VOLUME 1: RESEARCH VOLUME

Facial Emotion Processing in Neurodevelopmental Syndromes associated with Autism Spectrum Disorders (a review of the literature).

Processing of facial threat emotions after acquired brain injury: a structural neuroimaging study.

A thesis submitted to
The University of Birmingham
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DOCTOR OF CLINICAL PSYCHOLOGY

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Overview

This work comprises two volumes. Volume I contains two research papers on the topic of facial emotion processing in clinical populations.

The first is a review of the literature on facial emotion processing in genetic neurodevelopmental syndromes. The second is an empirical study examining the relationship between structural MRI scans and facial emotion processing deficits in brain-damaged patients.

Volume II contains five Clinical Practice Reports (CPRs) based on work conducted on clinical placements during Clinical Psychology training. CPR 1 (psychological models) presents the case of a 35-year-old woman with symptoms of anxiety formulated from cognitive and systemic perspectives. CPR 2 (service evaluation) assessed client satisfaction and possible change over time in client characteristics within a Brief Therapy service. CPR 3 (single case design) evaluated the impact of an a tape-based intervention on mood and time spent sorting through belongings in a 77-year-old man with a hoarding problem. CPR4 presents a case study in which a cognitive-behavioural approach was employed in therapy with a 15-year-old girl with Asperger’s Syndrome and selective mutism experiencing mood difficulties CPR5 was presented orally, and a single page summary is included here; this report described work carried out with a five-year-old girl with Smith-Magenis Syndrome displaying challenging behaviours.
Dedication

This thesis is dedicated to Danny, Stanley and Georgia, who will be glad to see the back of it, but who contributed enormously to its completion.

Acknowledgments

Empirical paper

Thank you very much to Pia Rotshtein for supervision of the empirical part of the thesis. Pia, I have learned an enormous amount from you, and have been very grateful for your frighteningly-intelligent, no-nonsense sense of perspective combined with endless good-humour and statistical tolerance. Thank you very much also to Glyn Humphreys for supervising/organising the beginning part of the research.

Many thanks to Pia and several undergraduate students who collected some of the data from both the patients and the control participants. Also to Magda Chechlacz and Nele Deyemere for expert technical help and advice.

*Enormous thanks to all the people who put so much time and effort into participating in the study.*

Literature review

Thank you very much to Chris Jones for supervising this part of my literature review, and for lots of very interesting discussions about research, sci fi and much else. Thank you also to Jo Moss and Chris Oliver for discussion of the subject matter.

General

Thank you again to Danny, whose very many talents include grammar, spelling, patience, tact and merciless mockery.

I am extremely grateful to all the Welhams, Westgates and Massesys who helped to entertain the kids during that thesis-filled Devon holiday which somehow still managed to be great.

*Finally, I am grateful beyond words to my wonderful Dad, who tirelessly attempted to teach me how to think clearly and logically, and to my lovely Mum, who taught me how to write what I mean to say.*
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Literature Review: Facial Emotion Processing in

Neurodevelopmental Syndromes associated with Autism

Spectrum Disorders
Abstract

Autism Spectrum Disorders (ASDs) are associated with atypicalities in the processing of emotion, including facial emotion, in others (e.g., Harms et al., 2010). Certain genetic neurodevelopmental syndromes are associated with an increased risk of ASD (e.g., Moss & Howlin, 2009). This literature review asks what is known about facial emotion processing in these syndromes, and how it might inform us about the relationship of the syndromes with ASD.

A literature search was conducted for papers empirically assessing facial emotion processing in each of the five syndromes most frequently associated with ASD in the research literature (Moss & Howlin, 2009): Fragile X Syndrome, Tuberous Sclerosis Complex, Rett Syndrome, Down’s Syndrome and Phenylketonuria. Of these, studies were found, and reviewed, for Down’s Syndrome and Fragile X Syndrome. In DS, there is evidence of possible reduced accuracy, in relation to typically developing children of matched intellectual ability, in facial emotion processing tasks (e.g., requiring people to match faces by their emotion). However, any impairment may be subtle, and the nature of the deficit is not clear. In Fragile X Syndrome, there is no evidence of reduced accuracy in such tasks, but studies using eye tracking, pupillometry, and functional Magnetic Resonance Imaging (fMRI) indicate atypicalities in emotion processing. Possible implications for ASD in these syndromes are discussed, along with possible future research directions.
Autism Spectrum Disorders and Facial Emotion Processing

Atypical social interaction is one of the determining features of Autism Spectrum Disorders (ASD). Alongside communication problems and repetitive behaviours/restricted interests, difficulties with social interaction form one of the core “triad” of impairments (Wing, 1981) necessary for a diagnosis of ASD (American Psychiatric Association, 2000; World Health Organization, 1992). Within this, differences in the processing of emotions in self and other are prominent. Kanner (1943) described autism as a “disorder of affective content” and Gillberg (1992) considered autistic disorders to be “empathy disorders”. DSM-IV-TR (American Psychiatric Association, 2000) diagnostic criteria include “lack of social or emotional reciprocity” and “marked impairments in the use of multiple nonverbal behaviours such as ... facial expression...”. ICD-10 (World Health Organisation, 1992) also specifies “a lack of socio-emotional reciprocity” and furthermore states that “There are always qualitative impairments in reciprocal social interaction. These take the form of an inadequate appreciation of socio-emotional cues, as shown by a lack of responses to other people’s emotions...”. Adaptive socialisation skills provide a key measure for diagnostic discrepancies in idiopathic ASD, for instance when the outcomes of the two gold-standard ASD assessments, the Autism Diagnostic Interview-Revised (Lord, Rutter, & Le Couteur, 1994) and Autism Diagnostic Observation Schedule (Lord et al., 2000), do not agree.

Empirically, it has been frequently demonstrated that people diagnosed with ASD process other people’s facial emotion atypically (see Harms, Martin, & Wallace, 2010, for a review). Eye tracking, electrophysiological and brain imaging studies consistently indicate that people with ASD process facial emotion in an unusual way. For instance, Spezio, Adolphs, Hurley, & Piven (2007a; 2007b) found that people with ASD made more saccades away from the eyes of emotional faces, especially when the eyes portrayed important information; O’Connor, Hamm, & Kirk (2005) found certain event related potentials to be
delayed or diminished in people with ASD on presentation of emotional face stimuli; Ashwin, Baron-Cohen, Wheelwright, O’Riordan, & Bullmore (2007) report different amygdala reactivity to fearful faces in ASD. There have also been numerous demonstrations of impaired ability in explicit facial emotion processing tasks (e.g., Celani, Battacchi, & Arcidiacono, 1999; Tantam, Monaghan, Nicholson, & Stirling, 1989), although the evidence on this is somewhat more mixed (see Harms et al., 2010), perhaps partly due to variations in participant selection as well as methodology. Abnormalities in facial emotion processing may contribute to some of the hallmark features associated with an ASD diagnosis.

**Autism Spectrum Disorders and neurodevelopmental genetic syndromes**

The influence of genetics in the development of ASD is substantial: some estimates of heritability exceed 90% (Bailey et al., 1995; Szatmari et al., 2007). “Idiopathic” ASD appears to result from combinations of genetic (and environmental) factors (e.g., Abrahams & Geschwind, 2008).

Of increasing recent interest in the academic literature are the relationships between known genetic causes of Intellectual Disability and the occurrence of ASD symptomatology (e.g., Meguid, 2012; Ji, Capone, & Kaufmann, 2011; Moss & Howlin, 2009; Moss, Howlin, Magiati, & Oliver, 2012). Intellectual disability in itself increases the risk of a diagnosis of ASD (e.g., Skuse, 2007). However, there is increasing evidence that certain intellectual disability-related genetic syndromes may be associated with a higher risk of ASD than expected based solely on their associated level of intellectual disability (see Moss & Howlin, 2009; although see also Skuse, 2007). Furthermore it is, of course, possible to be diagnosed with ASD for many different sets of reasons, and an increasing body of evidence suggests that ASD within specific syndrome groups differs significantly from “idiopathic” ASD and
from ASD within other genetic syndrome groups (e.g., Moss, Howlin, Magiati, & Oliver, 2012; Moss, Richards, Nelson, & Oliver, 2012).

This begs the question: what are the specific psychological corollaries of syndromes which increase the probability of ASD diagnosis? And how might syndrome-related characteristics affect the nature of an ASD presentation in people with a specific syndrome? Answers to such questions could enrich our understanding of the psychological manifestations of specific genotypes, the nature and meaning of the ASD diagnostic category and, ultimately, our general understanding of normal and abnormal developmental trajectories.

