EFFECTS OF ACTION OBSERVATION ON BRAIN ACTIVITY, FUNCTION AND STRENGTH

by

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ABSTRACT

This thesis aimed to examine whether observation of force based actions could moderate subsequent executed force and behavioural performance, and also brain activity during and following the action observation. There are six chapters, four that present empirical investigations, a general introduction (Chapter 1) and a general discussion (Chapter 6). Chapter 2 presents behavioural data that examined the effects of observing exerted force on an executed force response. The data revealed that the executed force was moderated by the condition observed so that observation of a 100% force caused increased force response compared to observation of a 50% and 0% force. Chapter 3 further examined whether bouts of observation could also moderate subsequent force and dexterity execution. Three experiments were conducted. In Experiments 1 and 2, observation of hand force based actions significantly moderated the executed hand dexterity. In Experiment 3, observation of leg force actions significantly moderated the executed leg force response. Overall, the data revealed that bouts of action force observation moderated the executed force and dexterity responses. Chapter 4 used fMRI to examine the brain activity during action force observation. The data revealed significant activity in the Superior Frontal Gyrus (SMA), part of the mirror neuron system. The finding was consistent with other findings in the literature, supporting the notion that observation of action force activates the same areas of the brain as those used for execution. To examine the relationship between action priming and brain activity, Chapter 5 again used fMRI, but to investigate resting brain activity. The data revealed significant mirror neurone system activity following action force observation compared to pre-observation and control conditions. The thesis is discussed (Chapter 6) in terms of how action observation could be used clinically for rehabilitation, and moreover, how further experimental directions could be added to these findings.

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Without the help of a number of people this work could not have been achieved, and I would like to take this opportunity to express my deep gratitude and sincere thanks to them.

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conditions on reach tapping dexterity. The dependant measure was the difference between post and pre measures. There was no significant difference between task or any interaction between observation condition and task. Error bars show standard deviation between participant responses.

occipital lobe). The image shows from left to right: coronal, sagittal, and axial section of the brain (the appropriate planes and directions shown below the images). Functional images are overlaid on an average high-resolution scan transformed into standard (MNI152) space. Coordinates for these areas are presented in Table 4.2.

heart).

and post-observation of the experimental strength based actions F [2, 27] = 7.42, p < 0.01. The images show increased activation for post-observation compared to pre-observation rest state in the following brain areas: bilateral Angular Gyrus, bilateral Supra Marginal Gyrus, posterior division, bilateral Lateral Occipital Cortex, superior division, bilateral Superior Temporal Gyrus, posterior division (BA 40), bilateral Inferior Frontal Gyrus, pars triangularis & pars opercularis, bilateral Frontal Orbital Cortex, bilateral Frontal Operculum Cortex (BA 44, 45, 47), left Premotor Cortex (BA6),left Primary Motor Cortex (BA4), left Corticospinal Tract & bilateral Cerebellar activity, posterior lobe, crus I & II. Each image shows from left to right, the coronal, sagittal, and axial sections of the brain (the planes and directions shown below the images represent Anterior and Posterior, Superior and Inferior, and Left and Right). Functional images are overlaid on an average high-resolution scan transformed into standard (MNI152) space. The colour bar represents the z values of normal distribution significance (ranging from 4.0 to 8.0). Note that the brain images are presented in the standard mirror format (i.e., the pictured left is the physical right side of the brain and vice versa).

standard mirror format (i.e., the pictured left is the physical right side of the brain and vice versa).

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CHAPTER 1:

GENERAL INTRODUCTION

1.1 Introduction

The aim of this thesis was to first of all investigate how the observation of strength and force based actions primes subsequent execution of action force and dexterity, and secondly, what aspects of motor system brain activity can explain the priming effects. The underlying purpose and original intention of the study was to develop knowledge that could be used for the development of clinical training paradigms following injuries that lead to strength loss. In this introduction chapter, I will start by introducing literature that has already measured the effects of action observation on execution (e.g., action priming). In the second part of the introduction, I will introduce the neural processes that are thought to underlie the priming effects. This latter part will focus on the 'mirror neuron system'; a network of neurons that are active both when the individual performs a motor action and when they observe somebody else performing a similar action. Evidence for the mirror neuron system will be presented from behavioural (e.g. using a reaction time paradigm), neurophysiological (e.g. TMS, EEG, and MEG) and brain imaging (e.g. fMRI) studies. In the final part of the thesis, a summary of the thesis chapters will be presented.

1.2 Action Priming

In the following section, I will introduce the literature that has reported that action execution can be primed following particular aspects of perception. I will start the review by briefly defining priming (section 1.2.1). Then, in sections 1.2.2 and 1.2.3, I will report the literature that has shown that action observation can prime subsequent execution.

1.2.1 The Priming Effect

In experimental psychology, priming paradigms are used to infer cognitive processes. It is considered that if a first behaviour primes a second subsequent behaviour, then the underlying cognitive processes for the two behaviours must be shared. In the simplest form, repetition priming shows that if a behaviour is carried out and then repeated, the first behaviour primes the second, presumably because the same cognitive processes also need to be repeated. This effect is also known as the practice effect.

There are many examples of priming effects in the literature. One of the more famous is that in the 'Stroop Effect' (Stroop 1935). In this effect, if participants are asked to say the colour of the ink that a word is presented in and the speed and accuracy of participants responses measured, the effect shows that compared to a control condition, participants are slow and show increased errors if the word names a colour and it is incongruent to the ink colour (for example, the word 'blue' written in green ink; the participant's required respond is 'green'). This is in contrast to congruency between the colour ink and colour name (for example, the word 'blue' written in blue ink; the participant's required respond is 'blue') or to the presentation of a control condition word (for example, the word 'tree' written in green ink; the participant's required respond is 'green'). In this effect, the participants are thought to automatically read the word and this behaviour primes the subsequent cognitive task of deciding upon and naming the ink colour. That is to say that the written word primes the naming of the ink colour showing that reading and saying a colour name must activate the same cognitive representations.

In the thesis here, I will focus on prime effects that have reported the behaviour of perception to prime the subsequent behaviour of action. In this sense, priming can be modulated by

several factors such as those related to the perceived object (e.g. size, weight or shape etc.), the perceived space (e.g., left vs. right side) or a perceived action performed by another person. In the next section that reviews the literature, factors in perception that influence subsequent action execution will be presented.

1.2.2 Action Priming and The Simon Effect

In the perception and action literature, the popular priming effect (that matches the popularity of the Stroop Effect) is that of the 'Simon Effect' (first reported by Simon & Rudell, 1967). The effect results from shared processes between space and effector (e.g., left or right hand) selection. For example, if a participant is required to respond using a right hand response, they are then faster and show less error to respond to a right target stimulus than a left target stimulus. Likewise, if the participant is required to select a left hand response, they are then quicker to respond to a left side stimulus than right. Interestingly, this spatial stimulus-response (S-R) matching also exists for non-spatial stimuli. For example, if the participant is asked to respond with their left or right hand to a verbal command of 'left' vs. 'right', participants respond faster with the congruent stimulus-effector conditions than non-congruent stimulus-effector conditions. This stimulus-response compatibility is proposed to be a consequence of congruency between the perceptual stimuli and the selection of effector for the executed action (Hasbroucq & Guiard, 1991).

1.2.3 Action Priming from Observation

In recent years, there has been a growth in evidence that viewing an action performed by another individual moderates the later execution of a similar action (see, for example, Brass, Bekkering, Wohlschlager, & Prinz, 2000; Castiello, 2003; Castiello, Lusher, Mari, Edwards, & Humphreys, 2002; Craighero, Fadiga, Umilta, & Rizzolatti, 1996; Dijkerman & Smit,

2007; Edwards, Humphreys, & Castiello, 2003; Gianelli, Dalla Volta, Barbieri, & Gentilucci, 2008; Griffiths & Tipper, 2009; Hardwick & Edwards, 2011; Jackson & Decety, 2004; Kilner, Hamilton, & Blakemore, 2007; Kilner, Paulignan, & Blakemore, 2003; Salama, Turner, & Edwards, 2011; Stanley, Gowen, & Miall, 2007 etc.). Like in the two previous examples (the Stroop and Simon Effects), the prime effect from action observation is thought to arise from a coupling effect between the perceived action (in observation) and action execution. The degree of congruency between the perceived and executed action conditions has also been termed ideomotor-compatibility, with data showing increases in ideomotor-compatibility have shown increased prime effects (Brass, Bekkering, & Prinz, et al., 2001).

An example of the research showing action observation to prime subsequent execution is that from Edwards et al. (2003). They were the first to have used motion-tracking analyses to examine the executed actions of sixteen subjects following the observation of either congruent or incongruent action stimuli. In the study, participants were asked to observe the experimenter performing reach and grasp actions and after observing the task, they were requested to perform a similar movement. The congruency between the observed and executed action involved changing the object that was acted upon. That is to say that the participants observed a grasping action to an object that was either small or large, and then had to execute a grasping action to either the small of large object themselves. The congruent condition involved observation and execution to the same size object (e.g., observe action to a small object, then execute action to a small object), and the incongruent condition involved observation and execution to different sized objects (e.g., observe action to a small object, then execute action to the large object). The findings of the experiment showed that observation congruency had a significant influence on the speed of response, especially in the initiation kinematics. In congruent condition, the participants reached the object significantly

earlier in the time to peak velocity compared to the incongruent condition. Edwards et al. (2003) suggested that the effect may have been caused by the observation condition priming the motor planning processes, the consequence of which lead to a faster initial execution of the planned action response.

In the above example, the action priming occurred for the observation of grasping objects. While there has been a tendency for the literature to focus on grasping or hand manipulative actions (e.g., Brass et al., 2000; Castiello et al., 2002; Dijkerman & Smit, 2007; Griffiths & Tipper, 2009), there is also evidence that spatial components of actions can be influenced. For example, recently Hardwick et al. (2011) used motion tracking analyses in an experiment that tested whether the observation of actions taking one of two spatial paths would prime execution. They tested eight participants that were asked to observe and execute similar reach and grasp actions. The congruency between the observed and executed action were manipulated by moderating the kinematic spatial path so that it followed a natural path, or followed an abnormally high path. The participant was then instructed to make a normal action execution response. Therefore, the experimenter reached and grasped the object, either with a normal reach (congruent to the participant response) or a high reach (incongruent to the participant response) action. Various objects were grasped, but differences between these were not analysed. One other manipulation also carried out involved manipulating the position of the observed action. That is to say that participants either observed the experimenter reaching and grasping an object from an opposite (180 degrees) or one side (90 degrees) position to the participant. The results from the experiment showed no effect of observed position, but did show a consistent significant effect of reach congruency. Participants reached the object with a 'normal' trajectory following observed normal reaching actions (congruent condition), but made higher reach trajectory action executions following

observation of the high reaching actions (incongruent condition). These findings are compatible with the previous studies that have shown that the congruency between the observed and the executed actions modulated action execution (Castiello, 2003; Castiello et al., 2002; Craighero, Fadiga, Rizzolatti, & Umilta, 1999; Dijkerman & Smit, 2007; Edwards et al., 2003; Ellis & Tucker, 2000; Griffiths & Tipper, 2009; Klatzky, Fikes, & Pellegrino, 1995; Riddoch, Edwards, Humphreys, West, & Heafield, 1998; Tucker & Ellis, 1998, 2001).

Apart from a paper published by Salama et al. (2011) (presented in Chapter 2 of this thesis), no other research in the published literature has so far considered whether action priming can influence executed force responses. In the study, I analysed force execution responses using a hand grip force measuring tool (a hand grip dynamometer) in order to examine the effect of action force observation on the subsequent executed force responses. The principle point of the study was to investigate whether the participants force execution response (trained to be 50% of the participant's maximum grip force) was moderated following the observation of baseline (no grip/no action; 0% force), congruent grip (50% force) or incongruent grip force (100% force) action force conditions. In particular, I was interested in whether the force observed could bring about different hand grip force responses as a function of increasing the force exerted in the observed action. Eighteen participants were tested and they were presented with video clips of various degrees of hand grip force (0%, 50% or 100% of a model's own maximum force). Prior to the experimentation, all of the participants were first trained to consistently respond at their own 50% maximum force level. The results of the study revealed that when participants observed an incongruent (100%) force, their own response was significantly increased in comparison to the baseline (0%) and congruent (50%) conditions. In the paper, I wrote that I assumed that observation of the incongruent (100%) force, relative to the baseline (0%) and congruent (50%) conditions yielded to greater primary

motor cortex excitability and consequently induced an increase in the participant's intended force response (by a small, but significant amount). One impressive aspect of these findings was that the observation condition moderated the response that the participants were trained to respond at, and the only response that they had to make throughout the experiment. Even so, observing another person's actions overrode the training to influence reproduction of force response, suggesting that prime effect may have been automatic (or non-conscious).

1.3 Mirror Neuron System

In the next section of this introduction chapter, the mirror neuron system brain areas thought to be involved in the priming between observed action and executed action are reviewed. In section 1.3.1, the non-human primate neurophysiology evidence for the mirror neuron system is presented. Then, in sections 1.3.2, 1.3.3 and 1.3.4, evidence from the human neurosciences literature is presented.

1.3.1 Mirror Neuron System: Evidence from non-human primates

Evidence for the mirror neuron system stems from original non-human primate research that discovered (siren dipity) particular activation profiles of neurons based in the ventral premotor cortex (area F5) of the macaque monkey (di Pellegrino, Fadiga, Fogassi, Gallese, & Rizzolatti, 1992; Gallese, Fadiga, Fogassi, & Rizzolatti, 1996; Rizzolatti & Craighero, 2004; Rizzolatti, Fadiga, Gallese, & Fogassi, 1996). The original aim of these studies was to investigate the activity of ventral premotor cortex (area F5) while participant monkeys performed grasping actions to different geometric shapes. In these studies, interestingly, they discovered evidence for neurons that were activated both when the animal performed a goal-directed hand actions and also when they observed another monkey or the human experimenter executing a similar action (Gallese et al., 1996; Rizzolatti et al., 1996). This for

the first time showed evidence of neurons in the motor areas of the brain that responded to perception of action, as well as execution, and further, showed evidence of neurons with two complimentary activation profiles (one for observed and one for executed actions). Rizzolatti et al. (1996) named these neurons 'mirror neurons'.

Since the discovery of mirror neurons, a number of investigations have been carried out with non-human primate participants in order to better understand the properties and functions of the mirror neurons. This research is still very much in progress. However, a key finding is evidence for two different types of mirror neuron, one based in the original premotor F5 area and generally active for the observation and execution of action, and another type typically in the parietal brain area and active during the observation or execution of an object object-directed action (Rizzolatti & Craighero, 2004; Rizzolatti & Luppino, 2001). These latter neurons have been named Canonical Neurons. On the basis of these findings, it has been argued that the mirror neuron system particularly represents the perception of and programmes the execution of goal directed actions. Thus, activation of the mirror neuron systems requires the existence of both an object (or goal) and an effector action (which has to be biological). Observation of the object alone with the absence of the effector, or observation of gestures (mimicking the action) with the absence of an object in the scene, does not cause mirror neurones activation.

Another functional aspect of the mirror neuron activation is that they appear to show degrees of matching (or congruency) specificity between the observed action and the executed action that they code. According to this, mirror neurones have been classified into two populations. One is "strictly congruent" and represents approximately one third of brain area F5 and the other is "broadly congruent" and represents the remaining two thirds of area F5. The "strictly

congruent" neurons are active for observation and execution of identical action (for example the clock-wise rotation of the wrist). The "broadly congruent" neurons show less specificity, with for example a mirror neuron being active for the observation of a pinch grip reach and grasp action and also active to the execution of a whole hand grip reach and grasp action (Gallese et al., 1996).

While these experiments continue, the relative difficulties associated with testing non-human primates cause the research to be slow. Much more research has been carried out using human neuroscience experiments. However, while these are able to further define the activations of the mirror neuron system, they are unable to measure the responses of the specific mirror neurons themselves (due to ethical constraints). In the next sections, this human mirror neuron system evidence is reviewed.

1.3.2 Mirror Neurons: Evidence from human fMRI research

Several brain imaging studies have been conducted in humans to explore the brain components that could be equivalent to the F5 mirror and premotor canonical neurons reported in experiments with non-human primates. One of the first papers to investigate these links was that by Grezes, Armony, Rowe, & Passingham (2003). Using fMRI, they aimed to investigate the existence and localization of the neural circuits similar to those discovered in macaque and also to examine the different neural circuits also invoked during action observation and execution. They presented participants with an observational condition that required the participants to passively observe only an object (OO), a hand grasp (OG) or an object being grasped (OGO). In an execution condition, the participants were requested to execute similar actions to those used in the observation condition (EO, EG and EGO). Two different conditions were used as baseline; either to observe a stationary background (OB) or

to execute a hand grasp while observing the same background (EB). The results showed that the observation of the object compared to observation of a stationary background (OO vs. OB) was associated with significant increased activation in the left ventral precentral sulcus and left intraparietal sulcus. The contrasts between observation of a hand grasp compared to observation of a stationary background (OG vs. OB) and execution of a hand grasp compared to executing a hand grasp while observing the same background (EG vs. EB) produced the same results, with both contrasts being associated with bilateral activations in the dorsal premotor cortex, intraparietal sulcus, superior temporal sulcus, the right parietal operculum (SII) and the left ventral precentral sulcus. Finally, contrasts between observation of object grasping compared to observation of a stationary background (OGO vs. OB) and execution of object grasping compared to executing a hand grasp while observing the same background (EGO vs. EB) also caused the same activations as those in the previous contrasts, except for the left ventral precentral sulcus. Therefore, the interesting finding of this research was that observation and execution of similar actions activated the same areas of the brain, supporting the mirror neuron concept that observation and execution activates shared areas of the human brain.

Since these initial findings, there have been a number of further experiments that have measure brain activity during action observation and execution. From these many research papers, a common network of activity has resulted. This consists of the brain areas; inferior frontal gyrus (IFG), superior and inferior parietal regions, the supplementary motor area and the lateral premotor cortex (Buccino, Binkofski, Fink, Fadiga, Fogassi, Gallese, Seitz, Zilles, Rizzolatti, & Freund, 2001; Buccino, Lui, Canessa, Patteri, Lagravinese, Benuzzi, Porro, & Rizzolatti, 2004b; Cochin, Barthelemy, Lejeune, Roux, & Martineau, 1998; Decety, Grezes, Costes, Perani, Jeannerod, Procyk, Grassi, & Fazio, 1997; Grafton, Arbib, Fadiga, &

Rizzolatti, 1996; Grezes et al., 2003; Johnson-Frey, Maloof, Newman-Norlund, Farrer, Inati, & Grafton, 2003; Lui, Buccino, Duzzi, Benuzzi, Crisi, Baraldi, Nichelli, Porro, & Rizzolatti, 2008; Manthey, Schubotz, & Cramon, 2003; Saygin, Wilson, Jr Hagler, Bates, & Sereno, 2004; Schubotz & Cramon, 2004). These areas have been reported to be the human homologue of monkey premotor area F5 (Rizzolatti & Craighero, 2004) and as the brain areas extend beyond the human premotor cortex, they have become known as the human mirror neuron system.

1.3.3 Mirror Neurons: Evidence from human TMS research

Evidence for human mirror neurons also comes from Transcranial Magnetic Stimulation (TMS) experimentation. As with fMRI, the method is non-invasive, and moreover it has the ability to provide a time accurate measure of primary motor cortex excitability. The method works by using electromagnetic induction to induce an electric current, and when applied to the scalp, the induced electric current causes neurons underneath the scalp (and at the focus of the electromagnetic coil) to become active. The method was first introduced and developed by Barker, Jalinous and Freeston (1985) and used to demonstrate correspondence between the primary motor cortex stimulation and recorded muscle action potentials reflecting the human homunculus. This research has since been extended, and been used to show how motor learning (or homunculus adaption) moderates primary motor cortex excitability (Wassermann, Pascual-Leone, & Hallett, 1994). Related to this, TMS has been used in the clinical setting as a valuable diagnostic evaluation of brain damage to the motor areas following stroke, dissiminated sclerosis and motor neurone diseases (see for example Currà, Modugno, Inghilleri, Manfredi, Hallett, & Berardelli, 2002).

For the assessment of mirror neurons, TMS was first used by Fadiga, Fogassi, Pavesi, & Rizzolatti, (1995) to investigate primary motor cortex activity during action observation. In the study, TMS was applied to the primary motor cortex of twelve participants while they observed the experimenter making object grasping actions, using their arm to trace a geometric shape in the air, or observing a flashing light. As in the example provided above, primary motor cortex excitability was measured using motor evoked potentials (MEPs) from the participant's hand muscles. Stimulation was made to the left hemisphere hand area of the homunculus and right hand muscles were recorded while the participants observed the actions or flashing light. The data showed that the recorded MEPs significantly increased during observation of the actions compared to the flashing light baseline. In addition, the data showed that MEPs for specific hand muscles were only modulated if the observed action involved use of the muscle. That is to say that the primary motor cortex that codes specific group of muscles was facilitated during the observation of movements that involved using those same muscles for execution. In the discussion, Fadiga et al. (1995) suggested that activity from the human premotor mirror neurons caused the increased primary motor cortex excitability and measured MEP relative to the comparison baseline condition (see also Strafella & Paus, 2000 for similar findings).

1.3.4 Mirror Neurons: Evidence from human EEG research

The final neuroscience method reviewed here that has been used to evaluate the human mirror neuron system is that of EEG. The method works by recording brain electrical activity through electrodes placed on the scalp. The electrodes measure the voltage fluctuations that are created as a function of neural activity causing current flows. Originally, EEG was used to record mirror neuron activity in primates (see Dum & Strick, 2002; Nishitani & Hari, 2000; Shimazu Maier, Cerri, Kirkwood, & Lemon, 2004; Tokuno & Nambu, 2000), but more

recent research has used EEG to examine the activity of the human mirror neurone system (see, for example, Muthukumaraswamy & Johnson, 2004; Muthukumaraswamy, Johnson, & McNair, 2004; Oberman, Pineda, & Ramachandran, 2007). Like TMS, EEG provides better temporal activity that fMRI. However, the advantage of EEG compared to TMS is that more areas of the brain can be measured at the same time (albeit with less spatial accuracy than fMRI).

