersoll, B. (2013b). Intervention fidelity: An essential component for understanding ASD parent training research and practice. *Clinical Psychology: Science and Practice*, *20*, 335-357.

Wainer, A. L., & Ingersoll, B. R. (2015). Increasing access to an ASD imitation intervention via a telehealth parent training program. *Journal of Autism and Developmental Disorders, 45*, 3877-3890.

Wallace, K. S., & Rogers, S. J. (2010). Intervening in infancy: Implications for autism spectrum disorders. *Journal of Child Psychology and Psychiatry, 51*, 1300-1320.

Walton, K. M., & Ingersoll, B. R. (2012). Evaluation of a sibling-mediated imitation intervention for young children with autism. *Journal of Positive Behavior Interventions, 14*, 241-253.

Want, S. C., & Harris, P. L. (2002). How do children ape? Applying concepts from the study of non human primates to the developmental study of 'imitation'in children. *Developmental Science, 5*, 1-14.

Warren, S. F., Fey, M. E., & Yoder, P. J. (2007). Differential treatment intensity research: A missing link to creating optimally effective communication interventions. *Mental Retardation and Developmental Disabilities Research Reviews*, *13*, 70-77.

Warren, Z., McPheeters, M. L., Sathe, N., Foss-Feig, J. H., Glasser, A., & Veenstra-VanderWeele, J. (2011). A systematic review of early intensive intervention for autism spectrum disorders. *Pediatrics*, *127*, e1303-e1311.

Watt, N., Wetherby, A. M., Barber, A., & Morgan, L. (2008). Repetitive and stereotyped behaviors in children with autism spectrum disorders in the second year of life. *Journal of Autism and Developmental Disorders*, *38*, 1518-1533.

Webb, S. J., Bernier, R., Henderson, H. A., Johnson, M. H., Jones, E. J., Lerner, M. D., ... & Westerfield, M. (2015). Guidelines and best practices for electrophysiological data collection, analysis and reporting in autism. *Journal of Autism and Developmental Disorders*, *45*, 425-443.

Webb, S. J., Dawson, G., Bernier, R., & Panagiotides, H. (2006). ERP evidence of atypical face processing in young children with autism. *Journal of Autism and Developmental Disorders, 36*, 881-890.

Webb, S. J., Merkle, K., Murias, M., Richards, T., Aylward, E., & Dawson, G. (2012). ERP responses differentiate inverted but not upright face processing in adults with ASD. *Social Cognitive and Affective Neuroscience, 7*, 578-587.

West, A., & Spring, B. (2007). Randomized controlled trials. Retrieved from http://www.ebbp.org/course_outlines/randomized_controlled_trials/

Wieder, S., & Greenspan, S. I. (2001). The DIR (Developmental, Individual difference, Relationship-based) approach to assessment and intervention planning. *Zero to Three, 21*, 11–19.

Williams, J. H., Waiter, G. D., Gilchrist, A., Perrett, D. I., Murray, A. D., & Whiten, A. (2006). Neural mechanisms of imitation and 'mirror neuron' functioning in autistic spectrum disorder. *Neuropsychologia, 44*, 610-621.

Williams, J. H., Whiten, A., & Singh, T. (2004). A systematic review of action imitation in autistic spectrum disorder. *Journal of Autism and Developmental Disorders, 34*, 285-299.

Williams, J. H., Whiten, A., Suddendorf, T., & Perrett, D. I. (2001). Imitation, mirror neurons and autism. *Neuroscience & Biobehavioral Reviews*, *25*, 287-295.

Wing, L. (1997). The history of ideas on autism legends, myths and reality. *Autism*, *1*, 13-23.

Wong, C., Odom, S., Hume, K., Cox, A., Fettig, A., Kucharczyk, S., & Schultz, T. (2013). Evidence-based practices for children, youth, and young adults with autism spectrum disorder. *Chapel Hill: The University of North Carolina*. Frank Porter Graham Child Development Institute.

Wong, C., Odom, S. L., Hume, K. A., Cox, A. W., Fettig, A., Kucharczyk, S., . . . Schultz, T. R. (2015). Evidence-based practices for children, youth, and young adults with autism

spectrum disorder: A comprehensive review. *Journal of Autism and Developmental Disorders, 45*, 1951-1966.

Yang, H. H., Savostyanov, A. N., Tsai, A. C., & Liou, M. (2011). Face recognition in Asperger syndrome: a study on EEG spectral power changes. *Neuroscience Letters*, *492*, 84-88.

Young, G. S., Rogers, S. J., Hutman, T., Rozga, A., Sigman, M., & Ozonoff, S. (2011). Imitation from 12 to 24 months in autism and typical development: A longitudinal Rasch analysis. *Developmental Psychology, 47*, 1565.

Zilbovicius, M., Saitovitch, A., Popa, T., Rechtman, E., Diamandis, L., Chabane, N., . . . Boddaert, N. (2013). Autism, social cognition and superior temporal sulcus. *Open Journal of Psychiatry,* 3, 46-55.

Zwaigenbaum, L., Bauman, M. L., Choueiri, R., Kasari, C., Carter, A., Granpeesheh, D., ... & Pierce, K. (2015). Early intervention for children with autism spectrum disorder under 3 years of age: recommendations for practice and research. *Pediatrics*, *136* (Supplement 1), S60-S81.

Zwaigenbaum, L., Bryson, S., & Garon, N. (2013). Early identification of autism spectrum disorders. *Behavioural Brain Research, 251*, 133-146.