**Facial Emotion Processing in ASD-associated Neurodevelopmental syndromes**

This literature review focuses on a crucial aspect of interpersonal functioning which has received theoretical and empirical research attention since Darwin (2005/1872): the recognition of facial emotions in others. As discussed in the previous two sections, 1) ASD is associated with difficulties/atypicalities in the processing of others’ facial emotion, and 2) certain genetic neurodevelopmental syndromes are associated with an increased probability of ASD. The review then asks the following questions: what do we know about the impact of ASD-associated genetic neurodevelopmental syndromes on the processing of facial emotion in others? How might this inform our understanding of the relationship between ASD and these syndromes?

**Paper selection for review**

Syndromes were selected for the literature search based on Moss and Howlin’s (2009) review paper. Moss and Howlin report the genetic syndromes most frequently cited as having an association with ASD, and the search focused on the “top 5” of these syndromes:
For these five syndromes, a further search was conducted. The terms “face” OR “facial” AND “emotion” (consulting Harms et al., 2010, for corroboration of relevant search terms) were input into the Web of Science and PsychInfo search engines. In each case search engine this was combined, using the AND operator, with each of the five syndromes identified above. The abstracts of all returned papers were examined. Empirical studies to the end of the year 2011, in which the processing of facial emotion was experimentally assessed within the syndrome group, were selected for review. The reference sections of the returned papers were also examined, and further searches were performed for key authors (identified as above), to identify any papers which may have been missed in the initial search. The results of this process are presented in Table 1.

1 The search strategy of Moss and Howlin was informally repeated to confirm that there was no obvious change to these “top five” since 2009.
<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Number of relevant papers to end of 2011. In title or as keyword: (“Face” OR “Facial” AND “Emotion”) AND (Syndrome name)</th>
<th>Details</th>
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<td>Hippolsyte, Barisnikov, &amp; Van der Linden (2008)</td>
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<td>Phenylketonuria</td>
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Table 1. Search outcomes

Due to the lack of literature on facial emotion processing in Rett Syndrome, Tuberous Sclerosis Complex and Phenylketonuria, the following review addresses primarily research on two syndromes: **Fragile X Syndrome** and **Down’s Syndrome**. It focuses first on papers assessing facial emotion processing in Down’s Syndrome, and then in Fragile X Syndrome,
in each case considering the strength of evidence for, and nature of, potential atypicalities in the processing of facial emotion. In each case, the potential implications for the syndrome’s possible association with ASD are considered.

**Literature Review**

**Facial Emotion Processing in Down’s Syndrome**

Down’s Syndrome (DS) is typically caused by full or partial trisomy of chromosome 21. Down’s Syndrome is the most common chromosomal cause of intellectual disability, occurring in approximately 10.3 in 10,000 live births (Bell, Rankin, & Donaldson, 2003) and accounts for the largest single grouping of children with intellectual disability of known aetiology. Down’s Syndrome is associated with mild to severe intellectual disability (Capone, Grados, Kaufmann, Bernad-Ripoll, & Jewell, 2005).

In the past, co-occurrence of ASD and Down’s Syndrome was considered rare. A relative preservation of social skills has traditionally been thought to characterise Down’s Syndrome, the stereotype of which includes a sociable and friendly persona (Gibbs & Thorpe, 1983) not generally associated with ASD. However, more recently, research has indicated that co-morbidity of ASD within Down’s Syndrome may be more common than had been thought, with estimates of prevalence from 5% to 39% (see Moss and Howlin, 2009; Moss et al., 2012). This has occurred alongside increased acknowledgment that people with Down’s Syndrome, despite being in some senses socially adept, may display disproportionate difficulty in certain areas of socio-cognitive understanding (e.g., Wishart, 2007). For instance, it has been suggested that many superficially elaborate or charming behaviours may not be truly social in the sense that people with Down’s Syndrome may show little reciprocity in interactions (see Wishart & Pitcairn, 2000). This may contribute to, or otherwise affect, diagnoses of ASD in some people with Down’s Syndrome. The past 10-
15 years have seen an increase in research with a social cognitive focus, with a number of papers directly testing the ability of children and adults with Down’s Syndrome to process emotion in the faces of others (see Table 2).

**Children**

Four studies (Kasari, Freeman, & Hughes, 2001; Wishart and Pitcairn, 2000; Williams et al., 2005; Wishart et al., 2007) have directly assessed the ability of children with Down’s Syndrome to complete tasks requiring the matching, recognition or labelling of facial emotion, compared with control participants matched on other aspects of ability.

One of the studies (Kasari et al., 2001) used felt puppets with detachable schematic emotional faces as stimuli, with the remaining three using facial photographs from the Ekman and Friesen series (Ekman & Friesen, 1976). The three studies which used photographic stimuli included a task in which participants had to match photographs (of differing identity) by their facial emotion (e.g., “This man looks sad. Can you find another picture [in a group of 3 pictures] of a man who looks sad?”; Williams et al., 2005). Wishart and Pitcairn (2000) and Kasari et al. (2001) also included a task requiring the explicit labelling of the emotion displayed on the stimulus (e.g., “this is a picture of Jim. Is Jim happy or angry?”; Wishart and Pitcairn, 2000). In Wishart and Pitcairn’s task, participants had the option of pointing to a schematic happy or angry face in response to this question.

In addition, Kasari et al. (2001) used a receptive recognition task in which participants had to point to a stimulus displaying a specific emotion identified by the experimenter (“where is the [e.g., sad] face?”), and Kasari et al. (2001) and Wishart and Pitcairn (2000) included a task in which participants selected the appropriate emotion stimulus to match a story (e.g., a story about getting an ice cream on a hot day required the selection of the “happy” face stimulus). All six “basic” emotions (Ekman, Sorenson & Friesen, 1969; Ekman, 1992) – anger, disgust, fear, happiness, sadness and surprise – were assessed (in certain tasks) by
Wishart and Pitcairn (2000), Williams et al. (2005) and Wishart et al. (2007). These three papers also include non-emotional face-processing tasks (e.g., identity matching) to distinguish difficulties with recognising facial emotion from general problems with the processing of facial stimuli.

Wishart and Pitcairn (2000), Williams et al. (2005) and Wishart et al. (2007) all found that participants with Down’s Syndrome performed significantly more poorly on the emotion-matching tasks than did mental age-matched typically developing control participants. This difference remained significant when participants in one of the studies (Williams et al., 2005) were matched for ability on a face recognition test. Wishart et al. (2007) also demonstrated no significant difference between Down’s Syndrome and typically developing groups on identity matching. The specific nature of the relative impairments varied slightly: Wishart and Pitcairn (2000) found that performance on fear and surprise was especially impaired, while Williams et al. (2005) and Wishart et al. (2007) note a particular problem with fear.

Wishart and Pitcairn (2000) and Kasari et al. (2001) also found significantly worse performance on explicit expression recognition in children with Down’s Syndrome compared with typically developing children and, in Kasari et al.’s case, with children with non-specific intellectual disability. Kasari et al. (2001) found this difference in a sample of children with Down’s Syndrome of mean mental age 4.2 years (chronological age 6.4), but not in a younger sample with mean mental age 3.4 years (chronological age 8.1), suggesting that a relative impairment may emerge over time. Consistent with this, Williams et al. (2005) found that, in contrast with their other two groups (typically developing and non-specific intellectual disability), there was no significant effect of chronological age on emotion matching performance in Down’s Syndrome (adolescents up to 17 years of age were included in the study).
All four studies included a group of children with non-specific intellectual disability. Only Kasari et al. (2001) demonstrated significantly poorer performance of the Down’s Syndrome group in relation to the non-specific intellectual disability group, although the trends in the data in the other papers were in this direction. Wishart et al. (2007) suggest that, with small sample sizes, specific impairments in facial emotion processing in Down’s Syndrome may only be reliably demonstrable in relation to typically developing groups.

Williams et al. (2005) found that there was less of a relationship between emotion matching and scores on other cognitive and linguistic assessment measures in the Down’s Syndrome group than in the other two groups.

Whilst the authors of these studies generally suggest that the data indicate relatively specific deficits in the emotion processing tasks within the Down’s Syndrome group, there were some, albeit more limited, indications in some of these studies that performance on non-emotional face processing tasks was also poorer in Down’s Syndrome groups. Williams et al. (2005) found that the Down’s Syndrome group performed more poorly on the identity matching control task than the typically developing group, although they explain this in terms of attentional factors.

**Adults**

Three papers specifically assessed performance in facial emotion processing tasks in adults with Down’s Syndrome in relation to typically developing control participants (Hippolyte et al., 2008; Hippolyte et al., 2009; Fernandez-Alcaraz et al., 2010).