Despite the value of EEG research methods for evaluating the effects of action observation on brain activity, very little research has investigated this area. Instead, researchers have focussed on a related question that considers how the mirror neuron system might be involved in observing social actions (or interactions). In this context, Oberman et al. (2007) examined the modulation of motor area mu rhythm as a function of changing the nature of various social stimuli. Twenty participants were asked to observe one of four video clip stimuli. These were: (i) a static non-action baseline, (ii) a non social interaction that involved three persons tossing a ball up and down, (iii) a social action that involved three persons tossing a ball to each other, and (iv) a social interaction that was similar to the third stimulus actions, except that the ball was occasionally and randomly thrown towards the participant to test the degree of their involvement in the social action presented. The data showed that the mu wave recorded from the mirror neuron system was modulated as a function of changing the degree of social interaction, with the highest mu suppression for the fourth social interaction condition and the lowest degree of suppression for the first non-social condition. Confounded with these data, the results showed that action observation and social interaction appeared to activate mirror neuron activity (Iacoboni et al., 2004).

1.3.5 Action Priming and the Mirror Neuron System

In this chapter, I have presented research showing that the observation of action primes subsequent executed action. I have also shown evidence from different neuroscience methods that the behaviours of action observation and execution activate the same areas of the brain[1]. It is believed that the mechanism explaining action priming is that the shared activity between observation and execution causes observation to prime execution, in the same way that action repetition priming would function (e.g., execution followed by the same execution; the latter execution showing improvements in performance compared to the former execution condition; the so called practice effect) (see Edwards et al., 2003).

1.4 Summary of the PhD Thesis

In this thesis, I for the first time in the literature, investigated whether the observation and execution of action force was represented by shared neural processes. I first addressed this question using action priming paradigms (Chapters 2 and 3), and then used fMRI brain imaging methods (Chapters 4 and 5) in order to measure specifically which brain areas were involved. In the rest of this section, a summary of each thesis chapter is provided.

In the first empirical chapter (Chapter 2; also Salama et al., 2011) I used a research method similar to that reported by Edwards et al. (2003). Participants were instructed to observe force based actions, and following observation had to execute a force response. The observed and executed actions used a hand grip dynamometer so that the force of the action could be accurately recorded. I tested eighteen participants and first trained them to respond at 50% of their own maximum force ability. Following training, I presented random stimuli trials that consisted of a model making different hand grip force responses of 100%, 50% and 0 % of

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[1] Though not necessarily the same exact neurons.

the model's own force ability. As in the previous research, the data showed a significant

increase in the participant's executed force when they observed incongruent (100%)

compared to congruent (50%) and base line (0%) stimuli. Therefore, these data replicate

other research presented in the literature and show that observation of action force primes

execution suggesting that observed action force must be represented in the same areas of the

brain as those used to execute force actions.

In the second empirical chapter (Chapter 3; also Salama et al., submitted), I wanted to extend

the findings of Chapter 2 by using a new research method design (so far not reported in the

literature). The rationale for the new research method design was based on the practicalities

of using action priming for clinical rehabilitation. I suggested that using the conventional

observation-execution priming paradigms in a trial-by-trial order would be practically very

difficult to run in a clinical setting. Therefore, in Chapter 3, I investigated whether bouts of

observation could prime subsequent executed force based actions. I ran three experiments in

which I used two different strength measuring tools (a hand and a leg dynamometer) and in

addition, I measured dexterity using Polhemus motion tracking. The aim was to examine

whether observed action force would prime executed force as in Chapter 2, and in addition

whether there would be any further priming of dexterity performance. The method measured

force and dexterity responses before and after the bouts of observation condition. The

observation conditions consisted of force-based actions and were compared to a control

condition that presented non-action stimuli. Each bout of observation lasted for

approximately 12 minutes. The results for Experiment 1 and 2 showed that the bouts of force

observation in comparison to the control condition significantly primed the executed

dexterity performance. Further, in Experiment 3, the results showed that the observation of

leg force action significantly primed the subsequent executed leg force response. These

findings replicate previous literature and suggest that bouts of observation rather than trial-by-trial observation may potentially provide a better method for clinical use of action observation for patient rehabilitation. This will be discussed in greater detail in Chapter 6. On the basis of the research findings from Chapters 2 and 3, Chapter 4 aimed to assess which brain areas were active during observation of action force. Using fMRI, I examined the heamodynamic changes (in BOLD signals) of the brain, and in particular, the mirror neuron system during observation of force-based hand and arm actions compared to control condition. Fifteen participants were scanned while they observed force-based hand and arm movements (experimental condition) or moving objects (control condition) that included heavy and light objects. The data analyses contrasted brain activity between the heavy and light objects for the experimental and control conditions. The results showed that observation of the heavy objects compared to the light objects in the experimental condition showed significant activations in the left superior frontal gyrus (the SMA of the mirror neuron system), left frontal pole and bilateral activation of the occipital lobe. Observation of the heavy objects compared to the light objects in the control condition only showed significant bilateral activation -of the occipital lobe. Therefore, these data support the findings of Chapters 2 and 3, showing that observation of action force appears to be represented in the mirror neuron system.

 In the final empirical chapter (Chapter 5), I again used fMRI to examine whether observation of actions compared to control stimuli modulated mirror neuron system activity. However, I for the first time in the literature used a new method of brain resting state activity in order to quantify how action observation moderates brain activity once the observation of action has finished (i.e., measuring activity following the stimulus presentation). The rationale for this investigation was based on understanding how mirror neuron system brain activity, reported

and shown in Chapter 4 to be active during action observation, leads to the prime effects reported in the literature, and in Chapters 2 and3. To gain a better understanding of how action observation primes subsequent action execution, I scanned the same participants as those tested in Chapter 4, and using the same stimuli. However, I examined brain activity during rest-states that were measured immediately prior to and following the observation conditions. Using PICA (Probabilistic Independent Component Analysis) I identified brain areas of significant activation in the contrasts between post-observation and pre-observation of strength based action. These were in the fronto-parietal areas and included areas typically associated with the mirror neuron system. Contrasts between post-observation and pre-observation of the non-action control stimuli showed no moderation of the mirror neuron system. I discuss these data in terms of them providing insight into how action observation may prime subsequent execution.

In the final chapter of this thesis (Chapter 6), a summary of the thesis is first presented and discussed in relation to the literature. Following this, the thesis strengths and limitations are discussed, and suggestions made that could improve the specific methods used in the thesis investigation. In the final section of the chapter, future experimentation is presented, primarily that considers how the findings of this thesis could be adapted and used for patient rehabilitation.

CHAPTER 2:

AUTOMATIC PRIMING OF GRIP FORCE FOLLOWING ACTION

OBSERVATION

The text and detail presented here exactly matches that of the published manuscript:

Salama, I. M., Turner, S., & Edwards, M. G. (2011). Automatic priming of grip force

following action observation. *The Quarterly Journal of Experimental Psychology, 64,*

833-838.

2.1 Abstract

Research shows that action observation can prime execution. Evidence for this comes from experiments that show action observation influenced temporal (e.g., speed) or spatial (e.g., peak grasp aperture or trajectory) aspects of executed movement. In the paper presented here, I for the first time show that observation can also prime executed action force. Following observation of force actions, participants executed grip-force responses using a dynamometer, and the data showed that their force was modulated by the condition observed. The findings of the study are discussed in terms of a likely cause of the force modulation effect and potential uses that the effect may have for strength rehabilitation.

2.2 Introduction

Recent research has shown that the observation of an action can prime subsequent execution (see for example Brass et al., 2000; Castiello et al., 2002; Dijkerman & Smit, 2007; Edwards et al., 2003; Gianelli et al., 2008; Griffiths & Tipper, 2009 etc.). These studies have tended to focus on the effects that observation has on temporal or spatial aspects of executed movement. For example, Brass et al. (2000) showed that observation of a congruent compared to incongruent simple finger movement facilitated the speed taken to make a simple finger response. Similarly, Castiello et al. (2002) and Edwards et al. (2003) reported that observation primed the speed of subsequent initiated movement. Spatial modulation has been reported whereby observation priming influenced executed grasp size and reach trajectory (Castiello et al. 2002; Dijkerman & Smit, 2007; Gianelli et al., 2008; Griffiths & Tipper, 2009). However, to date, no paper has tested whether observation can prime muscle force used in execution.

The rationale used to explain the prime effect between observation and execution comes from literature showing that both behaviours activate common neural areas in the brain. For example, in primate neurophysiology, 'mirror neurons' were activated during action observation and execution (see Gallese et al., 1996; Rizzolatti et al., 1996). In human brain imaging, action observation has been shown to activate the parietal and premotor areas; the same areas known to be activated during action execution (e.g., Buccino et al., 2001; Turella, Erb, Grodd, & Castiello, 2009). Also, Fadiga et al. (1995) showed modulation of Transcranial Magnetic Stimulation (TMS) Motor Evoked Potentials (MEP) while participant's observed actions (indicative of primary motor cortex excitability). In these data, specificity between the observed and executed conditions was demonstrated in that the MEP recorded corresponded

to observation of the same muscle being used. This suggests that observation of action had a direct influence on primary motor cortex and muscle activity, and supports the idea that observation can prime physical aspects of execution through common neural processes.

In the present paper, participant grip force execution on a handgrip dynamometer was recorded immediately after they observed video stimuli of a model making grip force response. Irrespective of the observed stimuli, participants were instructed to make handgrip force responses that were 50% of their own maximum immediately after watching each clip. I used observation stimuli of baseline (0%), congruent (50%) and incongruent (100%) conditions. Based on previous findings in the literature, I hypothesised that action observation would modulate the participant's execution force.

2.3 Methods

2.3.1 Participants

Eighteen undergraduate female[2] students aged 18-24 years (mean = 20.7) took part in the study. All participants were right-handed, had normal or corrected-to-normal vision, had no experience of strength training, and were naïve to the purpose of the study. The School of Sport and Exercise Sciences, University of Birmingham Ethics Committee approved the study.

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[2] Females were tested, as the handgrip dynamometer was only able to record a maximum response of 50kg. In previous research carried out in the laboratory, no female ever exceeded this amount, whereas some male participants did.

2.3.2 Apparatus and stimuli

The stimuli used for the action observation conditions were handgrip movements made using a handgrip dynamometer ("Li" Lafayette Instrument Co. Lafayette Indiana 47903) and displayed using video clips presented on a computer screen. The video clips were filmed using a high definition digital camcorder positioned approximately 2m away from a blank wall and 1m from the floor. Four right-handed volunteers (two female and two male) that were not associated with the study acted as models. They were seated holding the dynamometer in their right hand, with their elbow at a right angle perpendicular to their side. They held the dynamometer with a whole hand grasp and they were positioned to the right of the camera so that their fingers and handgrip were in the captured view. The dynamometer was positioned so that the back of the dynamometer was viewed (i.e., the dial face was not visible in the clip).

Each model performed five maximal grip force responses and an average was calculated which was then used to calculate their average 50% maximum grip. Each model was filmed making dynamometer responses in conditions of baseline - no grip / no action (0%), congruent grip (50%) and incongruent grip (100%) (see Figure 2a). Each model produced five clips for each condition, making a total of sixty clips. The stimuli were edited to five seconds and displayed the specific force of grip held throughout. That is to say that the beginning application and end removal of force was edited and deleted from the stimuli so that the participants only saw the execution of force and not the application and removal action phases of the force.

The experimental instructions and stimuli were presented using DMDX software (Forster and Forster, 2004) on a standard computer with 17" monitor. In the experiment, the software

presented each clip followed by a short time break. In this time, participants were instructed to make a response using the same dynamometer as that used to make the stimuli.

2.3.3 Procedure

At the beginning of the study, participants read an information sheet and completed a consent form. Participants were then seated 80cm centrally in front of the computer screen and instructed to hold the dynamometer in their right hand with their elbow at a right angle perpendicular to their side. The participant then made five maximum grip force responses and an average was calculated. From this, the participant's mean 50% maximum grip force was calculated. The participants were informed of this value and instructed to familiarise themselves with the necessary force needed to consistently achieve their 50% maximum grip force using the dynamometer dial for feedback. Once practiced (i.e., where they could achieve between 40% and 60% of their maximum force for three consecutive trials), the dynamometer was turned around so that the participants were not able to see the dial and hence could not use the dial for feedback during the experimental session. They were then instructed that in the experimental session, they had to respond at the 50% practiced maximal grip force after viewing each video stimulus. Each participant observed the sixty video stimulus clips in a random order, and made a response after each stimulus presentation. The experimenter recorded the participant's grip response and controlled the initiation of the stimuli by pressing the space bar after each response.

2.3.4 Data Analyses

The data were analysed using two repeated measures ANOVAs. In both, the independent variable was observed condition (baseline 0% vs. congruent 50% vs. incongruent 100%). In

the first ANOVA, the dependent variable was the mean absolute force difference between the actual grip response recorded and the participant's own initial mean 50% maximal force value (i.e., if the dependent measure was 'zero', it would indicate that the participant responded exactly with their own 50% maximal force value) (kg). In the second ANOVA, the dependent variable was the mean relative force response of the participant (%). Bonferroni Pairwise Comparisons were performed for any significant effects of condition.

2.4 Results

A simple regression between trial order (for the 60 trials) and mean relative handgrip response for the 18 participants showed no significant relationship (F[1, 59] = 0.6, p=.46) (r^2 = .009). This demonstrates that the responses were stable across the study and there were no effects of fatigue.

Analysis of both dependent measures, mean absolute and relative force were significant (F[2, 34] = 10.7, p<.001) and (F[2, 34] = 10.4, p<.001). Bonferroni Pairwise analyses showed significant differences between 50% and 100%, and 0% and 100% (p<0.05), and no difference between 0 and 50% for both dependent variables (see Figure 2b).
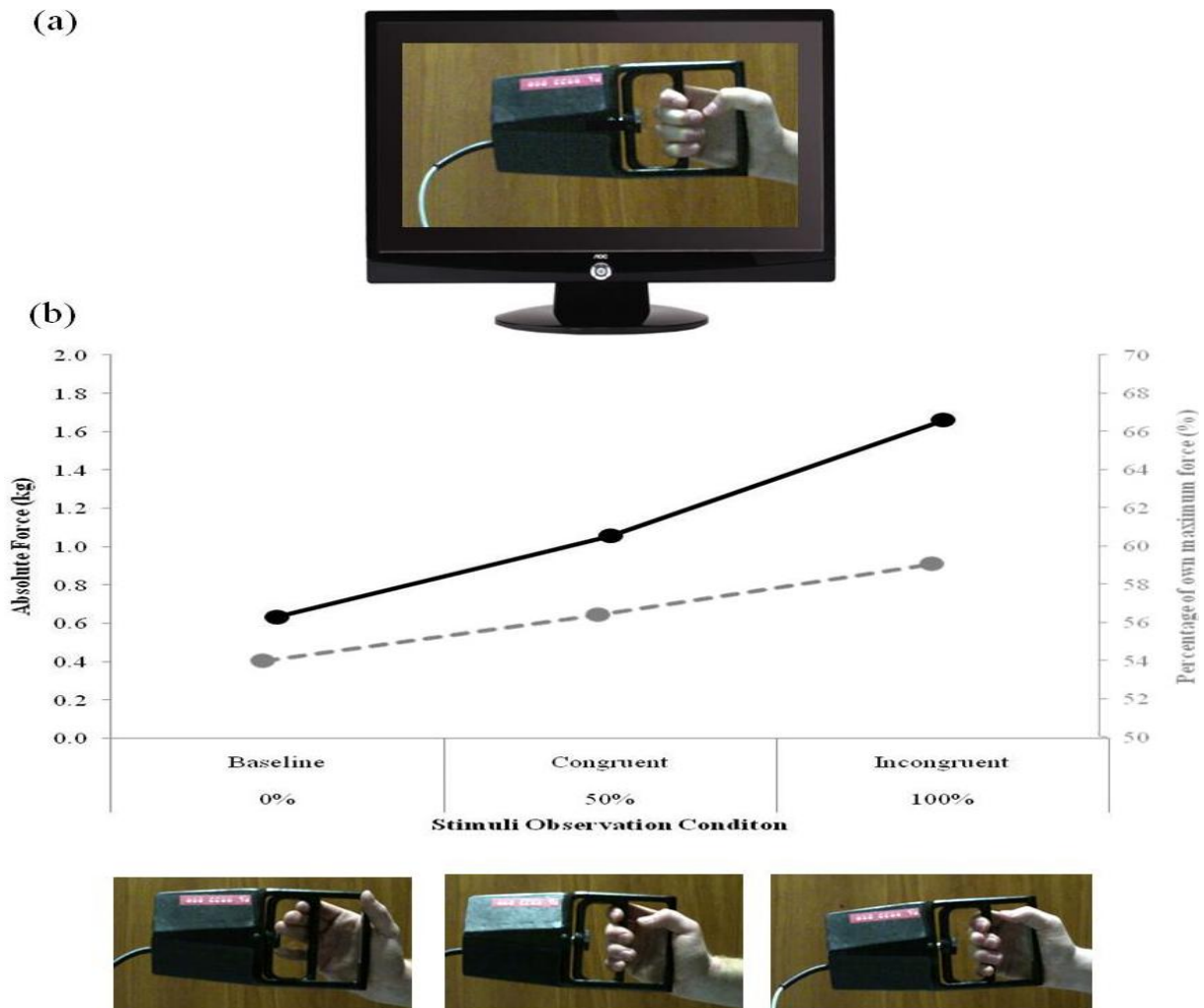
Figure 2: (a) Participants observed stimuli of a model making hand grip dynamometer responses that were 0%, 50%, or 100% of the model's own maximum force. The stimuli were depicted in a random order on a computer screen, and, after each, the participant immediately performed a hand grip response that was 50% of their own maximum (stimulus–response conditions of baseline 0%, congruent 50%, and incongruent 100%). (b) The graph with the black solid line shows the mean absolute force (kg), and the grey dashed line shows the mean relative force (percentage of participant's own maximum force; %). The mean standard errors were 1.9 kg, 1.8 kg, 1.9 kg, and 9.3%, 8.9%, 9.1%, for baseline 0%, congruent 50%, and incongruent 100% mean absolute force and mean relative force, respectively.

2.5 Discussion

In the present paper, I hypothesised that action observation would modulate participant's execution force responses. The data showed that when participants observed an incongruent (100%) force, their own response was significantly increased in comparison to the baseline (0%) and congruent (50%) conditions. These findings support Fadiga et al. (1995; see also Alaerts, Senot, Swinnen, Craighero, Wenderoth, & Fadiga, 2010a) where Transcranial Magnetic Stimulation (TMS) was applied to participant's primary motor cortex and Motor Evoked Potentials (MEP) measured in muscles that corresponded to the observed experimental movement condition. Their data showed that MEP activity was increased for action observation relative to non-action control conditions, suggesting that primary motor cortex excitability (increased through neural connections between the mirror neuron system and primary motor cortex; Fadiga et al., 1995) had a direct influence on specific muscle activity. In the data presented here, I show that muscle force responses were also influenced by the observation condition. I assume that greater primary motor cortex excitability arose from observation of the incongruent (100%) force, relative to the baseline (0%) and congruent (50%) conditions and that resultant increases in muscle activity increased the participant's intended force response (by a small, but significant amount).

One interesting aspect of these data was that the priming effects occurred for a particular response. Participants were trained to respond with a force that was 50% of their own maximum capability (i.e., until they were able to make consistent responses between 40% and 60% of their maximum force). Even with training to achieve the correct amplitude of the response parameter, observing another person's actions over-rode the training to influence production of force. In fact, the responses made were within the original accepted range of

response. That is, observed force influenced the participant's mean relative force by 5.1% over conditions. This suggests that participants continued to respond within the margins of the trained level, but within this level of response, were modulated by the observed force. I suggest that the data likely reflects force observation having an automatic effect on action execution, whereby the priming mechanism seems adaptable within the practiced and experienced responses measured (see Ocampo & Kritikos, 2010; Press, Bird, Flach & Heyes 2005 for similar findings).

These data are the first to show that action observation of force can prime subsequent executed force. This could be very interesting for applied research that uses action observation for rehabilitation. For example, Ertelt, Small, Solodkin, Dettmers, McNamara, Binkofski, & Buccino (2007) used observation rehabilitation therapy in eight patients and showed increased brain motor area activity for eight weeks following the intervention. Using similar methods, it could be that patients with strength loss through a broken a bone or lost limb function following brain injury (e.g., see Karlsson, Nilsson, Sernbo, Redlund-Johnell, & Obrant, 1996; Bohannon & Andrews, 1998 respectively) might be able to regain muscle strength through observation. These data here suggest that observation of action force would increase the excitability of the brain motor areas and in doing so, would stimulate the (strength loss) muscles through brain to muscle connections. Therefore, observation may provide a useful tool to support physical exercise in strength gain rehabilitation.

CHAPTER 3:

EFFECT OF ACTION OBSERVATION BOUTS ON ACTION FORCE AND TAPPING DEXTERITY BEHAVIOURS

The text and detail presented here exactly matches that of the submitted manuscript:

Salama, I. M., Springgay, S., Woska, B., Edwards, M. G. (2011). Effect of Action

Observation Bouts on Action Force and Tapping Dexterity Behaviours. *Submitted to*

Brain and Cognition.

3.1 Abstract

In a recent paper (Salama et al., 2011), I reported that the observation of grip force primed subsequent grip force responses and suggested that the positive effects could be used for neuropsychological strength rehabilitation of hemiparesis. In the present paper, I suggest that the typical observation-execution priming paradigm reported in the literature might be impractical for clinical use. Therefore, here I tested whether bouts of observation could also be used to prime subsequent force and tapping dexterity execution. The paper presents three experiments run on healthy control participants that measured force and tapping dexterity performance before and after action or control observation bouts. Overall, the data replicated our previous findings. In Experiment 3, observation of leg force significantly primed leg force execution, and in Experiments 1 and 2, observation of grip force compared to a control condition significantly primed dexterity. These data suggest that action bouts can be used to prime execution, a potentially better method for clinical applications. In the general discussion, I suggest how action observation could be used for rehabilitation in the clinical setting, and furthermore, suggest further experimental studies that could be investigated.