Hippolyte and colleagues (2008; 2009) assessed facial emotion processing in adults with Down’s Syndrome compared with typically developing children matched on a measure of receptive vocabulary. Both papers used tasks involving receptive emotion identification and emotion matching. In a third task (Emotion Recognition and Intensity Attribution)
participants were presented with a series of face photographs and had to indicate whether each face was happy, sad or neutral (neither happy nor sad). For “happy” or “sad” responses, the participants then decide between 2 emotional intensity levels. The authors also included a non-emotional identity matching task.

In neither study was there a significant difference between the control and Down’s Syndrome groups on identity matching. In both papers, the Down’s Syndrome group performed more poorly than the typically developing group on the receptive emotion identification and emotion matching tasks.

On the Emotion Recognition and Intensity Judgment task, Down’s Syndrome groups in both years performed more poorly than the typically developing control participants. This was driven by particularly poor performance on identifying the neutral emotion. Analysis of errors indicated a bias towards more positive responses (happiness); this effect did not reach significance in the 2008 paper (although the effect size was medium to large), but Hippolyte et al. (2009) found a significant positive bias.

Hippolyte et al. (2009) found that performance on a series of cognitive tasks, including receptive vocabulary, selective attention and non-verbal reasoning, correlated with aspects of the emotion processing tasks in the Down’s Syndrome group (as well as in controls). In particular, receptive vocabulary correlated with performance on the expression recognition task, with the relationship with the neutral expression being particularly strong.

Fernández-Alcaraz et al. (2010) investigated the facial emotion processing skills of 20 adults with Down’s Syndrome and moderate intellectual disability and 20 typically developing controls matched for sex and chronological age. Four computer-administered face processing tasks were carried out: one identity-matching task and three requiring the processing of facial emotion. As would be expected on the basis of difference in intellectual
ability, the Down’s Syndrome group performed significantly more poorly on all tasks. However, the authors’ main aim was to determine whether the relative ease of the tasks was similar for the two groups. There is no breakdown of results by emotion, so more detailed analysis of the results is difficult. In addition, the paper does not include control participants of similar ability in other areas, so cannot assess the presence (or otherwise) of a specific deficit in facial emotion processing. However, the paper broadly supports a position that there are similarities between the facial emotion processing of typically developing people and those with Down’s Syndrome.

**Adults and Children**

Porter et al. (2007) compared the emotion processing abilities of people with Down’s Syndrome and Williams Syndrome individually matched on gender, chronological age and mental age. Typically developing individuals matched to the Down’s Syndrome and Williams Syndrome groups on gender and chronological age were also tested, along with typically developing individuals matched to the Down’s Syndrome and Williams Syndrome groups on gender and mental age. Participants were given a forced-choice task in which a stimulus was presented and they had to indicate whether the expression in emotional faces and voices was happy, sad, angry or scared.

Overall on emotion recognition (combined analysis of facial and vocal expressions), the Down’s Syndrome group were significantly out-performed by the Williams Syndrome group and both of the typically developing groups, with a statistically significant difference on sadness individually. Separate data for facial and vocal tasks are not presented, but there was some indication that the particular problems with the sad expression were more driven by the vocal than the facial tasks. Gagliardi et al. (2003) found that the recognition of facial emotion in Williams Syndrome is worse than that of chronological age-matched, but indistinguishable from that of mental age-matched, controls. Given that the Down’s
Syndrome and Williams Syndrome groups in Porter et al.’s (2007) study are matched on mental age, the findings are consistent with the notion that people with Down’s Syndrome have more difficulty with the processing of facial emotion than would generally be expected on the basis of their overall cognitive ability. The authors note a positive bias in responses, with relative sparing of “happy”.

**Other related papers**

Certain papers intended to assess the facial affect recognition ability of people with ASD have used groups of people with Down’s Syndrome amongst their control participants. Celani, Battacchi, & Arcidiacono (1999) compared a group of children with ASD, a group of typically developing children and a group of Down’s Syndrome children, with all groups matched for Mental Age. Celani et al.’s (1999) Down’s Syndrome control group had a non-significantly lower score than a verbal mental age-matched typically developing control group, and a significantly higher score than the verbal mental age-matched ASD group on a delayed matching-by-emotion task using the emotions happy, sad or “wry”.

Turk and Cornish (1998) assessed facial emotion recognition in children with Fragile X Syndrome (discussed in more detail below), using IQ-matched people with Down’s Syndrome group as a control group. The Down’s Syndrome group performed more poorly on a task requiring participants to select a facial emotion to match a story. However, they also scored lower on a non-emotional facial recognition task.
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</thead>
</table>
| Turk and Cornish      | Happy, Sad, Fearful, Angry | • 14 boys FXS (CA 10.3; MA 5.7)  
• 14 boys DS (CA 10.8; MA 5.1)  
• 14 TD boys, MA-matched (CA 6.1; MA 6.2)  
DS and FXS matched on CA and MA | Receptive identification of emotions  
Matching vocalisation to facial expression  
Match facial expression to story vignette  
Face recognition (non-emotion task) | No differences on identification or matching of emotion.  
DS significantly lower scores than TD and FXS on matching facial expression to story vignette |
| Wishart and Pitcairn  | All 6 “basic”     | • 16 DS (mean CA 11.8)  
• 23 TD similar MA (mean CA 4.1), matched on facial recognition task  
• 16 NSID similar CA to DS group (mean 11.7)  
Matched on MA (DS and TD) or CA (DS and NSID) | Emotion Matching  
Match face to story  
Explicit labelling of facial emotion (angry or happy)  
Non-emotion face tasks | DS impaired relative to TD on emotion matching, especially for fear and surprise.  
DS also impaired on explicit labelling.  
DS group impaired relative to TD on one non-emotion task |
| Kasari et al (2001)   | Happy, Sad, Angry, Fearful | **Study 1:**  
• 20 DS (mean CA 6.4; mean MA 3.4)  
• 20 TD, MA-matched  
• 20 TD, CA-matched  
**Study 2:**  
• 36 DS (mean CA 8.1; mean MA 4.2)  
• 27 NSID, MA-matched | All 3 studies:  
Explicit emotion labelling  
Receptive emotion identification (pointing)  
Select emotion match vignette | Study 1: No differences from control groups  
Study 2: DS impaired relative to TD at expressive labelling and vignettes (significant for anger and fear). Impaired relative to TD and NSID on vignettes for anger and fear. |
<table>
<thead>
<tr>
<th>Paper</th>
<th>Emotions assessed</th>
<th>Participants and matching</th>
<th>Tasks</th>
<th>Key (selected) findings for DS groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kasari et al. (continued)</td>
<td></td>
<td></td>
<td></td>
<td>Study 3 (follow-up): lack of improvement</td>
</tr>
<tr>
<td>Williams et al. (2005)</td>
<td>All 6 “basic”</td>
<td></td>
<td>Emotion Matching</td>
<td>DS worse than TD on emotion matching (most impaired on fear)</td>
</tr>
<tr>
<td>Porter et al. (2007)</td>
<td>Happiness Sadness Anger Fear Faces and voices</td>
<td></td>
<td>Receptive Emotion Identification (faces and voices), forced choice between 4 emotions</td>
<td>DS outperformed by all other groups</td>
</tr>
<tr>
<td>Paper</td>
<td>Emotions assessed</td>
<td>Participants and matching</td>
<td>Tasks</td>
<td>Key (selected) findings for DS groups</td>
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<tr>
<td>Wishart et al. (2007)</td>
<td>All 6 “basic”</td>
<td></td>
<td>DS matched on MA (to WS, TD) or CA (to second TD sample)</td>
<td>DS outperformed by TD on emotion matching</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>No significant difference on identity matching</td>
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<td></td>
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<td>Emotion Matching</td>
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<td>Identity Matching</td>
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<td></td>
<td></td>
<td></td>
<td>Emotion Matching</td>
<td>Impairments in DS group, especially on neutral expression. Positive emotion response bias (non-significant)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Emotion Identification</td>
<td>Some indications of worse performance in DS group, but not significant.</td>
</tr>
<tr>
<td></td>
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<td>Emotion recognition and intensity attribution</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Identity processing (non-emotional) tasks</td>
<td></td>
</tr>
<tr>
<td>Hippolyte et al. (2009)</td>
<td>Anger, Happiness, Sadness, Surprise, Neutral</td>
<td></td>
<td>Matched on receptive vocabulary</td>
<td>Impairments in DS group on emotion matching (all emotions impaired except surprise) and emotion identification (surprise, anger and happiness most impaired).</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>Emotion Matching</td>
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<td></td>
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<td>Emotion Identification</td>
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</table>
### Table 2. Key characteristics of papers on facial emotion recognition in DS.