3.2 Introduction

In a recent paper, I reported that the observation of action force could prime subsequent action force execution (Salama et al., 2011). In the study, eighteen participants were required to make grip force responses that were 50% of their own maximum ability immediately after watching a video clip of a grip force action. The observed stimuli consisted of grip force corresponding to 0%, 50% and 100% of the model's maximum force ability. The aim of the study was to determine whether the observation condition influenced the action response. The results showed evidence that the observation condition influenced both absolute (kg) and relative (%) force differences (i.e., the participant's response relative to their own 50% maximum force ability). These findings were consistent with other action priming data showing that the observation of action can moderate subsequent execution (see for example Brass et al., 2000; Castiello et al., 2002; Dijkerman & Smit, 2007; Edwards et al., 2003; Gianelli et al., 2008; Griffiths & Tipper, 2009; Hardwick & Edwards, 2011).

In the literature, it is suggested that the likely mechanism thought to allow for the prime effects is that of the Mirror Neuron System (MNS; including the premotor, motor and parietal brain areas; Buccino et al., 2001). That is to say that action observation causes automatic activation of the MNS (Gallese et al., 1996; Rizzolatti et al., 1996) and that this activation moderates subsequent activation during action execution planning processes (Edwards et al., 2003). The two interesting points about Salama et al. (2011) was that firstly, it was the first paper to report that action observation priming could moderate force execution, suggesting that force of action must be represented during observation. Secondly, the data were consistent with neurosciences research showing that hand muscle Motor Evoked Potential (MEP) was increased from the combined presentation of action observation and primary

motor cortex Transcranial Magnetic Stimulation (TMS) (Alaerts et al., 2010a). MEP activity was increased for action observation relative to non-action control conditions, and furthermore, in correspondence with the force of the action observed (with greater force observation causing greater MEP activation). These data suggest that primary motor cortex excitability (increased through neural connections between the MNS and primary motor cortex; Fadiga et al., 1995) was moderated by observed action force, and thus supports the idea that the priming data reported by Salama et al. (2011) was likely caused by the same underlying neural activity.

In the action priming literature, there has been a tendency to suggest that the findings could be applied and used for rehabilitation. For example, in Salama et al. (2011), I suggested that the findings could be used to increase strength (or action force) in patients with limb strength (or action force) loss (e.g., with hemiparesis; reduced limb function as a consequence of contra-lateral brain damage). However, there have been relatively few papers that have investigated the use of action observation in the clinical rehabilitation sciences (see Celnik, Webster, Glasser, & Cohen, 2008; Ertelt et al., 2007; Iacoboni & Mazziotta, 2007; Pomeroy, Clark, Miller, Baron, Markus, & Tallis, 2005 for examples). I considered that one reason for a lack of investigation might have been a consequence of the perceived impracticability of using the prime effects. That is to say that the action prime effects reported in the experimental psychological sciences literature have been conducted over short time periods, with for example the observation prime condition presented for approximately five seconds before the measured execution response. In the clinical setting, it may be that presenting an observation condition immediately before having the participant perform a rehabilitation exercise might be difficult and costly if video stimuli were to be used requiring a computer for their presentation.

In the present study, I measured the effects of observation bouts (lasting approximately 12 minutes) on subsequent execution responses. The principle of the experiment was the same as that in Salama et al. (2011) in that I tested whether the observation of action brought about changes in action execution force. A pre-observation assessment was followed by an observation bout (observation of force actions vs. observation of a control condition) and then a post-observation assessment was conducted. The hypothesis was that observation of force actions would moderate performance after observation relative to before, and also relative to the observation of the control stimuli. The rationale for carrying out the study was to test whether bouts of observation also lead to priming effects. If I could show this, I considered that the findings might be more useful or practical to the clinical rehabilitation sciences. In addition to testing grip force (as in Salama et al., 2011), I extend the present paper by testing single-button tapping (Experiment 1) and two-button reach tapping hand dexterity (Experiment 2), and also leg force (Experiment 3) dependent measures.

3.3 Experiment 1: Handgrip force and single-button tapping dexterity

3.3.1 Methods

3.3.1.1 Participants

Ten undergraduate students (5 male) aged 20-32 (mean: 26) years of age took part in the study. All participants were right-handed, had normal or corrected-to-normal vision, had no experience of strength (action force) training, and were naïve to the purpose of the study. The School of Sport and Exercise Sciences, University of Birmingham Ethics Committee approved the methods used in the study.

3.3.1.2 Apparatus

In Experiment 1, there were experimental and control observation stimuli. The experimental stimuli consisted of ball squeeze, wrist curl and shoulder fly force-based actions and the control stimuli consisted of a moving tennis ball, mug and dumbbell object (with no body part or action presented). The experimental stimuli were filmed using a high definition digital camcorder positioned on a tripod approx 1.5m away from the model and 1.5m high. Two right-handed postgraduate volunteers from the University of Birmingham (one female and one male) that were not associated with the study acted as models. Each model performed the three different movement actions. For the ball squeeze and wrist curl actions, they were seated with their elbow against the lower part of the thigh to squeeze the tennis ball and to perform the wrist curl action, and when performing the shoulder fly, they were standing. Customising different animations to the control objects in PowerPoint made the control stimuli (13 slides were created with 13 different animations for each object). See Figure 3.1b for example pictures of the stimuli.

The experimental stimuli video clips were edited to only display the best thirty seconds of each action and each of the moving object presentations were created to last for thirty seconds. Stimuli were presented in blocks (i.e., experimental block consisted of ball squeeze, wrist curl and shoulder fly actions; and the control block consisted of an animated moving tennis ball, mug and dumbbell object). Within each block, each type of stimuli was repeated eight times, making twenty-four. These were presented in a random order and each block had an overall duration of twelve minutes. The experimental instructions and stimuli were presented using Windows Vista software on HP laptop with 15" monitor. They were presented using Media Player and PowerPoint presentation software.

The dependent measures used in Experiment 1 consisted of handgrip force and tapping speed dexterity. The participant's mean maximum handgrip force was recorded using a handgrip dynamometer ("Li" Lafayette Instrument Co. Lafayette Indiana 47903). To measure this, participants responded to the handgrip dynamometer for ten trials and the mean was calculated. Mean tapping dexterity was measured using Polhemus motion tracking equipment (200hz) and a tapping device constructed by the School of Sport and Exercise Sciences, University of Birmingham technical support services. The tapping device consisted of a square board (80cm x 80cm) made out of wood with 5 buttons (one central and four peripheral, 20cm apart; see Figure 3.1c). Tapping responses were measured by attaching one of the Polhemus motion tracking sensors to the back of the responding hand. Participants performed three trials where they tapped a single button (the closest button to the participant) for a period of 15 seconds. In this time, the number of taps was recorded by measuring the z-plane movements of the motion tracked hand movements. The mean tapping response was calculated from the total number of taps in the three trials.

3.3.1.3 Procedure

At the beginning of the study, participants read an information sheet and completed a consent form. They were then asked to perform the pre-observation measures of grip force and tapping dexterity. Following the pre-observation measures, participants were then seated 60cm centrally in front of the computer screen and instructed to watch either the experimental or control video clips (counterbalanced) for twelve minutes. Following observation, they were then tested for force and tapping dexterity using the same dependent measures as those used in the pre-observation condition. A week later, the same measures were taken, but this time for the observation of the control or experimental stimuli (i.e., the counterbalanced condition) (see Figure 3.1a).
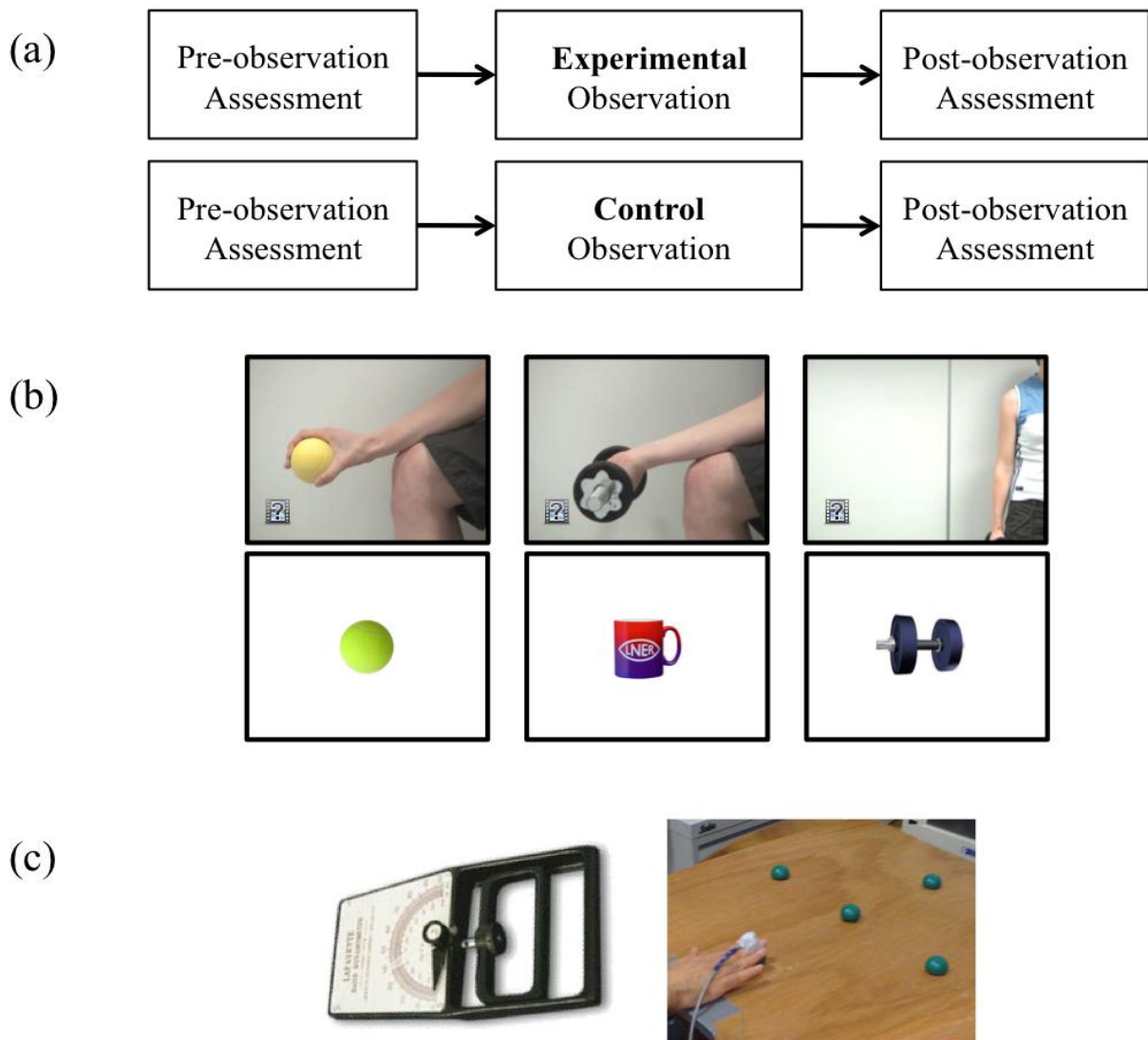
Figure 3.1: (a) Experimental design: Each participant carried out the experimental and control observation conditions, one week apart and with the order counterbalanced. (b) Independent measures were force versus control observation bouts presented for 12 minutes. The experimental condition consisted of repetitive force based actions involving a ball squeeze, wrist curl and shoulder fly, and in the control condition consisted of a non-action moving tennis ball, mug and dumbbell object. (c) Dependent measures were handgrip force and single button tapping dexterity. The button used was that which the hand is placed on. For each participant, the pre-observation dependent measure was subtracted from the post-observation in order to quantify the change in individual performance.

3.3.1.4 Data Analyses

The data were analysed using a repeated measures ANOVA. The independent variable was observation condition (Experimental vs. Control) and the dependent variables were the mean differences between pre- and post-observation for mean grip force and mean tapping dexterity. Therefore, a positive number would indicate an increase in force or tapping dexterity after observing the stimuli compared to that measured before observation. A three standard deviation from the mean confidence interval was used to remove any outlier data. This caused eight trials from 400 to be removed from maximum grip force and no trials from 120 to be removed from the tapping dexterity measure.

3.3.2 Results

The participant on average made 73 tap responses in the 15s recorded period and produced an average handgrip force response of 29.2 kg. The analysis of variance for handgrip force responses showed no significant difference between conditions ($F_{[1, 9]} = 0.10$, p=0.76). However, analysis of tapping dexterity showed that the experimental compared to control observation significantly influenced subsequent tapping dexterity ($F_{[1,9]} = 9.4$, $p < 0.05$). Participants on average tapped more following observation of the experimental compared to control stimuli (see Figure 3.2).

(a)

(b)
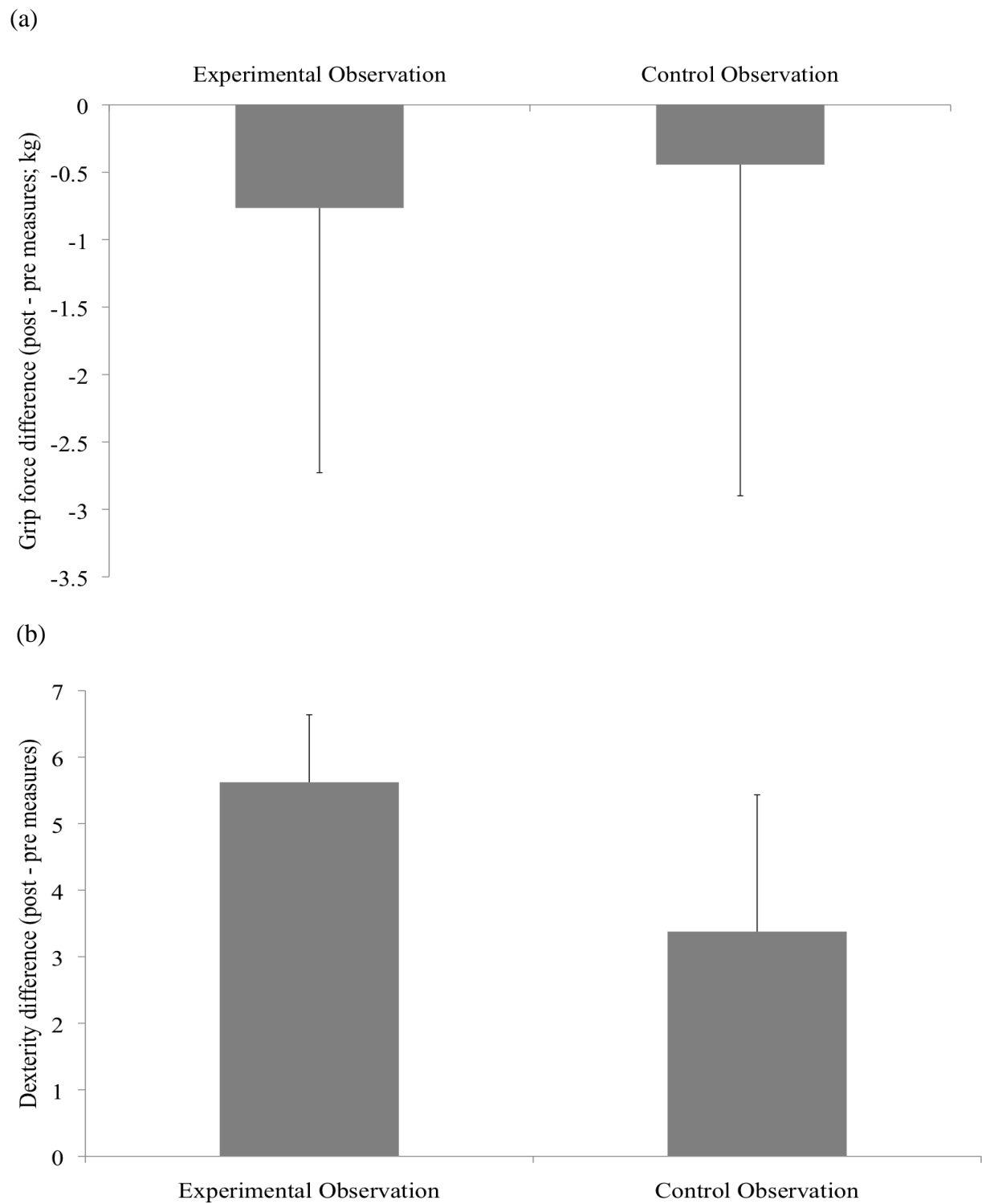
Figure 3.2: Effects of experimental force-based versus control observation conditions on (a) handgrip force (kg) and (b) tapping dexterity (number) difference between post and pre measures. Error bars show standard deviation between participant responses.

3.3.3 Discussion

In Experiment 1, I showed that the observation of experimental stimuli consisting of ball squeeze, wrist curl and shoulder fly actions caused participants show faster tapping dexterity responses in a single button tapping task compared to observation of non action control stimuli. These findings support the hypothesis that observation of the actions primed the motor system and lead to increased tapping dexterity. However, the data showed no effect of observation on the grip force response.

In Experiment 2, I aimed to replicate these effects, but by measuring more participants and also by measuring tapping dexterity using a more complex (though still simple) dexterity measure involving reach tapping movements between two buttons involving rotation of the shoulder.

3.4 Experiment 2: Handgrip force and two-button reach tapping hand dexterity

3.4.1 Methods

3.4.1.1 Participants

Sixteen undergraduate students (8 male) aged 20-32 (mean: 26) year of age took part in the study. All participants were right-handed, had normal or corrected-to-normal vision, and had no experience of strength (action force) training. Some of the participants tested also took part in Experiment 1. The School of Sport and Exercise Sciences, University of Birmingham Ethics Committee approved the methods used in the study.

3.4.1.2 Apparatus, Procedure and Analysis

The experimental instructions and stimuli used for the action observation conditions were the same as those used in Experiment 1 (experimental stimuli: ball squeeze, wrist curl and shoulder fly actions and control stimuli: moving tennis ball, mug and dumbbell object). The grip force response task was also the same as that in Experiment 1, and the tapping dexterity task was similar, except that the tapping responses were made between two buttons, positioned on the near versus far or left versus right buttons on the tapping apparatus presented in Figure 3.1c.

As in Experiment 1, participants first read an information sheet and completed a consent form. Following this, they completed pre-observation measures of grip force and tapping dexterity responses using the same apparatus as that in Experiment 1. Grip force was recorded in the same way, but to test their tapping dexterity, participants performed six trials where they tapped between two buttons on two tasks (right and left / near and far) for 15 seconds. The two buttons were 40cm apart from each other. As before, the tapping movements were recorded using Polhemus motion tracking equipment. Following the pre-observation measures, participants were then seated 60cm centrally in front of the computer screen and instructed to watch either the experimental or control video clips (counterbalanced with a week apart; each lasted twelve minutes). Following observation, they were then tested for force and tapping dexterity using the same dependent measures as those used in the pre-observation condition. One week later, the same measures were taken, but this time for the observation of the control (or experimental; counterbalanced) stimuli.

Data were analysed using a repeated measures ANOVA. The dependent variables were the mean differences between pre- and post-observation for grip force and tapping dexterity. For

both dependent measures, the independent variable was observation condition (experimental vs. control), and in addition, for tapping dexterity, there was an independent variable of task (right and left / near and far). Data that were outside of a three standard deviations from the mean were deleted. This caused one trial from 384 trials to be removed from the tapping dexterity measure and one trial from 640 trials to be removed from maximum grip force.

3.4.2 Results

The data showed similar findings to Experiment 1. Observation of force compared to control stimuli significantly influenced subsequent tapping dexterity measures ($F[1,15] = 5.7$, $p < 0.05$). However, there was no effect of task ($F[1,15] = 1.7$, $p = 0.22$) (near-far vs. left-right) and no significant interaction on tapping dexterity (see Figure 3.3). For the analysis of hand grip response, there was again no significant effect of condition ($F[1, 15] = 0.0$, $p = 0.95$) (experimental observation = -0.51kg vs. control observation = -0.56kg).
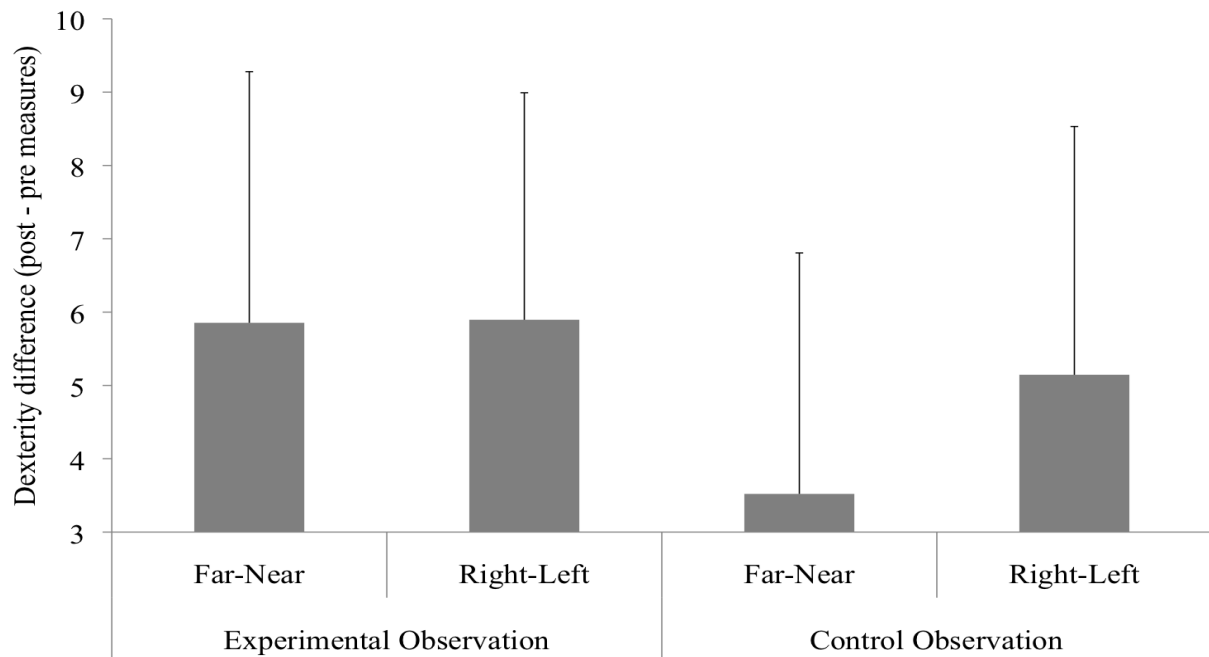
Figure 3.3: Effects of experimental force-based versus control observation conditions on reach tapping dexterity. The dependant measure was the difference between post and pre measures. There was no significant difference between task or any interaction between observation condition and task. Error bars show standard deviation between participant responses.

3.4.3 Discussion

These data in Experiment 2 replicated the findings presented in Experiment 1. Observation of the force-based stimuli compared to that of control stimuli caused an increase in tapping dexterity. The data from Experiment 2 were interesting as the findings extended to movements that required spatial positioning of the hand between two buttons and involving rotation of the shoulder. However, as in Experiment 1, the data showed no effect of observation on grip force, despite more participants tested.

The null finding showing that observation of the experimental compared to control stimuli had no effect on grip force responses was in contrast to the findings reported by Salama et al. (2011). To explain the null effects, I suggest that there were some issues that could have caused the inconsistent results between the study conducted in Chapter 1 and Experiments 1 & 2 of Chapter 3. One suggestion is that increased variance resulted from the use of force dynamometer between the pre- and post-observation measures. That is to say that in Salama et al. (2011), participants never removed their hand from the dynamometer during the experiment. In the experiments here, participants removed their hand from the dynamometer in between the two conditions. When considering this factor, I found that variance in peak grip force could be achieved by very slightly changing the hand posture distance between the fingers and palm of the hand on the tool (though still following the instructions to place the dynamometer in the palm of the hand, and the central sections of the digits on the bar of the dynamometer). Testing ourselves, I found that placing the bar in different positions of the central digit section resulted in different peak force responses. In the paper by Salama et al. (2011), this variation would have been limited as the participant always kept hold of the dynamometer and the analysis involved comparing relative differences in the grip force measure following a particular observation stimulus. A possible second reason for the null effect could have been caused by fatigue. In this chapter, participants were required to squeeze the dynamometer to the maximum of their ability, whereas in Chapter 2 participants were required to squeeze the dynamometer to 50% of their maximum ability. Therefore, for the ten trials before the observational conditions the muscle may have exhausted, and this could have affected the response following the observation. A final suggestion is that the participant's gender may have influenced the results. In Chapter 2, only females were tested, whereas in Chapter 3 mixed genders were tested.

In Experiment 3, I wanted to use a different experimental device that was available at the time of testing. Using a leg force dynamometer, I wanted to test whether it would be possible to achieve the force prime effect from bouts of observation. One of the reasons that I proposed to explain the null effects in Experiments 1 and 2 was that the amount of variance in the use of the handgrip dynamometer was too high. With the leg force dynamometer, participants pushed against the dynamometer and adjustments in posture appeared to have no influence on the force measure. Therefore, with the reduced variance in response measure, I now expected that observation of force stimuli would prime the force response. In addition, I also wanted to include a different control condition. In Experiments 1 and 2, the control condition involved observation of moving objects (without the presentation of a body part or action). Therefore, it could be that the priming was driven by generic observation of (any) action rather than specifically from the observation of upper-limb force based actions. In Experiment 3, participants observed both leg- and arm-based force actions. If generic action observation caused the tapping dexterity priming in Experiments 1 and 2, then both observation conditions would lead to a prime effect between the pre- and post-observation measures. However, if priming was based on specificity between the observed and executed actions, then observation of leg force actions should cause a greater prime effect than observation of arm force actions.

3.5 Experiment 3: Leg force responses

3.5.1 Methods

3.5.1.1 Participants

Fourteen undergraduate students (4 male) aged 20-33 (mean age of 21.8 years) participated in the study. All participants were right-handed and had normal or corrected-to-normal vision. The School of Sport and Exercise Sciences, University of Birmingham Ethics Committee approved the methods used in the study.

3.5.1.2 Apparatus, Procedure and Analysis

The experimental instructions matched those used in Experiments 1 and 2. The stimuli consisted of two separate sets of combined videos arm or leg force actions made by both a female and male model. The stimuli were filmed in a similar way to that in Experiments 1 and 2. The actions presented were exercises used by physiotherapists to improve strength (or action force) and were taken from the website (http://www.physiotools.com). These included for example, triceps dips and bicep curls for the arm exercises, and ankle raises and hopping for the leg exercises. For each or the exercises, the stimuli presented a series of repetitions. For each set, a total of fourteen clips were created and each lasted between 30 and 60 seconds. The stimuli bouts were matched in length and both lasted for 15 minutes.

The leg force responses were measured using a similar procedure to Experiments 1 and 2, though with a leg (rather than grip) force dynamometer. The participant was seated with their knee and the lower part of the front of the thigh positioned against a metal plate fixed to the dynamometer. The participant was required to use their thigh and leg flexors and extensors in

order to produce an upward force and push against the plate for five seconds. The force exerted was recorded from the dynamometer transducer using a computer and the Spike 5 software programme (Cambridge Electronic Design). The peak force exerted during the five seconds was recorded.

The design of the experiment and procedure was similar to that in Experiments 1 and 2, except that both observation conditions were ran in a single session. All participants started with a pre-observation condition where the participant performed six maximum force responses. Between each contraction, the participants were given a 30 second rest in which they were told to relax. Once this was recorded, half of the participants observed the experimental leg force stimuli and the other half of participants observed the control arm force stimuli (with participants selected randomly). Following observation, the participants performed another session of leg force measures (as in the pre-observation condition). Following these measures, the half of the participants that first observed the experimental leg force stimuli next observed the control arm force stimuli, and the half of participants that first observed the control arm force stimuli next observed the experimental leg force stimuli (that is, the observation conditions were counterbalanced). Following the second observation conditions, the participants again performed a session of leg force measures (as in the pre-observation condition).

The dependent measure was average maximum leg force (for the six trials) and the independent variable was condition (pre-observation, post leg force observation and post arm force observation). I chose to use the absolute force (measured in newtons) as a dependent variable so that I could determine whether the prime effects were a consequence of general action observation, whereby both observation conditions would show equal increases in force

responses compared to pre-observation, of whether the observation prime was specific, whereby only observation of leg force should prime the leg force dependent measure. The data were analysed using a single factorial repeated measures ANOVA.

3.5.2 Results

The analysis of the results now showed a significant effect of condition ($F_{[2,26]} = 5.3$, $p < 0.05$). Bonferroni Pairwise analyses showed that there were only significant differences between the observation of leg force condition and pre-observation baseline, and between the observation of leg force and observation of arm force. There was no difference between trials following observation of arm force compared to pre-observation baseline measure ($p > 0.05$) (see Figure 3.4).
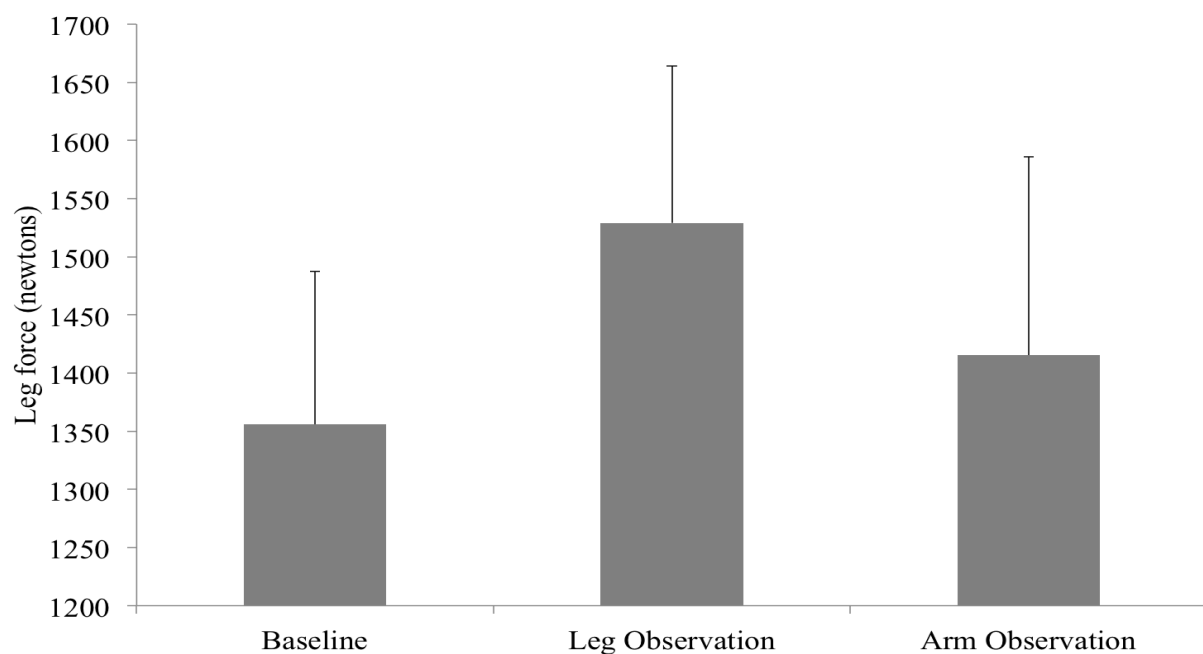
Figure 3.4: Effects of observing experimental leg force versus control arm force conditions on leg force responses compared to pre-observation baseline. Error bars show mean standard deviation within participant responses.

3.6 General Discussion

In this study, I set out to replicate Salama et al. (2011) and show that the observation of force could prime executed force. However, instead of measuring action execution immediately after the presentation of a single stimulus, I wanted to test whether bouts of observation lasting several minutes would prime an execution session. In Salama et al. (2011), I suggested that the effects of observation on execution for force might be useful for strength rehabilitation in patients with peripheral (bone or muscle etc.) or central (brain) injury that leads to strength loss. However, in the present paper I suggested that for clinical practice, a bout of observation might be easier to administer in the clinic. In Experiment 3 here, I replicated Salama et al. (2011) supporting the possible use of observation for rehabilitation. In addition to replicating Salama et al. (2011), I also showed that the observation bouts brought about positive increases in simple tapping (Experiment 1) and reach tapping (Experiment 2) dexterous actions. These additional findings further support the use of observation for rehabilitation improvements in function.

Although the data reported in this paper overall showed positive effects, there was one limitation being that I was unable to replicate the effects of force observation on grip force responses as reported in Salama et al. (2011). I suggest that the reason for the non-replication was because of increased variance in the measure caused by changes in the position by which the participant held the dynamometer in between the pre- and post-observation measures. In Experiment 3 however, I was able to replicate the priming effect of force observation on execution. I suggested that the reason for the success of Experiment 3 was simply a consequence of the dynamometer being only able to be used in one way (thus no variance in positioning as with the handgrip dynamometer). Furthermore, the leg dynamometer measure

was recorded using computer software rather than requiring the participant to read an analogue dial as on the grip dynamometer. This provided a more accurate measure, as with a dial, when the needle arrived between two markings for a given response, the experimenter had to subjectively estimate or round the measure on the basis of the relative needle position between the two possible readings. On the basis of these two points, I suggest that in order to assess strength gain using similar methods to those used in the present paper, it would be advisable to use dynamometers that provide consistent, accurate, low variance measures.

The primary aim of this research was to show that bouts of observation were able to prime subsequent execution in the same way that trial-by-trial stimulus-response methods can (e.g., Salama et al., 2011). I think that I have successfully demonstrated this as I showed that observation of upper limb force action relative to a control observation condition of moving objects primed simple and reach tapping dexterity (Experiments 1 and 2). I also showed that the effects were specific to the action observed. That is, in Experiment 3, priming of executed leg action only occurred following observation of leg force actions and not following observation of arm force actions, relative to a pre-observation measure. This latter result of specificity fits with the idea that the priming may come from mirror neuron system activity (Buccino et al., 2001; Gallese et al., 1996; Rizzolatti et al., 1996) and in turn moderates subsequent activation during action execution processes. This is consistent with evidence that MEP from TMS was moderated by the observation of force, and that there was specificity between the action observed and the MEP activity moderated (Alaerts et al., 2010a).

On the basis of the data presented here, and that reported by Salama et al. (2011), I suggest that observation of action force could be applied to clinical rehabilitation. I suggest that the method might be particularly effective if embedded into current clinical practice. That is to

say that I suggest a bout of specific observation should be presented to injured participants prior to receiving exercise or physical therapy. Of course, I suggest that a logical next step of this research would be to evaluate multiple clinical cases whereby one group of participants receives standard clinical exercises used by for example the physiotherapy services, and the other group of participants receives a bout of observation prior to the same exercises. The evaluation will assess whether the participants that received the observation benefit more (or faster) from the exercises than the participants that did not receive the observation.

In addition to the former suggestion, other research should consider how human mirror neuron system activity (assumed by measures of fMRI or TMS; e.g., Buccino et al., 2001 or Alaerts et al., 2010a), known to be active during observation of action, leads to priming after the observation conditions are complete. That is to say, how does the activity during observation lead to the prime effects reported here and in other published research (e.g., Brass et al., 2000; Castiello et al., 2002; Dijkerman & Smit, 2007; Edwards et al., 2003; Gianelli et al., 2008; Griffiths & Tipper, 2009; Hardwick & Edwards, 2011 etc). In order to assess this, measures need to be taken after observation, or at the time of execution. For example, does the mirror neuron system activity during observation remain active until execution? Or, is activity associated with action execution moderated by prior observation conditions? I suggest that future research should aim to answer these questions in order to better understand how action observation, or mirror neuron system processes can explain observation-execution priming.

CHAPTER 4:

EFFECTS OF STRENGTH BASED ACTIONS OBSERVATION ON BRAIN MOTOR AREA ACTIVITY

4.1 Abstract

In the literature, there is now overwhelming evidence that the observation of action can moderate or primes subsequent action execution. Evidence from the neurosciences has suggested that the observer's mirror neurone system, previously believed to be purely motor and involved in action planning, becomes active during action observation. It is suggested that representing observed action in the areas of the brain used for action planning might explain the priming effect, whereby the same areas of the brain represent the perception and action behaviours. From the findings already presented in this thesis (Chapters 2 and 3; see also Brass et al., 2000; Dijkerman & Smit, 2007; Edwards et al., 2003; Gianelli et al., 2008; Griffiths & Tipper, 2009; Salama et al., 2011; Salama et al., submitted), I might speculate that the observation of force-based actions compared to baseline and control actions also activates the mirror neuron system. In this Chapter 4, I fMRI scanned fifteen participants while they observed experimental stimuli involving arm and hand movements to heavy or light objects, or control stimuli involving non-action moving heavy or light objects. The results contrasted the brain activity between the observation of (experimental or control stimuli to) the heavy compared to light object. The results for observation of the experimental stimuli showed more significant activity in the Superior Frontal Gyrus (part of the mirror neurone system) and the Occipital Cortex when observing actions to the heavy than light objects. However, observation of the control stimuli only revealed significant differences in activity in the occipital cortex (and not in the mirror neurone system) for the observation of heavy compared to light moving objects. These data suggest that observation of force based actions specifically activated the mirror neurone system and supports the previous findings which suggest that mirror neurone activation during action observation might explain the mechanism behind the observation-execution priming effect reported in Chapters 2 and 3; (see also Salama et al., 2011; Salama et al., submitted).

4.2 Introduction

In Chapters 2 and 3 of this thesis (see Salama et al., 2011; Salama et al., submitted), I showed that the observation of action force could prime subsequent execution force and tapping dexterity. As presented in these chapters, the effect replicates previous literature (see for example Edwards et al., 2003). The explanation typically provided to explain the mechanism for the priming comes from research on the human 'mirror neurone system' (MNS). In these lines of research, the neuronal components of the MNS, previously assumed to be purely 'motor' and involved in action planning processes, were described to also be active in perceiving and interpreting actions executed by other people. In the observation context, and more specifically, for the representation of force (when considering the current thesis), research has shown that the observer has a surprising degree of accuracy to perceive or interpret the observed action, with for example, them being able to accurately judge the weight of objects being lifted by others. Previous research has shown that this ability seems reliant on 'mirror neuron system' activity, where for example, evaluation of the primary motor cortex excitability (part of the MNS) was shown to vary according to the observed force applied to an object in a grasping action (Alaerts et al., 2010a). That is to say that the motor cortex excitability was higher when observing actions made to heavy compared to light objects.

In Chapter 1 of the thesis, I have already provided a detailed review of the mirror neuron system. Therefore, here in Chapter 4, I only provide a review of the additional literature that have specifically explored the mirror neuron system for observation of strength or force actions. Currently, there are only several such papers that have explored how the observation of strength and force actions moderates perception and the mirror neuron system. In the first

papers, the focus was on how the observation of lifting actions moderated the perception of object mass (Runeson & Frykholm, 1981; Shim & Carlton, 1997). Following and related to this, there has been two brain stimulation studies and one brain imaging study (Alaerts et al., 2010a; Alaerts, Swinnen, & Wenderoth, 2010b; Hamilton, Wolpert, Frith, & Grafton, 2006 respectively) that investigated how observed actions to objects of different masses influence perceptual judgements and brain activity. In the following section, I will provide more details about these studies.

The paper by Shim and Carlton (1997) reported that observers could successfully perceive and identify the weight of an object being lifted by another person, simply from observing actions to a box object that contained a particular mass (5, 10, 15, 20 & 25 kg). The experiments used point light stimuli presentations. To make these stimuli, pieces of retro-reflective tape were attached to the head and to the major joints of a model's body. A light source was then directed towards these markers and the reflected light recorded and filtered to show just the body movements. Using the point light display stimuli, the participants were required to estimate the weight of a box from observing actions made by a model. These actions included either just the observation of action velocity during the lifting phase, or the observation of action velocity during the lifting phase, and also the placement of the object on a table, and walking while carrying the object. The data analyses showed that, although participants to some extent overestimated the weight inside the box, the estimated weight increased as a function of the increase in the actual lifted weight. That is to say that there was a positive correlation between the perceived and the actual mass showing that participants were able to perceive the weight of the object inside the box from the observation of the lifting action. There were no interactions between the observed actions and the mass of the object.

To our knowledge, there has so far only been one published functional brain imaging study that has explored the brain components used during action observation and requiring a judgement of perceived object mass (Hamilton et al., 2006). The study measured the motor brain networks known to be involved in the perception of observed actions and tested their involvement specifically for weight perceptual judgements while the participant both observed and executed an action to no object, or light and heavy object weights. The study involved 19 participants and while in the brain scanner, they performed either an experimental perceptual weight judgment task or a control task. In the experimental judgment task, the participants viewed a hand lifting a small box containing either a light or heavy weight, and placing the box on a shelf. As in Shim and Carlton (1997), the participants were requested to judge the weight of the box. However, in addition and at the same time as observing the action, the participant also had to either do nothing, lift light box that weighed 150g or lift a heavy box that weighed 750g. The boxes were plastic and compatible with the scanner (i.e., non-magnetic) and were placed on a platform above the subject's abdomen and chest. The control task involved two different conditions. These were, an *animacy control* where the participants were asked to judge the weight of a bouncing ball (with the absence of a biological effector) and a *task control* where the participants were asked to count the number of times a flickering square superimposed on a ball or a hand stimulus flickered. During the scans, the participants used their right hand to lift the object and their left hand to respond to the experimental or control task by pressing an appropriate key on a response box. As in standard brain imaging studies, the brain activity for the control tasks was subtracted from the brain activity of the experimental tasks. The main interest in the experimental task was to explore perception biases that resulted from the execution condition. A positive bias would indicate that participants judged the object to be heavier when lifting a light box or vice versa, whereas a negative bias would indicate that the participants judged the object to

be lighter when lifting a light box and vice versa. By contrasting brain activity for the bias effect, significant brain activity was found in the left extrastriate body area, inferior frontal gyrus and central Sulcus. Therefore, these data indicated that motor and perceptual processes for representation of weight appeared to be processed in similar brain networks, and were not as distinct or independent as was conventionally thought.

The final papers that I review measured how primary motor cortex excitability was moderated by the observation of actions to objects of different weight (Alaerts et al., 2010a; Alaerts, Swinnen, & Wenderoth, 2010b). As presented in the introduction to this thesis (Chapter 1), Transcranial Magnetic Stimulation (TMS) provides a method to investigate moderations in mirror neuron system activity due to the close connectivity between the premotor and primary motor cortex (Fadiga et al., 2005; Hallett, 2007). Alaerts et al. (2010a, b) were the first to use this technique to explore whether primary motor cortex excitability could be moderated by observing actions to objects with different weights. As described in Chapter 1, both papers (Alaerts et al., 2010a, b) calibrated the TMS equipment for each participant so that a single pulse of TMS delivered to the participants scalp would result in stimulation of the primary motor cortex and short thumb muscle; measured using EMG (see Chapter 1 for a detailed description of the method). The short thumb muscle was selected as the muscle would normally be used in a pinch grip and the physical lifting of the object.

In Alaerts et al. (2010a), two experiments were reported. In Experiment 1, eight participants observed an action made to an object that was either a light 10g piece of ribbon cable or a heavy 500g brass balance weight attached to the same ribbon. The actions always involved reaching to the object, grasping it, lifting it, holding it for a few seconds and returning it back to the initial location. Although the objects were of low frequency in everyday life, prior to

the experiment, each participant experienced grasping and lifting the objects. This reduced any potential effects that could have been related to unfamiliarity. During the experiment, TMS was applied during the observation of the lifting phase of action and EMG activity of the short thumb muscle recorded. The action to each object was presented 15 times, with the order of object presentation randomised. The results showed significantly higher MEP activity for observation of action to the heavy than light object, implying that primary motor cortex activation was greater during observation of the heavy than light objects. In the second experiment by Alaerts et al. (2010a), twelve participants were asked to observe actions made to objects that they had prior experience of interacting with and EMG activity was simultaneously recorded from the participant's opposition muscle of the right thumb and from the wrist flexors and extensor muscles (usually involved in power grip actions). The observed actions were presented in video clips lasting ten seconds each that depicted an actor lifting a bottle of three different weights (empty 0kg; half-full 1kg; and full 2kg). As in Experiment 1, a single pulse TMS paired to the recorded muscle activity was delivered during the observed lifting phase of action. EMG activity was contrasted for the independent variable of object weight in comparison to a baseline condition that recorded TMS-EMG activity during observation of a blank white screen without any action. The data showed significant MEP responses compared to baseline in the recorded muscles that would be actually involved in the action execution; the opposition and the extensor muscles, and not the flexor muscles. Moreover, the data showed increasing activity in correspondence to observing actions made to increased object weights (replicating their first experiment).