<table>
<thead>
<tr>
<th>Paper</th>
<th>Emotions assessed</th>
<th>Participants and matching</th>
<th>Tasks</th>
<th>Key (selected) findings for DS groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Happy</td>
<td></td>
<td>Emotion recognition and intensity attribution</td>
<td>Impairments in DS group, especially on neutral expression.</td>
</tr>
<tr>
<td></td>
<td>Sad</td>
<td></td>
<td>Identity processing (non-emotional) tasks</td>
<td>Positive emotion response bias (significant)</td>
</tr>
<tr>
<td></td>
<td>Neutral</td>
<td></td>
<td></td>
<td>No significant group differences</td>
</tr>
<tr>
<td>Fernandez-Alcaraz et al. (2010)</td>
<td>Happy</td>
<td>• 20 DS</td>
<td>Emotion Discrimination</td>
<td>DS group poorer performance all tasks (note groups not matched on performance measure)</td>
</tr>
<tr>
<td></td>
<td>Sad</td>
<td>• 20 TD</td>
<td>Emotion Naming</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Angry</td>
<td></td>
<td>Emotion Selection</td>
<td>Same order of ease of tasks in both groups</td>
</tr>
<tr>
<td></td>
<td>Fearful</td>
<td></td>
<td>Facial identity discrimination</td>
<td></td>
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<tr>
<td></td>
<td>Neutral</td>
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</table>

Abbreviations: FXS = Fragile X Syndrome; DS = Down’s Syndrome; WS = Williams Syndrome; TD = Typically Developing; MA = Mental Age; CA = chronological age; NSID = non-specific intellectual disability; fMRI = functional magnetic resonance imaging. See main text for further details (e.g., of tasks). Ages are given as group means in years. N.B. details selected from papers according to greatest relevance to this literature review (table does not attempt to present full details of all papers).
Summary: Facial Emotion Processing in Down's Syndrome

Papers published over the last 10-15 years have presented evidence that both children and adults with Down’s Syndrome, relative to typically developing control participants of similar ability in other domains, may be impaired in tasks which explicitly require the processing of facial emotion, including matching pictures by emotion (e.g., Williams et al., 2005; Wishart et al., 2007; Hippolyte et al., 2008, 2009), labelling the emotion in facial stimuli receptively (e.g., Kasari et al., 2001; Porter et al., 2007) and expressively (e.g., Kasari et al., 2001), and matching facial emotion to story vignettes (e.g., Turk and Cornish, 1998; Wishart and Pitcairn, 2000). Many tasks used within this research have been designed to minimize linguistic and other cognitive requirements (see, e.g., Wishart et al., 2007) and there is some evidence to indicate that the difficulties are relatively specific and not entirely accounted for by general intellectual or linguistic factors (e.g., Wishart et al., 2007; Hippolyte et al., 2008) or general face-processing difficulties (e.g., Williams et al., 2005). There is some indication (e.g., Williams et al., 2005) that performance in facial emotion processing tasks is less correlated with other aspects of ability in Down’s Syndrome than in other groups. However, other studies have found different cognitive abilities, such as receptive vocabulary and selective attention, to correlate strongly with performance on the emotion processing tasks (Hippolyte et al., 2009).

The conclusion that there are specific impairments in Down’s Syndrome on facial emotion processing tasks must currently be drawn only tentatively. In a number of the studies, there remains the confound associated with a “task dissociation” paradigm (see Jacoby, 1991, for a discussion and general possible solution). It is possible that the control tasks are simply less sensitive to performance deficits than the emotion processing tasks (e.g., Wishart et al., 2007; Williams et al., 2005; Wishart and Pitcairn, 2000), so the specificity of the possible facial
emotion processing difficulties remains partly an open question. The conclusion that there is a specific facial emotion processing deficit in Down’s Syndrome would have been strengthened had it been statistically demonstrated that the discrepancy in performance on emotional and non-emotional tasks was different across the groups. However, such analyses were not undertaken.

Several studies demonstrated poor performance by people with Down’s Syndrome on facial emotion processing tasks in relation to typically developing children matched for ability in other areas (e.g., Williams et al., 2005; Wishart et al., 2007). However, the evidence for impairment in relation to people with non-specific intellectual disability is weaker.

The specific nature of any impairment in facial emotion processing with respect to specific emotions is not consistent across the reviewed studies. The use of different sets of emotions in different studies also makes it hard to draw general conclusions. Some researchers (Hippolyte et al., 2008; 2009; Porter et al., 2007) note a possible bias towards mistaking negative emotions for more positive ones. There was also a possible problem with identifying emotionally neutral faces, although this could have been partially related to linguistic demands (Hippolyte et al., 2009). This is particularly interesting in relation to a study by Conrad et al. (2007), who conducted an EEG study of a small number of children with and without Down’s Syndrome while they watched video clips of differing affective content. There was evidence that, for happy, fearful and sad video clips, the Down’s Syndrome group displayed more intense emotional reactivity, which might be taken to indicate a bias away from emotional neutrality.
Down’s Syndrome, facial emotion processing, and Autistic Spectrum Disorders

How does an understanding of facial emotion processing in Down’s Syndrome alter our understanding of the ways ASD might present in people with Down’s Syndrome? Overall, evidence points to a (perhaps subtle) possible difficulty, relative to others of similar ability in other areas, with the processing of facial emotion in people with Down’s Syndrome. This has yet to be fully characterised. To the extent to which the possible deficit impacts on the social functioning of individuals with Down’s Syndrome, it may affect 1) the probability that people with Down’s Syndrome are diagnosed with ASD, and 2) the manner in which ASD might present.

Examination of diagnostic criteria for ASD (e.g., DSM-IV; ICD-10) indicate that diminished understanding of others’ facial expressions – as it seems may be the case in Down’s Syndrome – can contribute to a diagnosis of ASD. An impoverished understanding of facial emotion in people with Down’s Syndrome (over and above that explained by the level of intellectual disability) may increase the likelihood that a person with Down’s Syndrome will be diagnosed with ASD. To my knowledge, this remains a largely untested notion. No studies were found relating facial emotion processing difficulties to ASD symptomatology. In Down’s Syndrome, the manner in which impaired emotion-processing ability in Down’s Syndrome might interact with other factors – related and unrelated to Down’s Syndrome – remains to be elucidated. Numerous other factors (linguistic and other communicative abilities, social motivation, interests, and so on) would presumably interact with any facial expression perception difficulties to determine the overall manner in which the person presents. And this presentation, in turn, is in practice key to whether an individual will ultimately gain a diagnosis of ASD. For example, should a bias to interpret others’ emotions as more positive than they
are (Hippolyte et al., 2008; 2009) influence the real-world social interactions of people with Down’s Syndrome, one might imagine that this might contribute to the relatively indiscriminate social approach behaviour noted in the syndrome (although Porter et al., 2007, found no evidence of abnormal approach ratings alongside deficits in negative emotion recognition in their Down’s Syndrome group). It is conceivable that this could either increase or decrease the probability of being diagnosed with ASD depending on the context of other features of an individual. If approach behaviours present as extreme sociability, for instance, they may reduce the likelihood that clinicians and others would consider ASD as a diagnosis for an individual. If, on the other hand, the social insensitivity of the social approaches predominates in the impression given by the person, this could increase the likelihood of an ASD diagnosis.

Empirically, there is little evidence to elucidate a possible role for diminished facial expression in determining which people with Down’s Syndrome will obtain a diagnosis of ASD. Capone and colleagues’ analysis (Capone et al., 2005; Carter, Capone, Gray, Cox, & Kaufmann, 2007) did not indicate a strong role for social factors, more generally, in distinguishing people with Down’s Syndrome and ASD from those with Down’s Syndrome and no comorbid behaviour disorder. They instead found that unusual stereotypy and anxious behaviour were the main distinguishing variables. However, social withdrawal played a significant role in differentiating those with Down’s Syndrome-ASD from those with Down’s Syndrome and Stereotypic Movement Disorder (although Moss et al., 2012, found people with Down’s Syndrome and ASD may be less socially withdrawn than those with idiopathic ASD). The relationship between characteristics such as social withdrawal and facial emotion processing abilities has not been assessed in Down’s Syndrome.
Even if facial emotion processing abilities do not contribute to determining which people with Down’s Syndrome will also have ASD, it is possible that a facial emotion processing difficulty influences what ASD looks like when in combination with Down’s Syndrome. Whether, and in what way, this might be the case remains largely a question for future research. Interestingly, Turk and Cornish’s (1998) paper informs that, of five participants with ASD and Down’s Syndrome, parental reports indicated that 3 of the children showed “no understanding” of facial expression. This compares to 0 of 5 boys with ASD and Fragile X Syndrome and 6 of 18 boys with idiopathic ASD. This would be consistent with the notion that impaired facial emotion processing characterises ASD in Down’s Syndrome, although this is of course a small sample size, and also relies on parent report measures which are subject to reporting biases. The manner in which impaired ability to recognise others’ emotions may impact on this is not clear.