These findings support the previous effects of action observation on TMS-EMG findings reported in the literature (Borroni, Montagna, Cerri, & Baldissera, 2005; Fadiga et al., 1995; Gangitano, Mottaghy, & Pascual-Leone, 2001; Shim & Carlton, 1997) and provide further

evidence that action observation leads to brain activity modulations that are highly specific and represent the muscles recruited in execution. In addition, and new in these data, the areas moderated by action observation were further moderated according to the force exerted in the observed actions, such that, the greater the force required to lift an object, the higher the primary motor cortex excitability.

In a further paper reported by Alaerts et al. (2010b), they investigated the effects of the different effectors' and object related features that might contribute to an observer's ability to represent force in the observed actions. Three experiments were carried out. In the first experiment, the aim was to examine whether or not the kinematic motion pattern cues alone were sufficient to encode the exerted force related activity in the observer's motor system. The experiment presented participants with a video showing grasping and lifting movement kinematics to either a light or a heavy object, but the pressure and tension cues of the muscles contraction to the object were concealed. In the second experiment, the opposite video stimuli were presented. The stimuli instead presented pressure and tension cues to the object in the absence of the grasping and lifting kinematic pattern. In the final experiment, only the object (and any related weight cues) was presented to the participants (i.e., excluding kinematic and muscle state cues). Participants were asked to simply observe the presented stimuli. During the observation condition, single pulse TMS was delivered either during the lifting phase or during the holding phase (depending upon the experiment) and MEPs were recorded from the observer's muscles that match the actor's muscles being used in the observed actions. The results showed that all of the presented cues caused a moderation in the recorded TMS provoked MEP measure, with lift kinematics, muscle contraction and the object presentation, and that higher response occurred for the cues associated to the heavier than lighter objects.

In the present thesis chapter, I wanted to use fMRI methods to investigate how observation of force based actions to light or heavy object weight moderated mirror neuron system activity. From the research reported by Alaerts et al. (2010 a, b), I hypothesised that moderation of the primary motor or premotor cortex would occur; the areas thought to be measured by the TMS-MEP method (see Chapter 1). In addition, with fMRI, I wanted to explore whether objects of light and heavy mass moderated other parts of the mirror neuron system. That is to say that it might be that the moderation in mass results in a change in BOLD activity in the parietal part of the mirror neuron system. This is because previous fMRI studies have suggested that the parietal lobe represents objects used in actions (e.g., Buccino et al., 2001). By using fMRI methods, I was for the first time able to investigate whether manipulations in actions made to light and heavy object mass caused moderated BOLD activity across the mirror neuron system.

4.3 Methods

4.3.1 Participants

The experiment tested fifteen postgraduate student participants and consisted of seven females and eight males, aged 20-30 (mean: 25) years of age. All of the participants were right-handed and had normal or corrected-to-normal vision. As part of the pre-testing protocol, participants were screened and excluded for any potential problems associated with MRI experimentation (e.g., whether the participants had any metal implants, tattoos, history of brain injury). Participants gave written informed consent prior to participation. The Birmingham University Imaging Centre Ethics Committee approved the methods used in the study.

4.3.2 FMRI data acquisition and pre-processing

The fMRI data was obtained using a 3T Phillips Achieva scanner with an 8-channel SENSE parallel head coil. Images were acquired using a full-brain ascending gradient echo-planar T3* sequence (TR = 3000 ms; TE = 35 ms; FA = 85.3°; FOV = 240 x 240 mm^2; Matrix = 80 x 80; SENSE Factor = 2) and consisted of 156 slices of 3 mm thickness with no inter-slice gap. A block design was used and a total of 465 volumes (dynamics) in each session were collected. Two dummy scans were incorporated in each run to allow for steady state magnetization. High-resolution T1-weighted anatomical 3D images were also acquired to allow anatomical localization (TR = 8.4 ms; TE 3.8 ms; FOV = 288 x 232 mm^2; Matrix = 288 x 232; Voxel Dimension = 1.0 x 1.0 x 1.0) and consisted of 175 slices. Participants were instructed to keep their head still and head motion was minimized using the standard Philips head coil with ear pads. The data exported from the scanner were converted from PAR/REC (PAR= the text header file, REC= the binary file) or DICOM (Digital Imaging and Communications in Medicine) format to HDR (High Dynamic Range) format by use of MRICRO software and then to 'Nifti' format (standard MRI analysis format) by use of FSL software. These 'Nifti' files are usually compressed with gzip and stored as.nii.gz files.

4.3.3 Data Processing

The fMRI data processing was carried out using FEAT (FMRI Expert Analysis Tool) Version 5.98 that was part of the software package FSL (FMRIB's Software Library: www.fmrib.ox.ac.uk/fsl). The following pre-statistics processing were applied to the data: (i) motion correction using MCFLIRT (Motion Correction FMRIB's Linear Image Registration Tool) (Jenkinson, Bannister, Brady, & Smith, 2002); (ii) slice-timing correction using Fourier-space time-series phase-shifting; (iii) non-brain removal using BET (Brain Extraction Tool) (Smith, 2002); (iv) spatial smoothing by using a Gaussian kernel of 5 mm FWHM (Full

Width Half Maximum); (v) grand-mean intensity normalisation of all volumes by a single multiplicative factor; highpass temporal filtering (Gaussian-weighted least-squares straight line fitting, with sigma = 50.0s). Time-series statistical analysis was carried out using FILM (FMRIB's Improved Linear Model) with local autocorrelation correction (Woolrich, Ripley, Brady, & Smith, 2001).

After preprocessing, the functional scans were registered to the MNI152 standard space (average T1 brain image constructed from 152 normal participants at the Montreal Neurological Institute, Montreal, QC, Canada) with FLIRT (Jenkinson et al., 2002).

4.3.4 Experiment Design

The experiment presented two types of observation stimuli, one that was experimental and one that was control. The experimental stimuli were strength-based actions that consisted of an arm curl, wrist curl or shoulder fly action. These actions were either made to a light or heavy object weight. The control stimuli consisted of two moving objects, either a light chair or a heavy door. The experimental stimuli were filmed using a high definition digital camcorder positioned on a tripod approximately 1.5m away from a model and 1.5m high. A female right-handed postgraduate volunteer from the University of Birmingham that was not associated with the study acted as model. She performed the three different types of movement actions (arm curl, wrist curl and shoulder fly) using both her left and right hands. For each type of movement, she either lifted a bar with no weights on it (light object) or the bar with a 2.5 kg weight (heavy object). A total of twelve different video clips were recorded. For the wrist curl actions, the model was seated facing the camera and with her elbow against the lower part of the thigh. For the arm curl actions, the model was seated laterally with her

elbow apart from the thigh. Finally, for the shoulder fly, the model was standing laterally. See

Figure 4.1 for example pictures from the video stimuli.

The control stimuli consisting of chair and door movements were made by using different

animation features available in the software Microsoft Power Point and saving the sequences

as video clips. The chair and door were presented in two different orientations (left and right)

making four different movements (see Figure 4.2). In addition to the experimental and

control stimuli, a baseline condition of a fixation cross was also presented. All of the stimuli

were produced to display for a total of thirty seconds. Stimuli were presented using E-prime

software and were projected onto a screen within the scanner via a mirror fixed to the head

coil.

Figure 4.1: Experimental stimuli. Three panels of four pictures illustrate the wrist curl, arm curl and shoulder fly types of experimental observation stimuli. The left six pictures are examples of actions made with the light weight version of the object and the right six pictures are examples of actions made with the heavy weight version of the object. Within each pair of pictures (e.g., top left pair; wrist curl and light weight), a left and right hand version was created and the manner in which the movement was performed is illustrated by the extents in the range of motion with the left hand showing the beginning and the right hand showing the end of the movement. The top right pair shows the wrist curl and heavy weight using left and right hands. The middle left pair shows the arm curl and light weight and the middle right pair shows the arm curl and heavy weight. The bottom left pair shows the shoulder fly and the light weight and the bottom right pair shows the shoulder fly and the heavy weight.

Figure 4.2: Control stimuli. From left to right: chair with left orientation, chair with right orientation, door with left orientation and door with right orientation. The control stimuli were made by using different animation features available in the software Microsoft Power Point and saving the sequences as video clips. The dashed shapes with red and green arrows show some samples of different motion paths used (e.g. from left to right: spiral left, vertical figure of 8, heart and curvy right).

The experimental and control sessions were run on different days and the order counterbalanced across participants. For each experimental or control session, the stimuli were presented in three trial blocks (also called runs in the brain imaging literature), and each block (or run) lasted for approximately 7.5 minutes (making an approximate total of 22.5 minutes). For the experimental blocks (or runs), separate trials were presented that contained wrist curl, arm curl and shoulder fly actions (left vs. right and light vs. heavy), and in addition, three separate fixation cross video clips (each 30s long) were presented and used as base-line comparators. For the control blocks (or runs), the trials consisted of the moving door and chair (left vs. right orientation), and as in the experimental session, three separate fixation cross video clips (each 30s long). In both the experimental and control blocks (runs), the trial order was randomised. See Figure 4.3 and 4.4 for a schematic presentation of the experimental design used.

Experimental Session

Run:1 Experimental	AHML (30S)	AHMR (30S)	ALML (30S)	ALMR (30S)	SHML (30S)	SHMR (30S)	SLML (30S)	SLMR (30S)	WHML (30S)	WHMR (30S)	WLML (30S)	WLMR (30S)	FIX1 (30S)	FIX2 (30S)	FIX3 (30S)

Run:2 Experimental	AHML (30S)	AHMR (30S)	ALML (30S)	ALMR (30S)	SHML (30S)	SHMR (30S)	SLML (30S)	SLMR (30S)	WHML (30S)	WHMR (30S)	WLML (30S)	WLMR (30S)	FIX1 (30S)	FIX2 (30S)	FIX3 (30S)

Run:3 Experimental	AHML (30S)	AHMR (30S)	ALML (30S)	ALMR (30S)	SHML (30S)	SHMR (30S)	SLML (30S)	SLMR (30S)	WHML (30S)	WHMR (30S)	WLML (30S)	WLMR (30S)	FIX1 (30S)	FIX2 (30S)	FIX3 (30S)

Figure 4.3: The figure provides an example of how the experimental stimuli were presented. They were three runs and each run consisted of wrist curl (W), arm curl (A), shoulder fly (S) action types [Left (L), Right (R), Light Mass (LM) and Heavy Mass (HM)] and three fixation cross video clips (Fix 1, Fix2 and Fix 3). Each video clip stimulus lasted for a duration of 30s, and each total run lasted 7.5 min (with a total of 22.5 min for the three runs). Video clips were randomised in each run.

Control Session

Run:1 Control	DL1 (30S)	DR1 (30S)	CL1 (30S)	CR1 (30S)	DL2 (30S)	DR2 (30S)	CL2 (30S)	CR2 (30S)	DL3 (30S)	DR3 (30S)	CL3 (30S)	CR3 (30S)	FIX1 (30S)	FIX2 (30S)	FIX3 (30S)

Run:2 Control	DL1 (30S)	DR1 (30S)	CL1 (30S)	CR1 (30S)	DL2 (30S)	DR2 (30S)	CL2 (30S)	CR2 (30S)	DL3 (30S)	DR3 (30S)	CL3 (30S)	CR3 (30S)	FIX1 (30S)	FIX2 (30S)	FIX3 (30S)

Run:3 Control	DL1 (30S)	DR1 (30S)	CL1 (30S)	CR1 (30S)	DL2 (30S)	DR2 (30S)	CL2 (30S)	CR2 (30S)	DL3 (30S)	DR3 (30S)	CL3 (30S)	CR3 (30S)	FIX1 (30S)	FIX2 (30S)	FIX3 (30S)

Figure 4.4: The figure provides an example of how the control stimuli were presented. They were three runs and each run consisted of chair (C) and door (D) action types [Left (L), Right (R)]. Within each run, each stimulus was repeated three times (1, 2 and 3). As in the experimental session, three fixation cross video clips (Fix 1, Fix2 and Fix 3) were included. Each video clip stimulus lasted for duration of 30s, and each total run lasted 7.5 min (with a total of 22.5 min for the three runs). Video clips were randomised in each run.

4.3.5 Data analyses

A first level analysis was carried out individually on each run for each participant using FEAT (FMRI Expert Analysis Tool) Version 5.98, which was part of FSL (FMRIB's Software Library, www.fmrib.ox.ac.uk/fsl) and used to investigate the activity during the different experimental conditions. In this analysis, Z (Gaussianised T/F) statistic images were created using threshold clusters determined by a Z value greater than 2.3 for the significance $p = 0.05$ (Worsley, Liao, Aston, Petre, Duncan, Morales, & Evans, 2002). A second level analysis was then carried out using the same FEAT software and contrasts were combined for each participant in the first-level analyses. A final higher level analysis was carried out using FLAME stage 1 (FMRIB's local analysis of mixed effects) and used to compare the second level analysis across all participants for the different independent variables (Beckmann, Jenkinson, & Smith, 2003; Woolrich, 2008; Woolrich, Behrens, Smith, Jenkinson, & Beckmann, 2004).

4.4 Results

The experimental and control sessions of the experiment were analysed separately. For each, statistical mapping was first conducted for single subject analyses and then a random effect group analysis was run (one sample t-test). For the experimental stimuli, contrasts were made between the activations related to the experimental light object action stimuli relative to the experimental heavy object action stimuli (heavy – light activity). The data showed significant activations in the left hemiphere Superior Frontal Gyrus (SMA; part of mirror neuron system), Lingual Gyrus and the Frontal Pole. The data also showed significant bilateral

activations in the Lateral Occipital Gyrus, Occipital Fusiform Gyrus and Occipital Pole (see

Figure 4.5). Peak maxima activity for MNI (Monterial Neurological Institute) coordinates

and each of the Z scores for these areas are presented in Table 4.2.
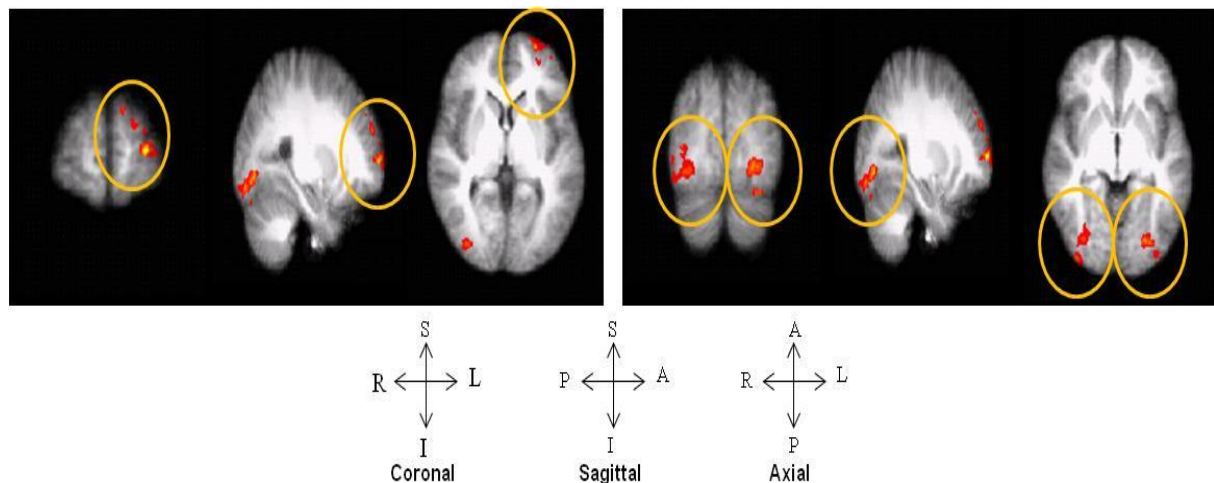
Figure 4.5: Brain areas that showed significantly increased activity for the contrast between observations of actions to heavy compared to light objects within the experimental condition. The left image illustrates the significant activation in the Superior Frontal Gyrus (SMA; part of MNS) and Frontal Pole. The right image shows the activation in the Occipital Lobe that included the lateral occipital gyrus, occipital pole, occipital fusiform gyrus and lingual gyrus. Each image shows from left to right: coronal, sagittal, and axial section of the brain (the appropriate planes and directions shown below the images). Functional images are overlaid on the average high-resolution scan transformed into standard (MNI152) space. Coordinates for these areas are presented in Table 4.1.

Table 4.1: Brain areas active for the contrast between observation of actions to the heavy and light object in the experimental stimuli. The areas selected are presented according to Harvard-Oxford Cortical Structural Atlas. The mark '' denotes bilateral activity.*

Area for Local Maxima	MNI			Z Score
	X	Y	Z	
[Heavy > Light] Left Hemisphere				
Superior Frontal Gyrus	-13	53	39	2.44
Frontal Pole	-27	61	6	4.73
Lateral Occipital Cortex*	-23	-90	-10	3.07
Occipital Pole*	-24	-91	-10	3.06
Occipital Fusiform Gyrus*	-24	-83	-10	3.61
Lingual Gyrus	-24	-82	-10	3.02
[Heavy > Light] Right Hemisphere				
Lateral Occipital Cortex*	39	-88	-10	4.19
Occipital Pole*	36	-91	-10	3.03
Occipital Fusiform Gyrus*	34	-82	-10	3.10

MNI: Montreal Neurological Institute.

For the control stimuli, contrasts were made between the activations related to the observation of control stimuli involving the heavy door object stimuli relative to the light chair object stimuli. Interestingly, the data did not show any activation in brain areas related to motor coordination, but rather only showed bilateral significant activation in the occipital lobe region, including the Lateral Occipital Gyrus, Occipital Pole, Occipital Fusiform Gyrus, and Lingual Gyrus. The data also showed significant activation in the left Intra-Calcarine and

Supra-Calcarine Gyri (also part of the occipital cortex) (see Figure 4.6). MNI coordinates and Z scores are presented in Table 4.2.
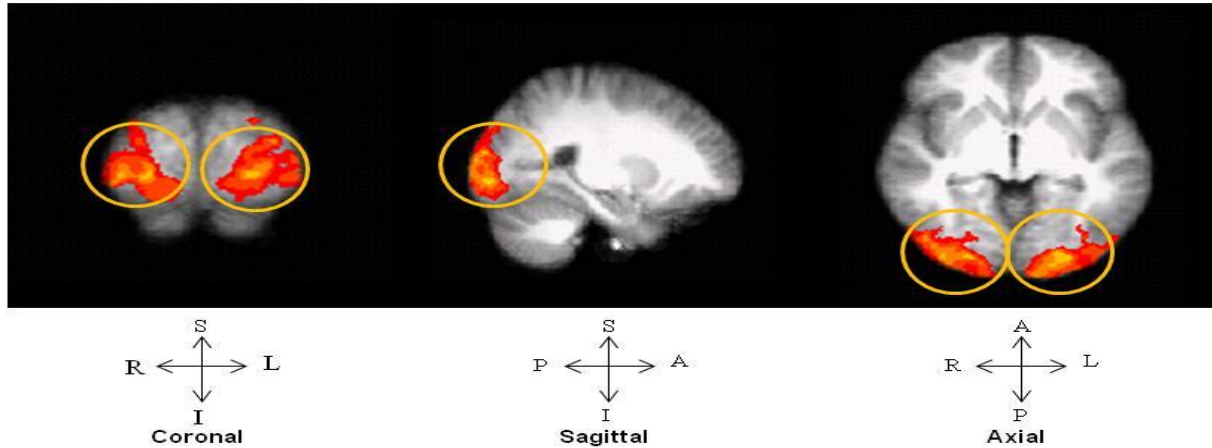
Figure 4.6: Brain areas that showed significantly greater activity for the contrast between observation of heavy (door) compared to light (chair) objects within the control condition. Activation only involved the Occipital Lobe. This included bilateral lateral occipital gyrus, occipital pole, occipital fusiform gyrus and lingual gyrus, and left intra-calcarine and supra calcarine gyri (parts of the occipital lobe). The image shows from left to right: coronal, sagittal, and axial section of the brain (the appropriate planes and directions shown below the images). Functional images are overlaid on an average high-resolution scan transformed into standard (MNI152) space. Coordinates for these regions are presented in Table 4.2.

Table 4.2: Brain areas active for the contrast between observation of the moving door compared to chair in control stimuli. The areas selected are presented according to Harvard-Oxford Cortical Structural Atlas. The mark '' denotes bilateral activity.*

Area for Local Maxima	MNI			Z Score
	X	Y	Z	
[Chair > Door] Left Hemisphere				
Lateral Occipital Cortex*	-28	-90	-3	4.65
Occipital Pole*	-18	-95	-2	4.67
Occipital Fusiform Gyrus*	-15	-95	1	3.96
Lingual Gyrus*	-16	-92	1	3.97
Intra-Calcarine Cortex	-15	-91	1	3.26
Supra-Calcarine Cortex	-15	-89	1	2.56
[Chair > Door] Right Hemisphere				
Lateral Occipital Cortex*	41	-85	1	4.62
Occipital Pole*	24	-97	3	3.93
Occipital Fusiform Gyrus*	26	-87	3	4.00
Lingual Gyrus*	19	-87	-8	3.24

MNI: Montreal Neurological Institute.

4.5 Discussion

The aim of the experiment reported here was to investigate, using fMRI methods, whether observation of force based actions would moderate mirror neuron system activity in comparison to a control condition. On the basis of the papers by Alaerts et al. (2010 a, b), I predicted that the observation of action to heavy compared to light objects would result in greater activity in the mirror neuron system. To carry out the experiment, I presented participants with video clips of actions made to heavy and light objects (experimental condition) or heavy and light objects moving without an action (control condition). To understand how the brain represented object weight, I contrasted brain activity between the heavy and light object video clips. The data showed a significant activity in the Superior Frontal Gyrus, Frontal Pole, and Occipital Cortex for the experimental action observation conditions, and Occipital Cortex for the control moving object conditions. Therefore, as hypothesised, these data showed some evidence that action observation to the heavy than light objects specifically involved the Superior Frontal Gyrus, an area reported by others as part of the mirror neuron system (Buccino et al., 2001; Buccino et al., 2004b; Cochin et al., 1998; Decety et al., 1997; Grafton et al., 1996; Grezes et al., 2003; Johnson-Frey et al., 2003; Lui et al., 2008; Saygin et al., 2004).