**Facial emotion processing in Fragile X Syndrome**

Fragile X Syndrome occurs in 1 in 3600 males and 1 in 8000 females, making it the most common known inherited cause of intellectual disability (Cornish et al., 2008). It arises from an excessive number (>200) of CGG repeats within the Fragile X Mental Retardation-1 (FMR1) gene, location Xq27-3. 5-40 repeats is classified as normal, 45-54 as an intermediate or grey zone, 55-200 as a pre-mutation and >200 as the full mutation (Maddalena et al., 2001). People with Fragile X Syndrome have lower levels of the FMR protein (encoded by the FMR1 gene), which has a cascade of developmental consequences. Fragile X Syndrome is generally associated with moderate to severe intellectual disability in males, with more variable (and generally less severe) intellectual disability found in females (Freund & Reiss, 1991; Reiss & Dant, 2003). Hyperactivity, attention deficits and social anxiety have also been associated with
Fragile X Syndrome (e.g., Reiss & Dant, 2003). Recent studies estimate the prevalence of diagnosable ASD in Fragile X Syndrome to be between 21% and 50% (although this is likely to be lower in females, Mazzocco, Kates, Baumgardner, Freund, & Reiss, 1997). In comparison with other known genetic neurodevelopmental syndromes (including Down’s Syndrome), the association between Fragile X Syndrome and ASD has been relatively well studied. The behavioural phenotype of Fragile X Syndrome is generally thought to share characteristics with idiopathic ASD.

Table 3 gives basic details of key studies on facial emotion processing in Fragile X Syndrome. Table 4 summarises key functional imaging findings where relevant.

**Initial behavioural studies**

Behavioural studies have found little indication of a deficit in facial emotion processing in Fragile X Syndrome. Mazzocco et al. (1994) assessed the ability of 46 females with the fragile X mutation (both unaffected carrier and expressing females) to match facial emotions, comparing their performance to that of a group of typically developing females. Performance was positively related to IQ but not to Fragile X Syndrome status.

Simon and Finucane (1996) assessed the ability of 15 adult males with Fragile X Syndrome and 15 individually age- and IQ- matched controls to identify facial expressions. Participants were shown a series of 48 pages of 6 faces, each displaying one of the “basic” six emotions, and were asked to point to a face displaying the emotion identified by the experimenter. There was no significant difference in emotion recognition between the two groups; neither was there any evidence that the relative difficulty of the different emotions differed. Wishart et al.’s (2007) study (discussed above) also indicated no impairments in facial emotion processing.
tasks in an Fragile X Syndrome group, relative to matched typically developing, non-specific intellectual disability and Down’s Syndrome participants.

Turk and Cornish’s (1998) first study assessed the facial emotion processing of 14 boys with Fragile X Syndrome (none of whom had received a diagnosis of autism), 14 boys with Down’s Syndrome matched on age and IQ, and 14 typically developing boys matched on IQ (and therefore with a lower chronological age). Children completed three facial emotion processing tasks (receptive emotion identification, matching a schematic face to an emotional noise such as sobbing, and selecting an emotional face to match a story vignette) and a facial recognition task. In none of these tasks was there a significant difference between the Fragile X Syndrome and typically developing groups’ performance. In a second study, 18 boys with Fragile X Syndrome, 45 boys with Down’s Syndrome and 42 with non-specific intellectual disability, matched on chronological age, were rated using a semi-structured interview with parents (Wing, 1980). One item reads: “How much can you control his behaviour by your facial expression without saying anything?”, to which a parent could respond that their child displayed no understanding of facial expression (score 0), that behaviour could be controlled by exaggerated expressions (score 1) or that behaviour could be controlled by small changes in facial expression (score 2). Although there were no significant differences between groups, it was noted that no boy with Fragile X Syndrome scored 0, whilst 20% of the Down’s Syndrome group and 16% of the non-specific intellectual disability group fell into this category. Two-thirds of the Fragile X Syndrome group demonstrated good understanding, whereas this was true of fewer than half of the Down’s Syndrome and non-specific intellectual disability groups. Over the three groups, participants with ASD were significantly more likely to show “no understanding” of facial expression than participants without ASD. None of the 5 boys with ASD and Fragile X Syndrome showed no understanding of facial expression, while 3 of 5 of the
Down’s Syndrome-ASD group and 6 of the 18 ASD-non-specific intellectual disability group showed no understanding.

**Pupillary Response (Autonomic Activity)**

Two recent studies have assessed autonomic activity, as indexed by pupillary dilation, in response to facial emotion in Fragile X Syndrome. Farzin et al. (2009) assessed 16 individuals with Fragile X Syndrome and 16 typically developing individuals matched for chronological age. Of the Fragile X Syndrome group, 8 were diagnosed with ASD. Farzin et al. (2011) used the same stimuli and experimental procedure to assess 15 individuals with Fragile X Syndrome and 20 typically developing controls, group-matched on chronological age. In this study, participants were tested twice, no more than two weeks apart.

Participants passively viewed 60 colour photographs of adult human faces each displaying a calm, happy or fearful expression. Each face was displayed for 3 seconds (preceded by a scrambled image of the face), during which participants’ eye movements and pupil diameter were recorded. Farzin et al (2009) found that participants in the Fragile X Syndrome group made fewer fixations, and spent less time looking at, the eye region of the faces. Also, participants with Fragile X Syndrome displayed greater pupil reactivity to emotional faces, compared with controls. Both groups showed most pupillary reactivity to the happy and fearful faces. In the Fragile X Syndrome group, pupil dilation in response to fearful faces correlated inversely with the number of fixations to the eyes of calm, happy and fearful faces.

Farzin et al. (2011) aimed to assess the feasibility and reliability of eye tracking and pupillometry as an outcome measure for evaluation of pharmacological interventions in Fragile X Syndrome. Their study confirmed Farzin et al.’s findings (2009) of significant differences in fixations and looking time for different facial regions between groups. For
instance, individuals with Fragile X Syndrome made significantly fewer fixations to the eye region of all faces. They also replicated the finding that participants with Fragile X Syndrome displayed greater pupillary reactivity than the typically developing group to faces in general (although they did not report an association of this effect with the emotion displayed on the face). Fixation count, looking time and pupillary response measures were all highly reliable across sessions.

The authors postulated that, during social interaction, people with Fragile X Syndrome - “both with and without autism” - experience excessive emotional arousal, which they then try to reduce using gaze aversion. The studies are, overall, consistent with the notion that increased autonomic arousal in response to emotion in others’ faces characterises Fragile X Syndrome. The impact of the specific emotion displayed remains to be elucidated (see also Hagan et al., 2008). In addition, the relationship of autonomic arousal with other cognitive, emotional and behavioural factors needs further exploration.

Functional neuroimaging studies

Two studies (Dalton et al., 2008; Hagan et al., 2008) have used fMRI to record brain activation during tasks in which participants made judgments about the emotional status of facial photographs. Dalton et al. (2008) compared people with Fragile X Syndrome with individuals with ASD and typically developing people. Hagan et al. (2008) compared females with Fragile X Syndrome with females. Different sets of emotions were assessed in the two papers, with different sets of response options. Dalton et al (2008) presented participants with happy, angry, fearful and neutral faces, and participants had to decide whether each face was “emotional” or “neutral” and respond with a corresponding button press. They also tracked participants’ eye movements. Hagan et al. (2008) presented happy, sad, neutral and
scrambled faces, to which participants responded (via a button press) “happy” (left button),
“sad” (middle button) or “neutral or scrambled” (right button). Hagan et al. (2008) made
comparisons, between the two groups of participants, of brain activation maps representing
specific contrasts between different types of stimuli. For example, typically developing and
Fragile X Syndrome groups were compared in their activation for “happy faces minus neutral
faces”. This contrast presumably represents the activation specifically attributable to a (happy)
emotional expression. In addition, the groups were compared in their activation for (e.g.)
“happy minus scrambled” faces, a contrast which presumably represents not only the specific
emotional expression but also the effect of “faceness”. Holsen et al. (2008) also conducted a
study of participants with Fragile X Syndrome (5 male) during the presentation of fearful faces;
participants judged whether each face was male or female. The authors conducted fMRI brain
scanning, and compared activation maps of the Fragile X Syndrome group to those of a
typically developing group matched on age, gender and handedness.

Overall, fMRI studies indicated neural atypicalities in the processing of emotional faces in
Fragile X Syndrome (see Table 4 for details). Hagan et al.’s (2008) study suggested that, in
females with Fragile X Syndrome (relative to age-matched typically developing females), there
may be emotion-specific differences in face processing. In particular, in the Fragile X Syndrome
group happy faces elicited greater activity in certain brain areas associated with emotion
processing, while sad faces elicited less activation than was found in controls. In Dalton et al.’s
study, people with Fragile X Syndrome displayed differences in brain activation and eye
movements when processing facial stimuli, with some of the atypicalities shared by a group of
people with ASD (e.g., Fusiform Gyrus, FG, hypoactivation) and some not. Regions which were
especially active in the Fragile X Syndrome group included the left postcentral gyrus and right
insula (both also especially active in response to happy faces in Hagan et al’s study). However,
these differences in Dalton et al.’s study were not related to the specific emotional status of the faces. Holsen et al.’s (2008) study indicated that possible regions of left and right frontal cortex may function differently in relation to social anxiety in people with Fragile X Syndrome. The manner in which this might relate to different facial emotions is unclear as only fearful faces were displayed.

The psychological interpretation of fMRI activation data is tricky (perhaps especially in people in whom brain development may be atypical), and there are many potential alternative ways to account for physiological data at a conceptual level. For instance, syndrome-specific activation patterns in the hippocampus (Dalton et al., 2008) may relate to numerous alternative emotion and/or memory functions. Hagan et al.’s study provides the most systematic investigation of activation in relation to different emotions (albeit it only happy, sad and neutral), and its power to do this was limited by a relatively short interstimulus interval (mean 1572ms). Overall, however, the studies add to the position that the emotional response to emotional and non-emotional faces may be atypical in Fragile X Syndrome. Brain activation data may be taken as consistent with the notion that, at least for some facial emotions, people with Fragile X Syndrome may respond with particularly pronounced emotional arousal (Dalton et al., 2008; Hagan et al., 2008). Hagan et al.’s study also raises the possibility that for sadness (an emotion not assessed by Dalton et al., 2008 or Farzin et al., 2009; 2011, see below) people with Fragile X Syndrome are less emotionally aroused than are typically developing people. There are also indications that the neural correlates of social anxiety are different in Fragile X Syndrome from those in typically developing people (Holsen et al., 2008).
<table>
<thead>
<tr>
<th>Paper</th>
<th>Participants and matching</th>
<th>Emotions included</th>
<th>Measures</th>
<th>Key findings (non-fMRI) for FXS group</th>
</tr>
</thead>
</table>
| Mazzocco et al (1994) | • 56 control (TD) women (CA 31.3)  
• 27 women carrying FXS premutation (CA 33.9)  
• 19 women carrying full mutation (CA 30.5)  
Matched on CA and gender | Happiness, Sadness, Anger, Fear, Shame, Contempt, Disgust, Interest, Surprise | Emotion matching | No significant group differences in accuracy |
| Simon and Finucane (1996) | • 15 FXS adults (all male. Mean CA 41.8)  
• 15 “non-FXS” adults (NSID?) (all male. Mean CA 43.5)  
Individually matched on CA and IQ | All 6 “basic”                      | Receptive identification | No significant effect of group on performance |
<table>
<thead>
<tr>
<th>Paper</th>
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<tbody>
<tr>
<td>Turk and Cornish (1998)</td>
<td>- 14 males FXS (CA 10.3; MA 5.7) &lt;br&gt;14 males DS (CA 10.8; MA 5.1) &lt;br&gt;14 TD males (CA 6.1; MA 6.2) &lt;br&gt;Matched on MA</td>
<td>Happy, Sad, Fearful, Angry</td>
<td>Receptive identification of emotions, Matching vocalisation to facial expression, Match facial expression to story vignette, Face recognition (non-emotion task)</td>
<td>No significant differences between FXS and TD &lt;br&gt;FXS superior performance to DS in some tasks (see Table 2)</td>
</tr>
<tr>
<td>Dalton et al (2008)</td>
<td>- 9 FXS (6 female, 3 male. None with clinical diagnosis ASD. Mean CA 20.7. Mean IQ 66.1) &lt;br&gt;- 14 ASD (all male. Mean CA 15.9. Mean IQ 87.2) &lt;br&gt;- 15 TD (3 female, 12 male. Mean CA 16.8) &lt;br&gt;Not closely matched on CA, or on gender. Groups not matched on IQ (FXS lowest) - included as covariate</td>
<td>Happy, Fearful, Angry, Neutral</td>
<td>Behavioural Task: Emotional or neutral judgment, Eye tracking, SCQ, fMRI</td>
<td>Behavioural: accuracy of FXS and ASD groups similar &lt;br&gt;Eye data: marginal tendency for FXS group to look less at the eyes than the TD group (no difference between ASD and FXS).</td>
</tr>
<tr>
<td>Paper</td>
<td>Participants and matching</td>
<td>Emotions included</td>
<td>Measures</td>
<td>Key findings (non-fMRI) for FXS group</td>
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<tr>
<td>Hagan et al (2008)</td>
<td>• 10 FXS (all female. Mean CA 16.4. Mean IQ 91)</td>
<td>Happy, Sad, Neutral, Scrambled</td>
<td>Behavioural Task: 3 button press – happy (left button), sad (middle button), neutral or scrambled (right button)</td>
<td>Behavioural: FXS lower accuracy (especially neutral and scrambled).</td>
</tr>
<tr>
<td></td>
<td>• 10 TD females (mean CA 15.6. Mean IQ 106)</td>
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<td>fMRI</td>
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<td></td>
<td>Groups matched for CA and gender. Not matched on IQ.</td>
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<tr>
<td>Holsen et al (2008)</td>
<td>• 11 FXS (6 females, 5 males. Mean CA 18.5)</td>
<td>Fear</td>
<td>Behavioural Task: male/female judgment. Eye tracking Measures of social anxiety</td>
<td>Different relationships between measures of social anxiety and brain activation for the different groups (see Table 4)</td>
</tr>
<tr>
<td></td>
<td>• 11 TD (6 females, 5 males. Mean CA 18.7)</td>
<td></td>
<td>fMRI</td>
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<td>Matched on CA, gender and handedness</td>
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<tr>
<td>Farzin et al (2009)</td>
<td>• 16 FXS (3 females, 13 males. Mean CA 17.0)</td>
<td>Calm, Happy, Fearful</td>
<td>Passive viewing Eye tracking and pupillometry</td>
<td>FXS greater pupillary reactivity to emotional faces FXS group: Pupillary response to fearful faces inversely correlates with number of fixations to eyes of all faces</td>
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<td>• 16 TD (3 females, 13 males. Mean CA 17.1)</td>
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<td>Matched on CA and gender</td>
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<tr>
<td>Paper</td>
<td>Participants and matching</td>
<td>Emotions included</td>
<td>Measures</td>
<td>Key findings (non-fMRI) for FXS group</td>
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<td>Farzin et al (2011)</td>
<td>· 15 FXS (3 females, 12 males. Mean CA 18.8)</td>
<td>Calm, Happy, Fearful</td>
<td>Passive viewing, Eye tracking and pupillometry</td>
<td>FXS greater pupillary reactivity to faces</td>
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<td>· 20 TD (10 females, 10 males. Mean CA 24.9)</td>
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<td>Not closely matched</td>
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Table 3. Key details of papers on facial emotion recognition and FXS (see Table 4 for neuroimaging findings). Abbreviations: FXS = Fragile X Syndrome; TD = Typically Developing; MA = Mental Age; CA = chronological age; NSID = non-specific intellectual disability; fMRI = functional magnetic resonance imaging. See main text for further details (e.g., of tasks). Gender of participants included due to specific relevance to FXS. Ages given as group means in years. N.B. details selected from papers according to greatest relevance.
<table>
<thead>
<tr>
<th>Paper</th>
<th>Key fMRI findings for FXS group</th>
<th>Possible interpretations (based on suggestions of authors)</th>
<th>Further notes/comments</th>
</tr>
</thead>
</table>
| Dalton et al. (2008) | 4 regions great activation for FXS than other groups:  
- Left hippocampus (correlated with SCQ)  
- Right insula  
- Left Superior Temporal Gyrus  
- Left postcentral gyrus  

Hypoactivation of left FG compared with TD (in common with ASD).  
FXS group: fixations to eye region correlate positively with FG activation.  
Activation in right FG correlates negatively with SCQ score (i.e., greater endorsement of ASD features = lower FG activation)  
Activation of left amygdala correlates positively with SCQ. |  
- Reduced habituation to emotionally salient stimuli?  
- Increased anxiety/orienting to emotional faces?  
- Compensatory brain activity specific to the fear emotion?  
- Enhanced cortical motor response?  