From these data, I might assume that either the Superior Frontal Gyrus or the Frontal Poles must specifically represent object weight for action. This is in contrast to the activations shown in the Occipital regions that were approximately common across the two types of stimuli. I suggest that this activation likely represents vision motion differences between the heavy and light stimuli that were not completely excluded in the subtraction between conditions, perhaps because the heavier object was usually visually larger than the light

object. While the finding that action observation to heavy than light weight activated the Superior Frontal Gyrus (SMA) of the mirror neuron system, the finding of significant Frontal Pole activity was unexpected. There is currently little understanding of what main function the Frontal Pole involves, with a variety of different functions suggested. However, one recent paper may shed some light on the finding presented here. Tsujimoto, Genovesio and Wise (2011) presented a literature review about the possible role of the Frontal Poles in behaviour and made the suggestion that the role was to monitor goal behaviour. Given this suggestion, it might be that the observation of the actions that I presented here may have triggered a goal representation, perhaps with the actions made to the heavier than light weights having a more purposeful goal; that is to exercise.

Based on this discussion, it is perhaps 'safe' to assume that the Superior Frontal Gyrus (SMA) activity may have been specifically responsible for object weight representations in action. This somewhat supports the research reported by Alaerts et al. (2010 a, b). One small problem was that I originally hypothesised that moderation of the primary motor excitability, as reported by Alaerts et al. (2010 a, b), was assumed to be a consequence of object weight being represented in the premotor cortex of the mirror neuron system. This assumption comes from the TMS-MEP literature that assumes the moderation in primary motor cortex excitability comes from premotor cortex activity (see Fadiga et al., 1995; also Chapter 1). However, these assumptions are difficult to prove with the TMS-MEP method, as there is no concurrent measure of brain activity taken. From the data presented in the current thesis, I suggest that the Superior Frontal Gyrus (SMA) activity must be responsible for moderating primary motor cortex in the TMS-MEP method, presumably through similar neural links between the Superior Frontal Gyrus and primary motor cortex. Using these same arguments, I might also assume that Superior Frontal Gyrus activity and subsequent moderations of

primary motor cortex excitability might explain the mechanism that causes observation of

action force to influence subsequent force and tapping dexterity execution (Salama et al.,

2011; Salama et al., submitted; Chapters 2 and 3).

One limitation of these data, and indeed similar research reported in the literature, is that the

neural areas reported active for action observation typically come from experiments that

measured brain activity concurrent to the observation stimuli (as in the present thesis). While

this provides knowledge of how action observation is processed by the brain, it does not

provide clear evidence of how the brain areas go on to influence subsequent neural processes,

such as primary motor cortex excitability, or influence action behaviours, such as in the case

of action priming. In order to measure which parts of the brain are used in the subsequent

processes after action observation, it is necessary to scan the brain after the observation of

action stimuli is complete. In the next chapter of this thesis (Chapter 5), I used a new

technique of brain imaging analysis in order to assess how action observation influenced

subsequent brain activity.

CHAPTER 5:

DOES OBSERVATION OF ACTIONS COMPARED TO MOVING OBJECTS MODULATE BRAIN RESTING-STATE ACTIVITY?

5.1 Abstract

There is substantial evidence reported in the literature showing that the observation of action activates areas of the brain associated with the mirror neuron system (the same brain areas used for execution) and also that action observation primes action execution. The two findings are hypothetically linked, with the suggestion that action priming occurs because of the shared neural processes for action observation and execution. However, so far, no study has investigated how brain activity during observation primes brain activity associated with execution. In the thesis chapter reported here, I investigated brain resting activity following an observational task in order to investigate how action observation influences brain activity after the observation condition ceases. Fifteen participants were scanned immediately before and after being exposed to observational stimuli that either included hand and arm strength based movements or control stimuli of moving objects. The data revealed that activity following action observational stimuli compared to baseline (pre-observation) and control (post-observation) stimuli successfully yielded significant widespread fronto-parietal and motor area brain activations. Interestingly, the brain regions shown to be significantly active following exposure to the experimental stimuli included the mirror neuron system. I suggest that the ongoing brain activity following observational stimuli might serve as the mechanism that explains how brain activity during observation, subsequently influences other brain activity or executed action performance.

5.2 Introduction

In the previous chapter of this thesis (Chapter 4), I reported that observation of actions to heavy compared to light objects moderated the observer's mirror neuron system brain activity, whereas there was no mirror neuron system activity in a control condition that involved the same participants observing moving (but non action) heavy compared to light objects. In the present chapter (Chapter 5), I again used brain-imaging measures, but this time examined brain activity during rest-states that were recorded immediately prior to and following observation of the same stimuli as that used in Chapter 4. The value of this measure was that I could evaluate how action observation influenced brain activity after the observation condition was complete, rather than during observation as presented in Chapter 4 and in the literature. I argue that measuring rest-state activity or activity after the observation condition might provide value for understanding how action observation can prime subsequent action execution; perhaps providing new knowledge for what brain areas cause the findings presented in Chapters 2 and 3 of this thesis.

The examination of rest-state activity in cognitive neuroscience or neuropsychology is a relatively new type of method. The measure involves assessing brain (BOLD fMRI) activity while the participant rests (i.e., representing the brain's baseline activity) and considers how former experiences in the absence of any immediate stimuli or performance influences the (resting) brain activity. Therefore, the measure involves recording brain activity while the participant is free to think about anything: the study, what they are going to do after the study, or something completely different. The only instruction is that they should keep their eyes open and look at a fixation cross presented on a visual display. Because of this freedom in possible activities that will be present during the recording, typically, long sessions of rest-

state are measured in order to average across all of the different thoughts that a participant may have (all of which will use different parts of the brain). The end result is that the recorded rest-state period will contain a variety of activity, usually referred to as noise. The main aim is to analyse the noise in order to determine whether there are any particular brain areas of activity that are active throughout the recording, perhaps indicating a non-conscious or automatic behaviour influenced by the prior to rest-state activity. To analyse rest-state, correlated brain populations have been defined and called the 'resting state network' (Damoiseaux, Rombouts, Barkhof, Scheltens, Stam, Smith, & Beckmann, 2006). Using Probabilistic Independent Component Analysis (PICA), evaluations of fluctuations in activity within these correlated networks are considered in relation to an independent variable, and compared to noise and error (i.e., the activity caused by the variety of participants cognitive thoughts, or by artefacts such those that result from head motion or physiological and autonomic changes; e.g., cardiac pulsations or respiratory cycle etc.) (Damoiseaux, et al. 2006; Hutchison, Leung, Mirsattari, Gati, Menon, & Everling, 2011; De Luca, Beckmann, Stefano, Matthews, & Smith, 2006).

In this chapter, I present the first research that has considered how action observation moderates rest-state activity. While there has been other papers that have used and examined the functional activity during the brain resting state (e.g., Albert, Robertson, & Miall, 2009; Biswal, Yetkin, Haughton, & Hyde, 1995; Damoiseaux et al., 2006; Krakauer & Shadmehr, 2006; De Luca et al., 2006; Miall & Robertson, 2006; Shadmehr & Holcomb, 1997 etc.), only one paper by Albert et al. (2009) has considered how visuomotor learning processes might moderate rest-state activity. I therefore provide a detailed review of this specific paper.

In the study carried out by Albert et al. (2009), two groups of participants completed a sensory-motor tracking task where the participant adapted joystick movements to a novel cursor position presented on a computer screen. The two groups consisted of an experimental and a control group. The experimental group performed the sensory-motor task without any explicit feedback, whereas the control group did receive explicit feedback. The difference therefore between the two groups of participants was that the experimental group experienced visuomotor learning whereas the control group learned the movements through instructional feedback. Both task groups under-went a resting state measure before completing the tasks, and later, under-went a second resting state measure after completing the tasks. Using Probabilistic Independent Components Analysis (PICA) of the BOLD signal, the authors were able to explore the networks involved during rest, and to measure changes in these neural networks for the after compared to before rest-state activity, as well as comparing the differences between the experimental and control groups. The analyses of data demonstrated that the experimental group, but not the control group had moderations in particular resting state areas. These were the frontoparietal and cerebellar networks; areas commonly active during the execution of actions (Damoiseaux et al., 2006). These data were the first to show that motor learning could be measured after the physical practice event. In measuring the 'resting brain', it was suggested that activity in the motor networks likely reflected neuronal connections of off-line automatic (or non-conscious) motor memory consolidation.

The findings by Albert et al. (2009) are particularly interesting to the current thesis in that the same measures could be used to determine how activity during the observation of action influences brain activity after the observation, and furthermore, whether rest-state activity can appear to explain the priming effects of observation on subsequent execution (Edwards et al., 2003; Salama et al., 2011; Salama et al., submitted; see Chapters 2 & 3). From existing

literature, I know that the observation of action activates the mirror neuron system (involving the Inferior Parietal Lobule, the premotor cortex and the Superior Frontal Gyrus; Buccino et al., 2001; Buccino et al., 2004b; Grezes et al., 2003; Lui et al., 2008; Rizzolatti & Craighero, 2004). However, these data only measure (assumed [3]) concurrent activity between observation and execution. For the prime effect, presumably, this activity must continue following the observation in order to influence motor planning processes for execution. Until now however, this hypothesis has not been explored.

In the present study, I wanted to replicate and extend the research by Albert et al. (2009) by, for the first time, measuring the effects that action observation has on resting state motor networks. I suggest that ongoing activity in the networks that overlap with the mirror neuron system, after compared to before the experimental observational task, the activity could be used to explain a possible mechanism behind the priming and motor planning for subsequent execution reported in Chapters 2 and 3. Based on Albert et al. (2009), I hypothesised that watching force based actions (experimental condition) would bring about more brain excitability in the motor area resting state networks compared to the pre-observation rest period (baseline condition) and also in comparison to changes between pre- and post-observation of watching (non-action) moving objects (control condition).

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[3] We say 'assumed' because it can be difficult to accurately measure the concurrent activity between observation and execution as there is a delay in the BOLD (composite) measure that doesn't start simultaneously with the neuron activity.

5.3 Methods

5.3.1 Participants

The experiment tested the same fifteen postgraduate student participants as that reported in Chapter 4 (seven female and eight male participants, aged 20-30, mean 25 years of age). All of the participants were right-handed and had normal or corrected-to-normal vision. Prior to the experiment, the participants were screened and excluded for any contraindications (e.g., metal implants, tattoos, history of brain injury etc). Participants gave written informed consent prior to participation. The Birmingham University Imaging Centre Ethics Committee approved the methods used in the study.

5.3.2 FMRI data acquisition and pre-processing

The fMRI data was obtained using a 3T Phillips Achieva MRI scanner with an 8-channel SENSE parallel head coil. Images were acquired using a full-brain ascending gradient echo-planar T3* sequence (TR = 3000 ms; TE = 35 ms; FA = 85.3°; FOV = 240 x 240 mm^2; Matrix = 80 x 80; SENSE Factor = 2) and consisted of 260 slices of 3 mm thickness with no inter-slice gap. A block design was used and a total of 707 volumes (dynamics) in each session were collected. Two dummy scans were incorporated in each run to allow for steady state magnetization. High-resolution T1-weighted anatomical 3D images were also acquired to allow anatomical localization (TR = 8.4 ms; TE = 3.8 ms; FOV = 288 x 232 mm^2; Matrix = 288 x 232; Voxel Dimension = 1.0 x 1.0 x 1.0) and consisted of 175 slices. Participants were instructed to keep their head still and head motion was minimized using the standard Philips head coil with ear pads. The data exported from the scanner were converted from PAR/REC (PAR = the text header file, REC = the binary file) or DICOM (Digital Imaging and Communications in Medicine) format to HDR (High Dynamic Range) format by using

MRICRO software and then to 'Niftii' format (standard MRI analysis format) by using FSL software. These 'Nifti' files are usually compressed with gzip and stored as .nii.gz files.

5.3.3 Data processing

Analysis was carried out using Probabilistic Independent Component Analysis (PICA) (Beckmann & Smith, 2004; Beckmann, DeLuca, Devlin, & Smith, 2005) and implemented using the software MELODIC version 3.10 (Multivariate Exploratory Linear optimized Decomposition into Independent Components; part of FSL FMRIB's Software Library: www.fmrib.ox.ac.uk/fsl). The following pre-statistics processing was applied: (i) motion correction was carried out using MCFLIRT (Motion Correction FMRIB's Linear Image Registration Tool) to remove any effects of participants moving their head during scanning (Jenkinson et al., 2002); (ii) slice-timing correction using Fourier-space time-series phase-shifting; (iii) spatial smoothing by using a Gaussian kernel of 5 mm FWHM (Full Width Half Maximum); (iv) removal of the non brain structures by using BET (Brain Extraction Tool) (Smith, 2002); (v) Intensity normalisation of all volumes by using grand-mean scaling, high-pass temporal filtering.

After preprocessing, the functional scans were registered to the MNI152 standard space (average T1 brain image constructed from 152 normal participants at the Montreal Neurological Institute, Montreal, QC, Canada) by using FLIRT (Jenkinson et al., 2002).

5.3.4 Experiment Design

The experiment consisted of two types of observation stimuli; one that was experimental and one that was control. The experimental stimuli consisted of typical strength-based actions, including arm curl, wrist curl and shoulder fly actions, and were made to light and heavy

weighted objects. The control stimuli consisted of two objects; a light chair and a heavy door

that randomly moved around the screen (i.e., with no actions). The stimuli were the same

stimuli as those reported in Chapter 4 (see Figure 5.2 and 5.3) and details of how the stimuli

were created are presented in Chapter 4.

The experimental and control stimuli were presented in separate sessions (as in Chapter 4).

Within each type of stimuli presentation (i.e., experimental and control), there were three trial

blocks whereby the specific type of stimuli was presented randomly in each trial block using

E-prime software. The total time for the stimuli presentation of the three trial blocks was

approximately 22.5 minutes (as described in Chapter 4). Immediately prior to and following

the presentation of the stimuli (experimental or control), the participants participated in two

rest phases. Each of the four rest periods (i.e., pre- vs. post-observation of the experimental or

control stimuli) lasted for 360s. During these rest phases, participants were told to do nothing

except for looking at a fixation cross that was projected onto a screen within the scanner via a

mirror fixed to the head coil. The experimental and control sessions were run on different

days, and the order of sessions was counterbalanced across the different participants tested

(see Figure 5.1).
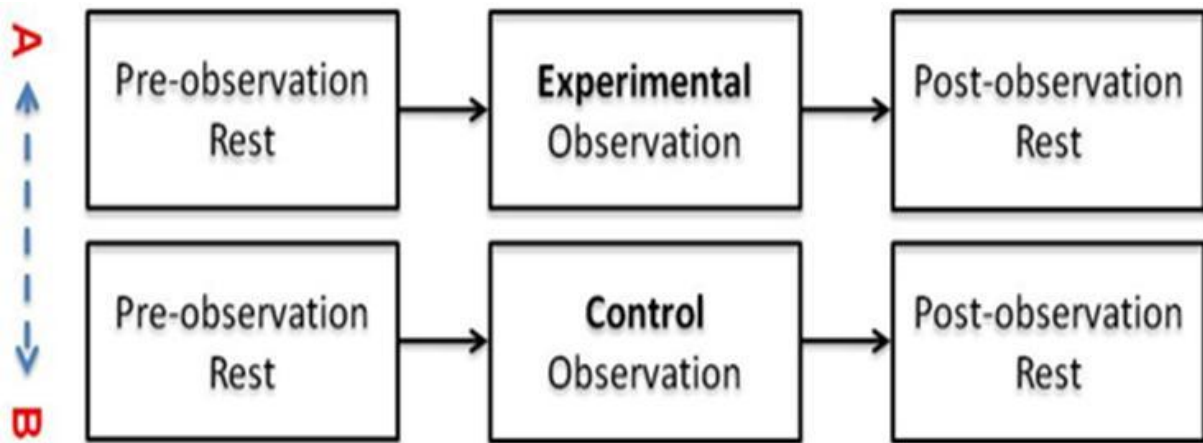
Figure 5.1: Experimental design. The experimental and control observation sessions were run on different days (A and B), and the order was counterbalanced across the different participants (AB vs. BA). Immediately before and after the observation stimuli were presented, the participants received two rest phases, a pre-observation and a post-observation rest.

5.3.5 Statistical analyses

A modified version of the tensor-PICA approach was used for statistical analyses (Beckmann & Smith, 2005). This allowed for the definition of the resting state networks in order to measure changes in these networks between the pre-observation and post-observation rest phases, and to compare the differences between the experimental versus control observation conditions. A total of sixty individual data sets were acquired from fifteen participants and analysed. The four types of data sets were independently decomposed into groups of vectors that described signal variation in the spatial (maps), frequency (time-courses), and subject domain by optimising for non-Gaussian spatial source distributions using a fixed-point iteration technique (Beckmann & Smith, 2005; & Hyvärinen, 1999). Eighteen to twenty one dimensional subspaces (components) were determined and the number of these components was estimated using the Laplace approximation to the Bayesian evidence of the model order (Beckmann & Smith, 2004). Estimated Component maps were divided by the standard

deviation of the residual noise and thresholded by fitting a mixture model to the histogram of intensity values. Z (Gaussianised T/F) statistic images were thresholded at the alpha level of $p = 0.05$ (uncorrected).

In the first part of the analyses, differences between the experimental and control sessions were contrasted for the pre-observation condition only. One problem with contrasting activity between the sessions was that any differences in activity might reflect different head positions in the scanner between the two different recorded sessions. Therefore, the purpose of this first analysis was simply to show that baseline pre-observation was roughly similar across the two separate sessions (for the same participants). In the main second part of the reported analyses, contrasts were made between the rest-state activations for post-observation compared to pre-observation of experimental and separately, the control stimuli (see Figure 5.1). Differences between the experimental and control observation conditions was not analysed, but instead, subjectively compared.

Figure 5.2: Experimental stimuli. Three panels of four pictures illustrate the wrist curl, arm curl and shoulder fly types of experimental observation stimuli. The left six pictures are examples of actions made with the light weight version of the object and the right six pictures are examples of actions made with the heavy weight version of the object. Within each pair of pictures (e.g., top left pair; wrist curl and light weight), a left and right hand version was created and the manner in which the movement was performed is illustrated by the extents in the range of motion with the left hand showing the beginning and the right hand showing the end of the movement. The top right pair shows the wrist curl and heavy weight using left and right hands. The middle left pair shows the arm curl and light weight and the middle right pair shows the arm curl and heavy weight. The bottom left pair shows the shoulder fly and the light weight and the bottom right pair shows the shoulder fly and the heavy weight.

Figure 5.3: Control stimuli. From left to right: chair with left orientation, chair with right orientation, door with left orientation and door with right orientation. The control stimuli were made by using different animation features available in the software Microsoft Power Point and saving the sequences as video clips. The dashed shapes with red and green arrows show some samples of different motion paths used (e.g. from left to right: spiral left, vertical figure of 8, curvy right and heart).

5.4 Results

In the first phase of the analyses, I compared the activity for the pre-observation rest states between the experimental and control observation conditions. A combined single PICA analysis was used with a between groups-contrast. The data showed that only one component from the 20 defined components had a significant variation between conditions $F [2, 27] = 3.67, p < 0.05$. This involved brain stem and cerebellar activity (see Figure 5.4). As these contrasts considered activity for the same participants, pre-observation, but in different test sessions, it could be that the difference actually reflects noise or error due to differences in head position between scans or autonomic changes (e.g. cardiac cycle, respiration or cerebrospinal fluid fluctuation) on the different days tested. However, as a consequence of

this finding, any post-observation subjective differences between experimental and control activations for the brain stem and cerebellar activity may be considered with caution. None of the other nineteen defined components showed any significant differences between the experimental and control testing sessions (for pre-observation rest state).
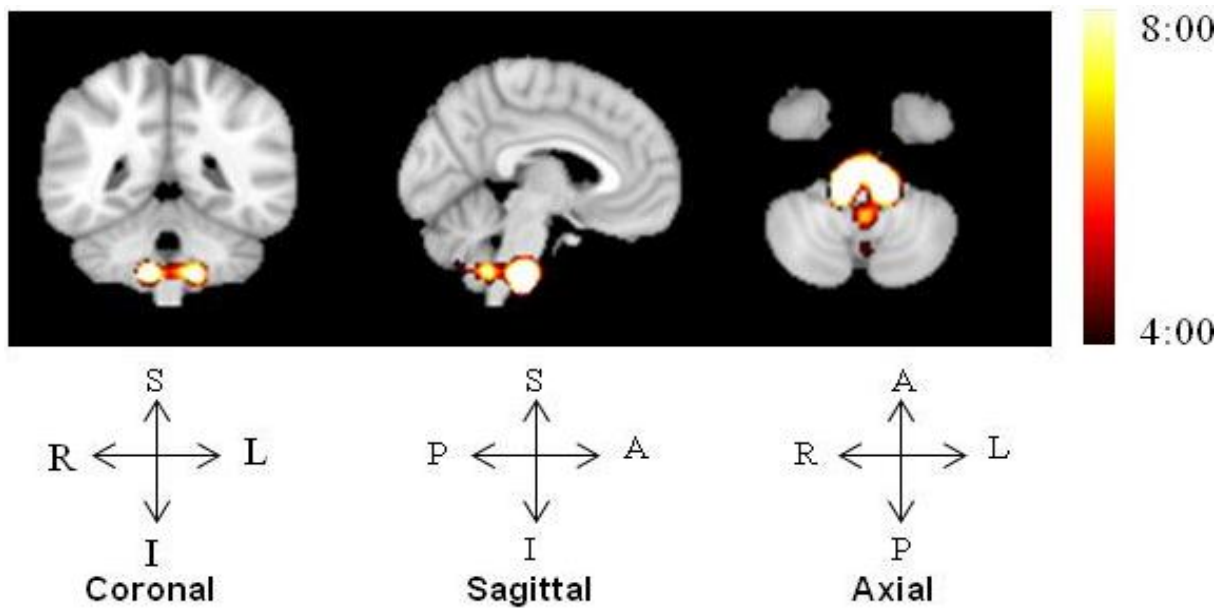
Figure 5.4: Significant activations for the contrast between pre-observation of the experimental and control stimuli. The image shows activation for brain stem and to certain extent bilateral cerebellar activity. Each image shows from left to right, the coronal, sagittal, and axial sections of the brain (the planes and directions shown below the images represent Anterior and Posterior, Superior and Inferior, and Left and Right). Functional images are overlaid on an average high-resolution scan transformed into standard (MNI152) space. The colour bar represents the z values of normal distribution significance (ranging from 4.0 to 8.0). Note that the brain images are presented in the standard mirror format (i.e., the pictured left is the physical right side of the brain and vice versa).

In the second phase of analyses, I contrasted post-observation to pre-observation rest state activity for either the experimental or control conditions. For a combined single PICA analysis of the conditions, twenty-one components were identified. In the analysis of the experimental condition, four separate components showed a significant increase in activity between the post-observation compared to pre-observation (see Figures 5.5-5.8). However, analysis of the control condition showed no significant differences between the post-observation compared to pre-observation phases. Interestingly, the significant components of the experimental condition showed increased BOLD signal activity post-observation compared to pre-observation in the motor and memory areas of the brain.

Figure 5.5: Component 1: Significant activations for the contrast between pre- and post-observation of the experimental strength based actions (F [2, 27] = 16.64, p < 0.001). The images show increased activation for post-observation compared to pre-observation rest state in the following brain areas; right Frontal Pole (BA 46), right Supramarginal Gyrus, right Angular Gyrus, right Superior Parietal Lobule, right Lateral Occipital Cortex (BA 40), right Middle Frontal Gyrus, right Superior Frontal Gyrus (BA 6), right Inferior Frontal Gyrus, pars tringularis (Broca's Area BA 44/45), right Paracingulate Gyrus (BA 46), right Cingulate Gyrus, posterior division, right Precuneous Cortex (BA 31) and the left Crus of the Cerebellum. Each image shows from left to right, the coronal, sagittal, and axial sections of the brain (the planes and directions shown below the images represent Anterior and Posterior, Superior and Inferior, and Left and Right). Functional images are overlaid on an average high-resolution scan transformed into standard (MNI152) space. The colour bar represents the Z values of normal distribution significance (ranging from 4.0 to 8.0). Note that the brain images are presented in the standard mirror format (i.e., the pictured left is the physical right side of the brain and vice versa).
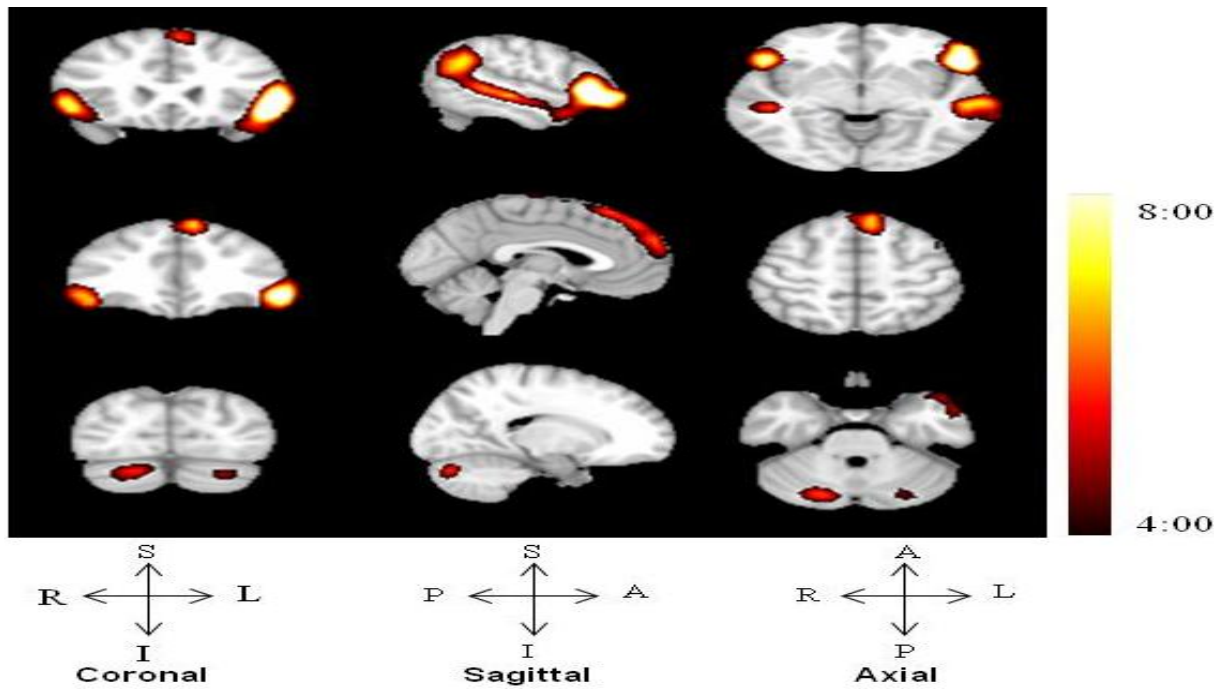
Figure 5.6: Component 2: Significant activations for the contrast between pre- and post-observation of the experimental strength based actions F [2, 27] = 7.42, p < 0.01. The images show increased activation for post-observation compared to pre-observation rest state in the following brain areas: bilateral Angular Gyrus, bilateral Supra Marginal Gyrus, posterior division, bilateral Lateral Occipital Cortex, superior division, bilateral Superior Temporal Gyrus, posterior division (BA 40), bilateral Inferior Frontal Gyrus, pars triangularis & pars opercularis, bilateral Frontal Orbital Cortex, bilateral Frontal Operculum Cortex (BA 44, 45, 47), left Premotor Cortex (BA6),left Primary Motor Cortex (BA4), left Corticospinal Tract & bilateral Cerebellar activity, posterior lobe, crus I & II. Each image shows from left to right, the coronal, sagittal, and axial sections of the brain (the planes and directions shown below the images represent Anterior and Posterior, Superior and Inferior, and Left and Right). Functional images are overlaid on an average high-resolution scan transformed into standard (MNI152) space. The colour bar represents the z values of normal distribution significance (ranging from 4.0 to 8.0). Note that the brain images are presented in the standard mirror format (i.e., the pictured left is the physical right side of the brain and vice versa).

Figure 5.7: Component 3: Significant activations for the contrast between pre- and post-observation of the experimental strength based actions F [2, 27] = 9.91, p < 0.001. The images show increased activation for post-observation compared to pre-observation rest state in the following brain areas: bilateral Central Opercular Cortex, bilateral Heschl's Gyrus (includes H1 and H2), bilateral Planum Polare, bilateral Planum Temporale (BA 13/22), bilateral Precentral Gyrus, bilateral Juxtapositional Lobule Cortex (formerly Supplementary Motor Cortex), bilateral Cingulate Gyrus, posterior division & anterior division. Each image shows from left to right, the coronal, sagittal, and axial sections of the brain (the planes and directions shown below the images represent Anterior and Posterior, Superior and Inferior, and Left and Right). Functional images are overlaid on an average high-resolution scan transformed into standard (MNI152) space. The colour bar represents the z values of normal distribution significance (ranging from 4.0 to 8.0). Note that the brain images are presented in the standard mirror format (i.e., the pictured left is the physical right side of the brain and vice versa).
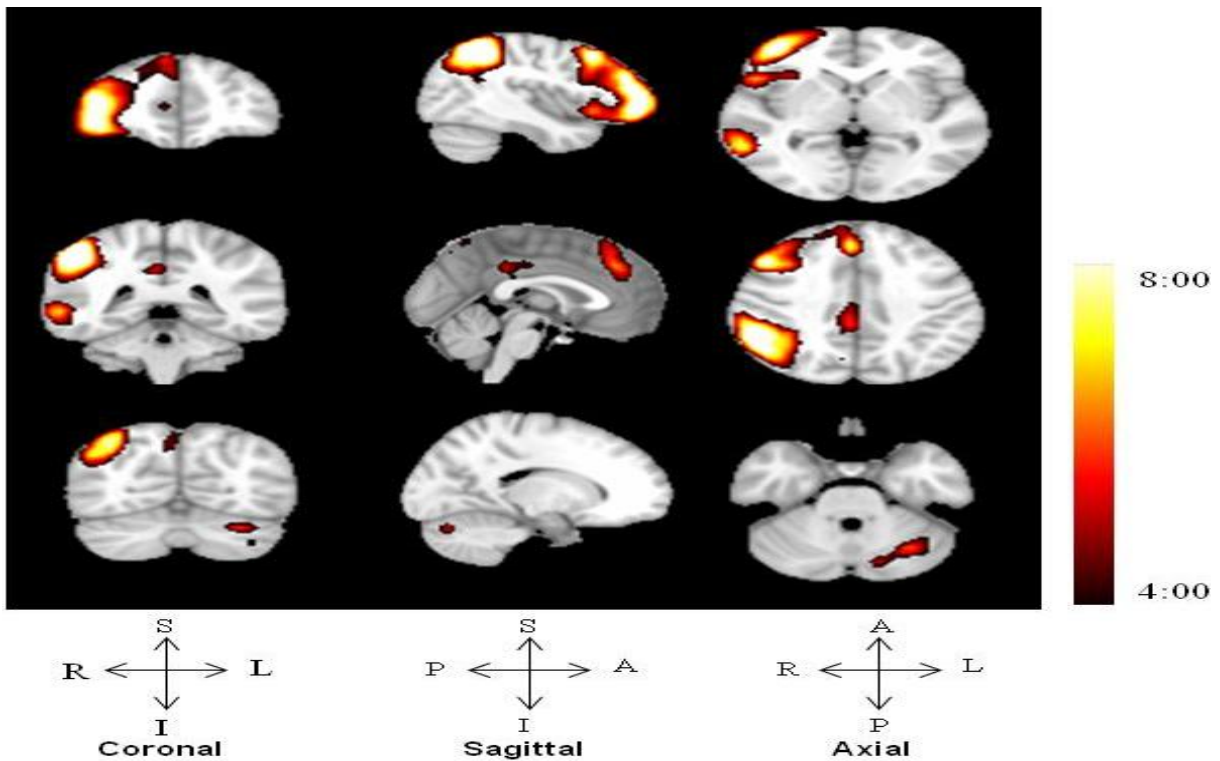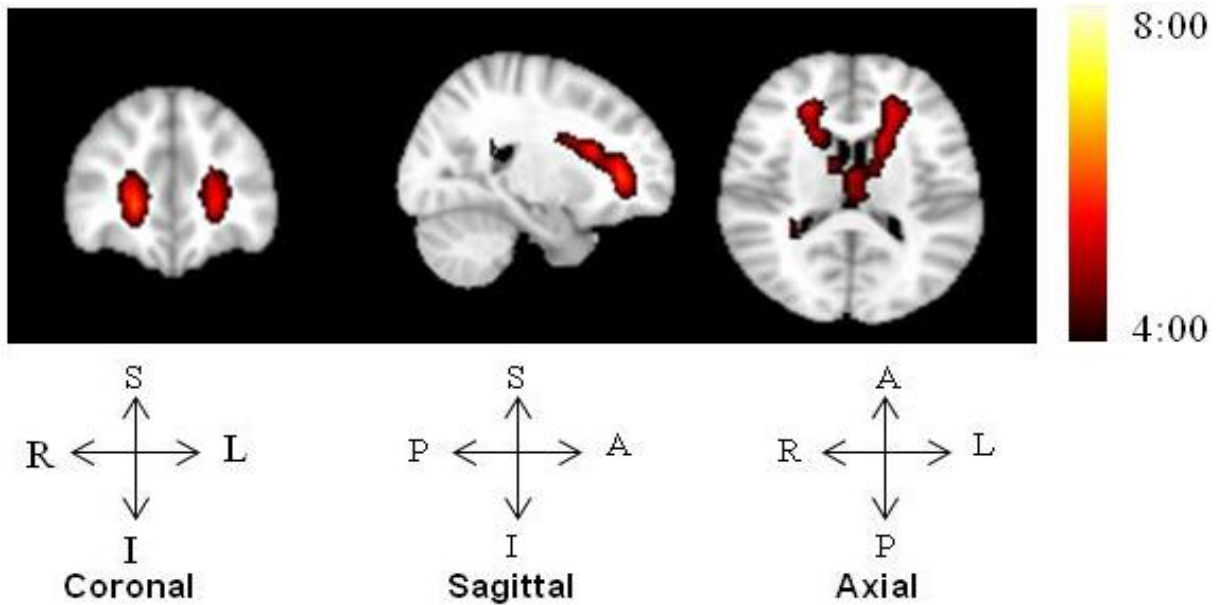
Figure 5.8: Component 4: Significant activations for the contrast between pre- and post-observation of the experimental strength based actions F [2, 27] = 5.38, p < 0.05. The images show increased activation for post-observation compared to pre-observation rest state in the following brain areas: bilateral Callosal Body, left Lt Corticospinal Tract, and bilateral Superior Occipito-Frontal Fascicle. Each image shows from left to right, the coronal, sagittal, and axial sections of the brain (the planes and directions shown below the images represent Anterior and Posterior, Superior and Inferior, and Left and Right). Functional images are overlaid on an average high-resolution scan transformed into standard (MNI152) space. The colour bar represents the z values of normal distribution significance (ranging from 4.0 to 8.0). Note that the brain images are presented in the standard mirror format (i.e., the pictured left is the physical right side of the brain and vice versa).

5.5 Discussion

In this chapter, I for the first time present an experiment that investigated how action

observation moderates brain rest-state activity. I hypothesised that measuring resting brain

activity following an action observational task might show prolonged activity from the same

areas active during action observation, and perhaps provide a further understanding of how

action observation leads to the priming of subsequent action execution; as I reported in

Chapters 2 and 3 of this thesis. Using PICA analysis to measure the fluctuations in the BOLD

signals of the resting brain following an action observation compared to before observation,

and in contrast to observation of a control condition, I was able to test the plausibility of our

assumption. Interestingly, the data showed that the pattern of activation following

observation of strength based action compared to before observation included several regions

that were originally predicted by our hypothesis; namely the fronto-parietal regions that

include the mirror neuron system. This was in contrast to observation of the control condition

of non-action moving objects that did not show any differences in activity between the post-

and pre-observation conditions (relative to noise / error).

An interesting aspect of the components shown to be significantly active post-observation

compared to pre-observation of the experimental strength based actions was that they

encompassed the same brain areas which have been reported to be active concurrent to

observing action (the mirror neurone system). In the data presented here, these areas of brain

activity included the Superior Frontal Gyrus, premotor cortex (BA 6), Inferior Frontal Gyrus,

pars tringularis (Broca's area BA 44/45), Primary Motor Cortex (BA 4) and the

Supplementary Motor Cortex. These are the same areas shown by other studies to be active

during action observation (see for example Buccino et al., 2001, 2004b; Cochin et al., 1998;

Decety et al., 1997; Grafton et al., 1996; Grezes et al., 2003; Johnson-Frey et al., 2003; Lui et al., 2008; Saygin et al., 2004). This suggests, as I hypothesised, that there appears to be a persistence of the activity in the observer's brain regions stemming from activity during observation of specifically relevant actions, and also following observation when the stimuli were no longer present.

From these data, I suggest that the prolonged activity in the motor areas of the brain may plausibly provide a clue of how observation can prime subsequent action execution. The findings in this chapter are compatible with the data presented in Chapters 2 and 3 of this thesis (see also Salama et al., 2011; Salama et al., Submitted). These chapters showed that observation of force based actions compared to control observation conditions moderated executed force and tapping dexterity responses. Moreover, the data is consistent with other previous studies showing that action observation primes action execution (see for example, Brass et al., 2000; Castiello et al., 2002; Dijkerman & Smit, 2007; Edwards et al., 2003; Gianelli et al., 2008; Griffiths & Tipper, 2009).

One point worth mentioning is that the compatibility between these data presented here and those presented in Chapter 3 are the most compatible. In Chapter 3, I presented used a similar design to that used here. Participants observed bouts of either experimental strength based actions or control non-strength based actions. Strength and tapping dexterity responses were measured pre- and post-observation, and the observation conditions were run on different days. The data in Chapter 3 (Salama et al., submitted) were the first to show that bouts of action observation could prime subsequent execution compared to the both the control condition and pre-observation measures. Here, the same observation resulted in mirror

neuron system activity following the action observation conditions, also compared to pre-observation, and in subjective comparison to the control condition.

A critical examination of the findings here in comparison to Chapter 2 (Salama et al., 2011) or the literature (e.g., Brass et al., 2000; Castiello et al., 2002; Dijkerman & Smit, 2007; Edwards et al., 2003; Gianelli et al., 2008; Griffiths & Tipper, 2009) might suggest the findings are not as informative as I suggest. That is to say that the single trial stimuli presented immediately before an action execution response, shown to moderate priming in Chapter 2 and the literature, may necessarily result in rest-state moderations. In fact, it would be extremely difficult and expensive to measure rest-state brain activity moderations from the presentation or observation of single trial stimuli. Instead, I suggest that future studies may attempt to include a block of rest (or no stimulus) after the presentation of observation stimuli in an fMRI event related design. That way, brain activity during and after the observation stimulus could be measured and compared. An alternative would be to measure primary motor cortex excitability using TMS and measure how excitability is moderated following the observation stimulus. On the basis of the current findings, I expect that there would be activity in the mirror neuron system that occurs immediately after the observation condition, and it is this activity that moderates subsequent action execution performance in the action priming literature (and also explaining the effects reported in Chapter 2).

In the data presented in this chapter, I used a linear decomposition of the data sets using PICA analysis. The method aims to tease apart activity caused by the manipulation of an independent variable relative to noise. One problem with the approach is that it lacks the ability to include functional connectivity between brain networks that may show a nonlinear correlation (Friston, Mechelli, Turner, & Price, 2000). This could result errors in the

identification of brain networks selected for the investigation. In order to improve the identification of brain areas, I suggest that combined use of Electroencephalograpy (EEG) with fMRI techniques could add more temporal and spatial connectivity information in order to better understand the brain resting state activity (see for example Britz, Van De Ville, & Michel, 2010; Goldman, Stern, Jerome, Engel, & Cohen, 2002; Laufs, 2010; Martínez-Montes, Valdés-Sosa, Miwakeichi, Goldman, & Cohen, 2004; Musso, Brinkmeyer, Mobascher, Warbrick, & Winterer, 2010). Developments in these types of analysis will provide more specificity to the exact areas and networks of the brain implicated by the intervention condition (i.e., stimuli presented prior to the recorded rest-state).

Another limitation that makes this approach clinically impractical is that it can only currently measure the functional rest-state activity at group level and presently cannot consider the individual participant level. One of the main aims of this thesis was to determine whether observation of strength based actions could be used for clinical application to improve strength and tapping dexterity in patients with strength and dexterity loss, for example following stroke. In the research following this thesis, I hope to apply the findings of the thesis to clinical investigations. To do this, it may be useful to use similar methods to those reported here in this chapter, and determine how the effects of observation (or other interventions) influence the damaged brain rest state activity. In order to carry this out, modifications in the data analyses used will be required.

Despite these limitations, these data presented here indicate a promising new area of investigation that considers how the brain areas active during action observation cause priming of action execution. On the basis of the correspondence between the methods presented in Chapter 3 and the current chapter (Chapter 5) of this thesis, and the findings of

Chapter 4, I suggest that action observation activates the mirror neuron system, and that once the observation event is complete, the mirror neuron system remains active and this activity moderates activity usually associated with planning and executing action. The behavioural effect of this moderated brain activity likely explains why action execution kinematics are moderated or primed by observation (e.g., Edwards et al. 2003).

CHAPTER 6:

GENERAL DISCUSSION

6.1 Introduction

The global aim of this thesis was to investigate whether the observation of action force would prime subsequent execution, and furthermore, how force observation would modulate the observer's brain activity, specifically in the mirror neuron system area, both during and after the observation condition. The studies presented in the four empirical chapters of this thesis showed that combining human recording studies with data acquired using experimental psychology and brain imaging methods can provide a more comprehensive understanding of how action observation modulates the observer's brain activity and executed motor performance. In the final chapter of this thesis, I will first review the data presented in the empirical chapters of this thesis (Chapter 2, 3, 4, and 5) in relation to key literature. Following this, I will summarise the limitations of the thesis, and particularly suggest specific issues that could have improved the experiments. In the final section of this chapter, I present plausible directions for future research.

6.2 Summary of the Thesis Results

In the literature, several behavioural studies have reported that action observation can prime subsequent execution (e.g., Brass et al., 2000; Castiello et al., 2002; Dijkerman & Smit, 2007; Edwards et al., 2003; Gianelli et al., 2008; Griffiths & Tipper, 2009; Hardwick et al 2011 etc.). These studies have mainly focussed on how temporal or spatial details in the observed action influence subsequent action execution. However, so far in the literature, no studies have investigated how the observation of action force influences execution.

In the first empirical chapter of this thesis (Chapter 2), I for the first time investigated whether the observation of action force would prime subsequent action force execution. Participants were required to make responses of 50% of their maximum force ability immediately after observing stimuli depicting a model making force responses that were labelled baseline (no grip/no action; 0%), congruent grip (50%) or incongruent grip force (100% of a model's own maximum response). Both the observed and executed responses were made to a hand gip dynamometer and the procedure used matched other experiments reported in the literature (e.g., Edwards et al. 2003). The results from the experiment showed the participant response was significantly increased after they observed an incongruent (100%) force in comparison to the baseline (0%) or congruent (50%) force observation conditions. I argued that the reason for the increase was perhaps caused by greater primary motor cortex excitability following observation of the incongruent 100% force, relative to the baseline (0%) and congruent (50%) conditions. The rationale for this argument was based on findings showing that primary motor cortex excitability was increased during action observation (Fadiga et al., 1995) and furthermore, that observation of actions to heavy objects caused more primary motor cortex excitability than observation of actions to light objects (Alaerts et al., 2010). The finding that observed action force could prime force execution was particularly interesting as the effect occurred even though the participants had to make the same (trained) response throughout the experiment. In fact, I defined that a participant was trained when they were able to make a consistent train of responses without feedback that were within a 10% range of their 50% maximum force ability. Interestingly, the results of the experiment showed that participants continued to make responses within this margin, but that the responses were influenced by the observation conditions. I suggested that the reason for the modulation might have therefore been automatic or driven by a non-conscious neural mechanism. These findings and interpretation replicate the current literature showing that

action observation primes execution responses (e.g., Brass et al., 2000; Castiello et al., 2002; Dijkerman & Smit, 2007; Edwards et al., 2003; Gianelli et al., 2008; Griffiths & Tipper, 2009; Hardwick et al 2011 etc.), but in addition, they extended the literature by showing priming for action force (see Salama et al., 2011).