Neural mechanisms in common with ASD  
Specific FXS-related relationship between behavioural features and FG activation  
Relationship between ASD symptomatology and FG activation atypicalities in FXS  
Specific relationship between amygdala and ASD symptomatology |  
ASD data included for comparison  
ASD symptomatology assessed in FXS group in relation to fMRI data  
Not possible to determine which fMRI aspects related specifically to emotion |
<table>
<thead>
<tr>
<th>Paper</th>
<th>Key fMRI findings for FXS group</th>
<th>Possible interpretations (based on suggestions of authors)</th>
<th>Further notes/comments</th>
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<tr>
<td>Hagan et al. (2008)</td>
<td>Sad minus neutral faces: FXS lower activation in parts of the right and left insula, and pre- and post-central gyri</td>
<td>Lower emotional arousal in FXS in response to sadness? (reduced empathy?)</td>
<td>Specifically assesses correlates of processing emotion in faces</td>
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<td></td>
<td>Sad minus scrambled faces: Lower activation in left claustrum, putamen and caudate and left superior and middle frontal gyri</td>
<td></td>
<td>No assessment of ASD symptomatology</td>
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<td></td>
<td>Happy minus neutral faces: FXS group increased activation in certain areas, including the precentral gyrus, right middle frontal gyrus and right insula</td>
<td>Higher emotional arousal in FXS in response to happiness?</td>
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<td>Dorsal Anterior Cingulate Cortex (dACC): FMRP levels correlated positively with activation (although when IQ was covaried out, the correlation remained significant only for the happy minus scrambled faces contrast).</td>
<td>Biochemical evidence for modulation by FXS genetics of a paralimbic area associated with emotion processing</td>
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### Table 4

<table>
<thead>
<tr>
<th>Paper</th>
<th>Key fMRI findings for FXS group</th>
<th>Possible interpretations (based on suggestions of authors)</th>
<th>Further notes/comments</th>
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<td>Holsen et al. (2008)</td>
<td>For faces which were later remembered: In regions of left and right frontal cortex, higher brain activation associated with lower social anxiety. Opposite correlation observed in control participants. Lower activation of prefrontal regions (including superior and medial areas)</td>
<td>Specific neural mechanisms behind social anxiety in FXS Social cognition networks activated alongside social anxiety in controls do not function normally in FXS Inability to recruit social cognition related areas appropriately</td>
<td>Behavioural task not emotion-related Not possible to determine which fMRI aspects related specifically to emotion</td>
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</table>

Table 4. fMRI findings for facial emotion processing in FXS (see Table 3 for other aspects of papers). Abbreviations: FXS = Fragile X Syndrome; SCQ = Social Communication Questionnaire (Rutter, Bailey, & Lord, 2003); FG = Fusiform Gyrus; TD = Typically Developing; dACC = dorsal Anterior Cingulate Cortex; FMRP = Fragile X Mental Retardation Protein; fMRI = functional magnetic resonance imaging.

N.B. details selected from papers according to greatest relevance.
Facial Emotion Processing in Fragile X Syndrome: What can we learn about the ASD association?

Task Accuracy

There is little indication in the reviewed literature that accuracy in explicit facial emotion processing tasks (e.g., receptive identification of emotion, Turk and Cornish, 1998, Simon and Finucane, 1996; matching pictures by emotion, Wishart et al., 2007; selecting facial emotion pictures based on a story, Turk and Cornish, 1998) is specifically impaired in Fragile X Syndrome.

In idiopathic ASD, whilst the evidence is mixed (see Harms et al, 2010, for a review), it has long been considered that there may be specific impairments in performance on emotion-processing tasks such as matching pictures by emotion (Bormann-Kischkel, Vilsmeier & Baude, 1995; Hobson, 1986; Lindner & Rosén, 2006, and numerous others). Based on current evidence (albeit following less investigation), there are no such deficits in these tasks in Fragile X Syndrome populations.

What might this tell us about the relationship between ASD and Fragile X Syndrome? There are few studies of facial emotion processing specifically in people with comorbid Fragile X Syndrome and ASD (although see Dalton et al., 2008; Farzin et al., 2009). However, the apparent absence of impairment in facial emotion processing tasks in Fragile X Syndrome overall may be consistent with the notion that people with Fragile X Syndrome-ASD have social skills which are less impaired than in people with idiopathic ASD (e.g., Kau et al., 2004). This picture is complicated by the results of studies indicating that within groups of people with Fragile X Syndrome, it is socialisation skills which seem to best predict ASD diagnosis.
Kaufmann et al. (2004) assessed boys with Fragile X Syndrome with and without ASD, and concluded that it was Reciprocal Social Interaction domain of the Autism Diagnostic Interview-Revised (ADI-R) (Lord et al., 1994) which formed the main distinction between the groups of participants. Facial emotion processing is a key component of effective reciprocal social interaction. The socialisation scale of the Vineland Adaptive Behaviour Scales (VABS; Sparrow, Balla, & Cicchetti, 1984) was also a strong predictor of ADI-R score. Budimirovic et al. (2006) also found that 6 items on the VABS socialisation scale accounted for the correlation between this scale and ASD diagnosis, and revealed that these items represented recognition of emotions and verbal labelling of emotions (e.g., “label happiness, sadness, fear and anger in oneself”; “respond appropriately when introduced to others”) and the recognition and application of rules of social behaviour. Such abilities may well be related to facial emotion processing skills, although it is possible that deficits as reported on these questionnaires are assessing different or additional abilities from those assessed in empirical studies of emotion processing. At present there is no evidence that facial emotion processing abilities as measured empirically are correlated with ASD symptomatology in Fragile X Syndrome. The relationship between questionnaire measures of facial emotion processing and empirical investigations of the ability may need to be assessed. For instance, it is possible that an IQ-appropriate ability to recognise emotions within an experimental setting does not translate into a socially appropriate use of this ability.

**Autonomic Arousal and Eye movements**

Whilst behavioural performance on facial emotion processing tasks is not obviously impaired, the manner in which emotion in faces is processed does appear to be atypical within Fragile X Syndrome populations.
First, people with Fragile X Syndrome may show a greater autonomic response to at least some emotions when displayed on other people’s faces, which in turn may affect their behaviour (Farzin et al., 2009). In particular, it may be that in order to regulate this autonomic response, there is a tendency to avert gaze from faces, especially from the eye region. Intuitively, it seems likely that a characteristic associated with the avoidance of eye contact might, all other things being equal, increase the likelihood of a person being diagnosed with ASD. It is therefore intriguing that, in Farzin et al.’s study, there were no significant associations between symptoms of ASD (measured by the SCQ and ADOS) with any of the fixation, dwell time or pupil reactivity measures. It is possible that Farzin et al.’s finding of a lack of relationship between eye fixations and ASD symptoms reflects that people with Fragile X Syndrome in their sample all, or almost all, display enough gaze avoidance for this to potentially classify as characteristic of ASD. Therefore, variance in ASD measures would be more substantially related to other aspects of ASD symptomatology: whether or not a person with Fragile X Syndrome also has a diagnosis of ASD could depend on other, more variable, characteristics (e.g., communication skills). If this were the case, the autonomic arousal associated with processing others’ facial emotions could be a factor linking Fragile X Syndrome and ASD, but not play a substantial role in which people with Fragile X Syndrome will also be diagnosed with ASD.

It could also be that the type of gaze avoidance associated with Fragile X Syndrome and demonstrated by Farzin et al. (2009) does not present as ASD symptomatology and thus does not covary with scores on ASD measures. It has been suggested that people with Fragile X Syndrome may avert gaze due to social anxiety whereas people with ASD tend to display more social indifference, suggesting possible difference in underlying mechanisms and presentation (see, e.g., Budimirovic et al., 2006). Interestingly, there are some indications of reduced
autonomic activity in response to emotional faces in idiopathic ASD (Hubert, Wicker, Monfardini, & Deruelle, 2009). This raises the possibility that different types of atypical autonomic responses characterise ASD and Fragile X Syndrome in response to facial emotions. This may add to the position that similar presentations (e.g., avoidance of eye contact) in the two conditions occur for different reasons.