After running the research for Chapter 2, I immediately considered that these findings could be very useful for clinical research that uses action observation for neural rehabilitation. For all of the reported evidence that action observation influences execution, there are very few examples that have applied the effects to practice. For example, Ertelt et al. (2007) reported that eight patients showed significant increased brain motor area activity following an action observation intervention therapy. There have been very few papers that have replicated or continued the research, and an unpublished examination with neuropsychology clinical practice showed little use or knowledge of the potential therapy.

I considered that the findings of Chapter 2 (Salama et al., 2011) could be particularly useful to regain muscle strength following strength loss through for example a broken bone (Karlsson et al., 1996) or limb function loss following brain injury (Bohannon & Andrews, 1998). However, I first considered that a change to the paradigm might facilitate use of the effects in clinical practice. That is to say that I assumed that the poor uptake of using action observation priming in the clinical setting was because the conventional observation-execution priming paradigms were based on trial-by-trial methodology that might be impractical for clinical use. That is to say that clinicians might find it difficult or too time consuming to present an action for the participant to observe immediately before asking the participant to perform an action exercise. In Chapter 3 I decided to extend the literature by evaluating whether bouts of action observation could also prime execution. The rationale for

this change was that if I could show observation bouts to prime execution, I would be in a position to propose that clinical practice could more easily use action observation priming for clinical rehabilitation.

Chapter 3 investigated three experiments and tested the effects of observation on arm (Experiments 1 & 2) and leg force (Experiment 3) responses, and on simple (Experiment 1) and complex tapping dexterity (Experiment 2). For the effects of action observation on execution force, I was unable to replicate the findings of Chapter 2 showing that observation primed grip force responses. Rather than suggesting that the effect cast doubt on the previous finding, I provided a number of reasons to explain the null effect. One of these reasons included the way in which I recorded the grip force response. In changing the dependent measure to a more precise leg force measure, I was then able to replicate the findings of Chapter 2. Observations of leg strength actions were able to prime leg force responses in comparison to observation of arm force and pre-observation measures. The effects of action observation on subsequent tapping dexterity were clearer. The data showed that observation of action force primed both simple and complex tapping dexterity, showing significant increases in tapping speed dexterity relative to baseline or control conditions.

The findings of Chapter 3 added to the literature on two dimensions. First of all, they showed that action observation priming also worked when the observation condition consisted of a long bout of trials followed by the execution (replicating Salama et al., 2011). Secondly, the observation force prime effects extended beyond priming the specific action observed. Action observation also primed tapping dexterity. For this last finding, I suggest that the priming of tapping dexterity was simply caused by a priming of execution force, and that with a greater force capacity, the participants were able to perform faster tapping dexterity responses.

The third empirical chapter of this thesis (Chapter 4) explored whether observation of force based actions compared to control condition would moderate mirror neuron system activity. Based on the data reported by Alaerts et al., (2010 a, b), I expected that observation of actions to heavy in comparison to light objects would elicit greater activity in the mirror neuron system. I fMRI scanned participants while they observed video clips of either experimental or control conditions. The experimental condition included hand and arm actions made to heavy or light objects and the control condition included non-action moving heavy or light objects with the absence of the effector. Within each condition, contrasts were made between the brain activity as a function of observation of heavy compared to light objects. The results showed that for the experimental condition, there was significant activity in the Superior Frontal Gyrus (SMA), Frontal Pole, and Occipital Cortex for observation of actions to heavy compared to light objects. However, for the control condition, there was only significant activity in the Occipital Cortex. Therefore, as originally hypothesised, these findings showed that action observation of heavy compared to light objects moderated activity in the Superior Frontal Gyrus; an area reported by other researchers as part of the mirror neuron system (Buccino, et al., 2001; Buccino, et al., 2004b; Cochin, et al., 1998; Decety, et al., 1997; Grafton, et al., 1996; Grezes et al., 2003; Johnson-Frey, et al., 2003; Lui et al., 2008; Saygin et al., 2004). In the discussion of these data, I suggested that both the Superior Frontal Gyrus and the Frontal Poles might represent object weight during action observation and that activation of the Occipital Cortex across both experimental and control conditions was likely responsible for processing visual information. The finding that the Superior Frontal Gyrus (SMA) of the mirror neuron system was active for observation of actions to heavy compared to light mass was expected, the finding of significant activation in the Frontal Pole was unexpected. Currently there is limited understanding of what behaviour the Frontal Pole contributes to. One recent study by Tsujimoto et al., (2011) is that the Frontal Poles may be

used for monitoring goal behaviour. On the basis of this, I suggested that the goal of exercise may have caused observation of the actions to the heavier than light weights facilitating the Frontal Pole activity; the goal representation for interacting with heavy objects having a greater goal representation than that for interacting with lighter objects.

The findings of Chapter 4 therefore supported Alaerts et al., (2010 a, b), and showed that the mirror neuron system, specifically the Superior Frontal Gyrus (SMA), was moderated by observation of action to the heavy than light object. These findings provided a possible mechanism to explain the priming effects reported in Chapters 2 and 3 (Salama et al., 2011; submitted). It could be suggested that observation of action force (or interaction with a heavy compared to light object) brought about increased mirror neuron activity, and that this activity influenced subsequent activity when planning to execute a force or dexterous action (for example as in Brass et al., 2000; Castiello et al., 2002; Dijkerman & Smit, 2007; Edwards et al., 2003; Gianelli et al., 2008; Griffiths & Tipper, 2009; Hardwick et al 2011 etc.).

While above I argue that data of Chapter 4 can be used to explain the prime effects findings of Chapters 2 and 3 (using a similar rationale as that presented in Edwards et al., 2003), one might argue that the rationale is incomplete. That is to say that the finding that action observation causes increased activity in the same areas of the brain known to be involved in action execution does not necessarily support the idea that action execution activity is facilitated by the action observation activity. It is not understood whether the activity during observation remains active until the time of execution planning. It might be that the activity during action observation immediately ceases once the action observation stimulus is complete. In Chapter 5, I tested this by measuring rest-state activity before and after

observation. I predicted that there would be persistent activity in the same areas active during action observation. The observational conditions used were similar to those used in Chapter 4. These were either 'experimental' which included force based hand and arm actions or 'control' which included moving objects. The same participants as those tested in Chapter 4 took part in the experiment, and they were fMRI scanned immediately before and after observation of either the experimental or control stimuli. The experimental or control stimuli lasted for 22.5 minutes and each of the resting phases lasted for six minutes. For the contrast between pre-observation of the experimental and control, the data showed that only one component from the 20 defined components had a significant variation between conditions. This involved brain stem and cerebellar activity. Contrasted activations for the post-observation compared to pre-observation of experimental stimuli showed significant widespread fronto-parietal activity (regions associated with the mirror neuron system). Interestingly, these brain regions shown to be significantly active following observation of the experimental stimuli involve the same brain regions that were active during action observation findings reported in Chapter 4. and reported by other studies (see for example Buccino et al., 2001, 2004b; Cochin et al., 1998; Decety et al., 1997; Grafton et al., 1996; Grezes et al., 2003; Johnson-Frey et al., 2003; Lui et al., 2008; Saygin et al., 2004).

From these data in Chapter 5, I suggested that the persistence of activity following action observation might provide an explanation of the mechanism behind this priming effect. I suggested that the ongoing activity following action observation might underlie the action priming effects reported in Chapters 2 and 3 (Salama et al., 2011, submitted). These finding are also compatible with the findings demonstrating that action observation priming can be used for clinical rehabilitation (Ertelt et al., 2007).

The data reported in the four chapters of this thesis full-filled the main thesis aim. That was to test whether the observation of action force would prime subsequent execution, and furthermore, how force observation would modulate the observer's brain activity, specifically in the mirror neuron system area, both during and after the observation condition. The data presented here showed that the observation of force actions primed executed force, tapping dexterity performance, brain activity and resting brain activity through activation of the mirror neuron system. In meeting these aims, the data represent new findings that support existing literature. In addition to this, I also demonstrated two new methods, one showing that bouts of observation can prime execution and one measuring brain activity after the stimulus has ceased and measuring brain activity that can influence execution planning processes. However, there are a number of aspects in the experimentation that I suggest could have been improved, or could be addressed in future experimentation. There are presented in the next section.

6.3 Strengths and Limitations

This thesis used both human recording (Chapters 2 and 3) and brain imaging (Chapters 4 and 5) methods. The human recording tools, used in Chapters 2 and 3, provided data regarding participant motor responses as a function of the observed visual stimuli. This allowed to cost effectively acquire data with high level of spatial accuracy using accurate dynamometer and motion analysis equipment. However, the use of human recording tools alone would be unable to provide an understanding of the brain structures active while observing a specific motor stimulus. The brain imaging tools, used in Chapters 4 and 5, allowed for the

examination of the brain structures active during and after observation of similar stimuli to those used in Chapters 2 and 3. Together, the use of these complementary tools provides a robust and complete approach to meet the aims of the thesis, allowing for a higher opportunity to contrast and compare data acquired from human recording experiments in context with the brain imaging evidence underlying their design. However, there are number of unique limitations specific to each approach used in the thesis, and these are addressed below.

In Chapter 2, I tested how the observation of grip force influenced executed grip force. There was one potential problem with the study. This was that I chose to present action force observation stimuli that depicted model force responses of 0%, 50% and 100% (no force, congruent to execution force and incongruent to execution force). The results showed that observation of the 100% incongruent force caused a greater execution force response. I assumed that the observation condition primed the increased execution force. However, it could be that the greater executed force was actually a consequence of the incongruent compared to congruent prime. If the effect was a consequence of incongruence alone leading to increased force execution, I might expect that observation of an incongruent 25% force may have also cause an increased execution force. Because of this, I suggested that future experiments should consider presenting a range of observation conditions (e.g., 0% no action; 25% incongruent low force action; 50% congruent force action, and; 75% incongruent high force action; in relation to the executed force response).

In Chapter 3, the main limitation has already been discussed and involved the use of the dynamometer before and after observation conditions. The data overall in Chapter 3 revealed positive effects, but there was one limitation regarding the use of the hand grip dynamometer

measuring tool. The problem with the tool was that a variance in the results was created as a function of changing the posture of the hand on the hand dynamometer before and after the observation conditions. I believe that the increased variance was the main reason for the non-significance of the action observation prime effect. On the basis of this null finding, and to avoid this variance, in Experiment 3 of Chapter 3, I used a non-adjustable leg dynamometer. This enabled us to acquire the same type of data, but without increased variance. With this modification to the measure, the data became significant and replicated the findings of Chapter 2. From this experience, I recommend that future research should carefully select the strength measuring methods used to measure strength responses, either by using non-adjustable strength measuring tools as those used in Experiment 3, or by keeping the participants hand on the hand grip dynamotor (as in Chapter 2).

In Chapters 4 and 5, the methods used matched other similar experiments reported in the literature and both chapters presented new and original data. Apart from the expense limitation, the main limitation in these chapters was the appropriateness of the experimental stimuli in contrast to the control stimuli. In the case here, I presented video clips of strength based action observation in the experimental condition and contrasted brain activity resulting from the experimental conditions compared to brain activity resulting from the observation of moving objects. There are potentially two limitations with regard to the choice of stimuli used. The first is for the control stimuli. In brain imaging, the purpose of the control comparison condition is to remove brain activity that is active in the experimental, but not relevant to the hypothesis. In the thesis, the control stimuli were heavy and light moving objects. Our original aim was to remove brain activity associated with moving objects, which were not moved by actions. However, in hindsight, it could have been that other activities could have also been removed. For example, in Chapter 4, occipital activity was greater for the experimental heavy than light objects, which I argued to be a consequence of the visual

size of the objects moved. Similarly, I argued that the Frontal Pole activity in the experimental condition might have been caused by the actions to the heavy objects having more goal representation than the actions to the light objects. To control and remove both of these activations from the experimental data, it may have been better to have control stimuli that matched object size between the light and heavy objects, and also that contained goal presentations. It may have also been the case that these additional factors also influence the data in Chapter 5.

The second limitation in Chapters 4 and 5 was that the experimental action observation conditions consisted of a range of different strength based actions. While I can say that in general, observation of strength based actions compared to the control conditions brought about the reported findings, it may be that only some of the observed actions exerted an influence. That is to say that there may have been some particular types or presentations of the action stimuli that caused a greater effect than the others. However, because of the experimental design and analysis methods used, I was unable to investigate whether this was the case. Future studies may attempt to determine what types of experimental action observation stimuli bring about the greater brain activation (prime) effect. In the following section, summaries of additional possible future directions are presented (that exclude the points raised in this section).

6.4 Future Directions

As presented in the previous section, one of the strengths of this thesis was in the use of motion tracking, force recording and brain imaging measures in order to understand the effects of force or strength based action observation on execution. Based upon these studies and the findings revealed, there are several directions the future research could consider. In

this section of the General Discussion, two proposed direction themes will be presented. In the first direction theme, the methods of motion tracking and force recording measures will be considered. In the second direction theme, brain imaging measures will be discussed. Both themes consider the potential use of these approaches to examine whether the effects could be used for rehabilitation. The last part of the section will discuss this point in greater detail.

6.4.1 Motion tracking and human recording approaches

The findings reported in the first two empirical chapters of this thesis (Chapters 2 and 3) are compatible with the hypothesis that action observation primes action execution through activation of the mirror neuron system, and for the first time, for force based actions. These findings are novel and promising for clinical application to improve performance and muscle strength in patients that have strength loss. The same hypothesis could be further examined, through testing patients with either central or peripheral motor system abnormalities that cause muscle function loss or weakness, for example following stroke, motor neuron diseases (MND) or bone injury. Based upon the findings reported in Chapters 2 and 3, the patients could be either presented with force based actions or daily life motor actions (e.g. grasping, using tissues, eating or walking movements etc.) and then tested for the executed responses following the observation conditions compared to a baseline or control condition (like those used in the present thesis). Testing patients would provide the opportunity to investigate whether the reduced functioning muscles could also benefit from observation. If so, it would be expected that when observing force based actions or daily life actions, patients would respond faster following observation. The future study could extend either Chapter 2 or 3, though I suggest that using bouts of force or daily life action observation that the patients watch in their own convenience or before they undertake the active physiotherapy may be easier to manage than presenting individual stimuli prior to a single response. In addition to

this, future studies could consider the relative benefits of action observation versus physical (physiotherapy) practice, and versus a combined approach. I expect that using a combined observational and active intervention might give the better results in comparison to physical (physiotherapy) practice alone (Ertelt et al., 2007).

6.4.2 Brain imaging approaches

The vast majority of paradigms reviewed in the chapters of this thesis (Chapters 1-5) have tended to focus on investigating the general effects of action observation on the human mirror system. In Chapters 4 and 5, I explored the effects of action observation force (or strength) on the activity of the mirror neuron system during (in Chapter 4) and after (Chapter 5) participants were exposed to the experimental action observation and compared to control conditions. The data in Chapter 4 supported our original hypothesis in that it revealed a significant activity in the Superior Frontal Gyrus (SMA), previously defined to be a part of the mirror neuron system. The data in Chapter 5 supported these findings and further was revealed a significant activity in the mirror neuron system as well in other brain areas with motor significance. I suggest that future studies could test the influence of action observation on the activity of the mirror neuron system by exploring functions of the mirror system in patients with a likely impaired function of the mirror neuron system (e.g. after stroke particularly with Fronto-Parietal lesions). It might be that instigating the effects of action observation in these patients using either brain imaging or action priming methods may yield new knowledge about how specifically the mirror neuron system is involved in these behaviours.

6.4.3 Mirror Neurons and stroke rehabilitation

One of the most common neurological deficits results from a stroke. Stroke is caused by disturbance in the blood supply to the brain and usually leads to a permanent loss of brain function and behaviour. In the case of a unilateral parietal / motor area lesion, this can cause partial paresis (often called hemiparesis), that reduces mobility and leads to a deterioration in muscle function in one or more limbs on one side of the body. As previously discussed in this chapter, there is plenty of evidence that action observation activates the observer's motor or mirror neuron system. Facilitation of the motor system during mere observation of actions is an extremely appealing mechanism for rehabilitation of motor functions (see e.g. Buccino et al., 2006; Celnik et al., 2008; Eng et al., 2007; Ertelt et al., 2007; Pomeroy et al., 2005). Exploring the function of the mirror neurone system particularly in stroke patients would provide further evidence regarding the plausibility of our original assumptions that observation could be harnessed as a rehabilitative approach in clinical settings.

An example of the possibility of using observation as a rehabilitative tool was presented in an empirical study by Ertelt et al. (2007). This study was the first to use observation as a rehabilitative tool combined with active exercise. The study tested two groups of patients with motor disability caused by stroke. One group was the experimental group and they received physical training combined with observational stimuli that included daily life arm and hand actions. The other group was the control group. They received the same physical training, but the combined condition involved observation of sequences of geometric figures and letters. The data showed that in the experimental group, patients demonstrated a significant improvement of motor performance compared with the pre-intervention baseline and also the control group. In the same study, the authors used fMRI to examine the brain activity before and after treatments. Interestingly, the data showed a significantly higher

activity after treatment in the mirror neuron system. On the basis of these findings, they proposed that action observation lead to improvements in the patients that were beyond that which would normally result from current physical exercise conditions (e.g., physiotherapy).

In addition to exploring the activity of the mirror neuron system in patients using behavioural action priming and fMRI (as in Ertelt et al., 2007), I propose that future studies should aim to analyse the effects that action observation on activity after the observation condition, and in rest-state. One current problem with measuring rest-state activity is that the analyses that use PICA (the tool used to analyse the resting brain activity) are currently only able to analyse group (or multiple participant) data. For clinical use, it could be more useful to explore the brain at an individual subject level instead as individual differences between the location of the brain injury may be critical. Therefore, I suggest that the future research could find a way where I can examine the resting state activity of the brain at an individual level.

6.5 Conclusion

The central aim of this thesis was to investigate the influence of force based action observation on the subsequent action execution and to investigate the underlying mechanism behind the priming effect by measuring brain activity in correspondence to the observation conditions. The data showed that force based action observation was able to prime force and tapping dexterity execution, replicating previous findings in the literature. The thesis also found that observation of action force activated the mirror neuron system, concurrent to action observation and also following action observation. Together, these data support existing literature and suggest that action observation, through representations in the mirror neuron system, prime action execution processes. In this discussion, I have suggested some points about how the experiments in the current thesis could be improved in future studies, and I also propose that the thesis findings support the development of action observation for strength gain in patients that have strength loss.

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LIST OF ACRONYMS AND ABBREVIATIONS

ANOVA   Analysis Of Variance, a collection of models, which statistically test whether or not the averages of several data sets are all equal

BA   Brodmann Area, an area of the cerebral cortex defined based on its cytoarchitectural (histological) organisation of its neurons. A map of 52 distinct brain areas were described by the German Neurologist 'Korbinian Brodmann'

BET   Brain Extraction Tool, part of FSL, used for extracting brain from non-brain structures in structural and functional data analysis

BOLD   Blood Oxygen Level Dependent, in magnetic resonance imaging, the hemodynamic changes measured by FMRI tool

DICOM   Digital Imaging and Communications in Medicine, a format in which FMRI data is acquired

ETC   Et Cetera, Latin expression which means 'and so forth'

EEG   Electroencephalography, an approach for recording the electrical activity of the brain via multiple electrodes placed on the scalp. It has a widespread research based and clinical applications

EMG   Electromyography, an approach for recording the electrical activity of Muscle cells via electrodes placed on the skin covering the muscle being examined. It is used clinically to detect medical abnormalities or in research to examine the kinematics of human or animal movement

ET AL   'et alii' or 'et aliae' or 'et alia' a Latin expression which means 'and the rest'

FA   Flip Angle, in magnetic resonance imaging, the degree of perturbation of the average axis of the protons produced by radiofrequency signals relative to the direction of the main static magnetic field.

FEAT   FMRI Expert Analysis Tool, part of FSL, used for FMRI data preprocessing and statistical analysis

FILM   FMRIB's Improved Linear Model, part of FSL, used for FMRI data first

level (time series) analysis with prewhitening

FLAME   FMRIB's Local Analysis of Mixed Effects, part of FSL, used for FMRI data higher level analyses of multiple subjects/sessions

FLIRT   FMRIB's Linear Image Registration Tool, part of FSL, used for FMRI data linear inter-model and intra-modal registration

FMRI   Functional Magnetic Resonance Imaging, a neuroimaging approach for measuring the hemodynamic changes produced as a function of neural activity in the brain or spinal cord

FMRIB   Oxford Centre for Functional Magnetic Resonance Imaging of the Brain

FOV   Field Of View, the size of the 2 or 3 dimensional spatial encoding area of an image. It is defined in units of MM². Therefore, the smaller the FOV, the smaller the voxel size and consequently the better the resolution

FSL   FMRIB's Software Library, a collective software package used for functional and structural brain imaging analysis

FWHM   Full Width Half Maximum, full width between half maximum values of a function

HDR   High Dynamic Range, a format in which FMRI data is acquired

HZ   Hertz, a frequency measuring unit which is equivalent to the number of cycles per second

IFG   Inferior Frontal Gyrus

MCFLIRT   Motion Correction FMRIB's Linear Image Registration Tool, part of FSL, used for motion correction of FMRI data as well as for linear inter-model and intra-modal registration

MEP   Motor Evoked Potentials, changes in a muscle activity following stimulation either directly or through TMS

MNI   Montreal Neurological Institute

MNI152   MNI152 template is a standard-space average of 152 brains

MNS   Mirror Neuron System, as brain system which has been shown to fire both when an individual executes an action and when they observe another individual executing an identical action.

NIFTI   Neuroimaging Informatics Technology Initiative, a format in which

FMRI data is acquired

PAR/REC PAR = the text header file, REC = the binary file, a format in which FMRI data is acquired

PICA Probabilistic Independent Component Analysis, Part of FSL, used for FMRI data analysis and in particular of the brain resting activity

SMA Supplementary Motor Area, an area located on the medial surface of the cerebral cortex just in front of primary motor cortex

TE Echo Time, in magnetic resonance imaging, the time between the application of the 90° pulse and the peak of the echo signal in spin echo and inversion recovery pulse sequences. Usually defined in milliseconds

TMS Transcranial Magnetic Stimulation, a noninvasive approach which uses electromagnetic induction to induce electric current and consequently facilitates motor cortex excitability allowing the function of the brain to be studied

TR Repetition Time, in magnetic resonance imaging, the time between scanning consecutive brain volumes. Usually defined in milliseconds