**Neurological correlates**

Dalton et al.’s (2008) functional imaging study (described above) included an idiopathic ASD group and certain similarities were found between ASD and Fragile X Syndrome participants’ brain activation patterns. However, the degree to which these similarities (e.g., in FG hypoactivation) specifically reflect the emotion processing aspect of the task is not clear. The study also specifically assessed autistic symptomatology (measured by the SCQ) both in Fragile X Syndrome and people with idiopathic autism, in relation to brain activation maps and eye movements. The study indicates that the processing of emotional faces in Fragile X Syndrome is different from both typically developing and ASD groups with respect to brain activation maps. In addition, activation in certain areas which were specifically active in participants with Fragile X Syndrome (notably left hippocampus) was correlated with SCQ score. This was not the case in participants with idiopathic autism, suggesting potentially different neurophysiological pathways to ASD symptomatology, perhaps (a notion suggested by the authors) reflecting a reduced habituation to emotion in stimuli specifically in people with Fragile X Syndrome. This result is in need of replication.

Structural imaging studies of ASD and Fragile X Syndrome have generally indicated some possible similar neuroanatomical correlates (e.g., increased caudate size, e.g., Langen, Durston, Staal, Palmen, & Van Engeland, 2007; Reiss, Abrams, Greenlaw, Freund & Denckla, 1995;
reduced cerebellar vermis, Kaufmann et al., 2003). However, a VBM study directly comparing the two found numerous differences (e.g., in basal ganglia and frontal cortex). Whilst many of the common and unique specified areas have been associated with social functions including facial emotion recognition (e.g., basal ganglia; frontal areas), how the anatomical similarities and differences between typically developing individuals, those with ASD and those with Fragile X Syndrome might relate to socio-emotional functioning remains to be fully investigated.

In summary, studies indicate brain activation atypicalities in people with Fragile X Syndrome during facial emotion processing tasks as well as atypicalities in eye gaze and autonomic arousal. These may be partially distinct from those in idiopathic ASD. However, the precise nature of the atypicalities remains unclear. For instance, there may be a difference between the nature of abnormal processing for different individual emotions (e.g., sadness vs. happiness, Hagan et al., 2008), but this requires replication and current conclusions are limited by the use of only a subset of the basic emotions in the cited studies, with different emotions utilised in different studies. The relationships between Fragile X Syndrome, facial emotion processing and ASD may be highly complex. Dalton et al. (2008) found activation in certain brain areas (FG, possibly amygdala) to be correlated with symptoms of ASD during an emotion processing task. However, there was no evidence that this specifically related to the emotional aspects of the tasks and, of course, it is difficult to say conceptually what these differences represent. One study (Farzin et al, 2009) failed to establish a statistical link between autonomic and gaze atypicalities in response to emotional faces and ASD symptomatology. Given the potential importance of emotion and face processing in other people to ASD diagnoses, the established atypicalities in facial emotion processing within idiopathic ASD (Harms et al., 2010), and questionnaire-based findings that facial emotion-related difficulties
account for variance in ASD diagnosis in Fragile X Syndrome (Budimirovic et al., 2006), this warrants further exploration.

**Other Syndromes of note**

The phenotypic interpersonal characteristics of certain other syndromes suggest that research into the processing of facial emotion in people with the syndromes may not only further elucidate aspects of the phenotype, but also its relationship with ASD. For instance, in Angelman Syndrome, the behavioural phenotype includes a strong tendency for smiling (e.g., Pelc, Cheron, & Dan, 2008; Zori et al., 1992). “Simulation” theories of facial emotion perception (e.g., Goldman & Sripada, 2005) propose that similar neural mechanisms are involved in producing one’s own facial expressions and perceiving facial emotion in others. Does a bias towards happy facial expressions in people with Angelman Syndrome correspond to a bias to perceive happiness in others? If so, how might this relate to possible ASD presentations? In Smith-Magenis Syndrome, a strong preference for adult attention has been noted, which can be a prominent reinforcer of challenging behaviour (e.g., Taylor & Oliver, 2008). Does a tendency to work for adult attention in circumstances when negative emotions may be displayed correspond with a difficulty distinguishing facial emotions? How might it affect discrimination between other emotions? Might this also relate to ASD presentations? These questions are currently unanswered.

**Summary and conclusions**

Of the five genetic syndromes most frequently associated with ASD in the literature (Moss and Howlin, 2009), papers empirically assessing facial emotion processing were found for two: Fragile X Syndrome and Down Syndrome. The papers indicate (different) possible abnormalities in facial emotion processing in these groups.
Processing of facial emotion in others is widely recognised as a crucial skill for normal social functioning, and atypicalities feature in the diagnostic criteria for ASD. In a broad sense, we are beginning to understand a little about the different ways in which ASD might present within syndrome groups (e.g., Capone et al, 2005; Budimirovic et al, 2006; Moss and Howlin, 2009; Moss et al., 2012; Meguid, 2012). However, in order to appreciate how genetic syndromes may translate into ASD diagnoses, an understanding of the cognitive and emotional corollaries of the syndromes is important. Empirical investigations of abilities such as facial emotion processing in specific syndrome groups are beginning to emerge and, in some cases, investigators are also measuring the relationship between such abilities and measures of ASD (e.g., Dalton et al., 2008; Farzin et al., 2009).

The emergent picture to date is somewhat complex and the profile of facial emotion processing abnormalities in Down’s Syndrome and Fragile X Syndrome is still emerging. Furthermore, the links between abilities such as facial emotion processing and ASD diagnoses remain largely hypothetical within syndrome groups. Whilst one might pontificate on the potential impact of (for instance) a possible facial emotion recognition impairment in Down’s Syndrome, or a decreased ability to regulate emotional responses to others’ emotions in Fragile X Syndrome, on the development of ASD symptomatology, further research is required to better characterise the possible connections.

In the case of Down’s Syndrome, studies of the facial emotion recognition abilities of people with comorbid Down’s Syndrome and ASD are called for. In addition, studies using implicit measures of facial emotion processing, including gaze fixation, autonomic measures and neurological activity during facial emotion processing tasks may help to bridge the gap in understanding between the chromosomal abnormality and the possible facial emotion recognition difficulty. Such methods could also aid disentanglement of facial emotion
processing from linguistic and other cognitive demands, which is difficult in the behavioural tasks used to date. It is also implicit, non-linguistic aspects of facial emotion processing in which facial emotion processing atypicalities are most reliably found in people with ASD (Harms et al., 2010), and thus understanding of such aspects in Down’s Syndrome could illuminate the connection between the two disorders.

Fragile X Syndrome research is more developed than research into Down’s Syndrome in its relationship with ASD and in the breadth of methods used to study facial emotion processing. The links between genetic mutation and the manner in which facial emotion is processed in the brain, between the genetic mutation and ASD symptomatology, and between facial emotion processing and ASD symptomatology have received some research attention. Still, many questions remain. How do autonomic responses and/or emotion-regulation atypicalities relate to specific emotions? How do these autonomic response differences relate to those found in idiopathic ASD? What do brain activation correlations with ASD symptoms during facial emotion processing in Fragile X Syndrome represent? While people with Fragile X Syndrome may not have specific problems recognising and labelling basic facial expressions (happiness, sadness, disgust, fear, surprise and anger) from static photographs, do they have more difficulty with more subtle or ambiguous facial emotions, using more complex, partially occluded, briefly presented or otherwise ecologically valid facial stimuli, which could contribute to an ASD presentation?

Experimental investigation of the social cognitive correlates of genetic neurodevelopmental syndromes is, in many cases, still in its early stages. The possible relationship of social cognitive skills such as facial emotion recognition to diagnoses of ASD in syndrome groups remains largely unclear. However, research trends may indicate that the elucidation of links
between specific genetic syndromes, social cognitive phenotypes and behaviourally-defined categories such as ASD will continue in coming years.

References


the official publication of the International Society of Psychiatric Genetics, 144B(1), 87–94.


Processing of facial threat emotions after acquired brain injury: a structural neuroimaging study.

Abstract

Fear, anger or disgust in the face of another person all alert the observer to the presence of some form of possible threat. There is currently no consensus on whether these emotions are represented categorically (e.g., Ekman, 1972) or dimensionally (e.g., Russell, 1980). Categorical models predict dissociable neural substrates in the brain, whilst dimensional models predict that the three threat emotions are processed by similar neural circuitry. This study assessed the ability of 26 chronic neurological patients with anatomically diverse, stable brain lesions, to recognise fear, anger and disgust in pictures of emotional faces (Ekman & Friesen, 1976), and compared their performance with 29 healthy age-matched individuals. The patient group performed significantly worse on all three emotions. For the 26 patients, we then used voxel-based morphometry (VBM) (Ashburner & Friston, 2000) to assess in an unbiased fashion the relationship between accuracy of recognition of fear, anger and disgust (individually and then together) and the integrity of grey matter across the whole brain. We found evidence to support both categorical and dimensional hypotheses of emotion representation: some brain areas were associated specifically with recognition of anger, fear or disgust, and some were associated with accuracy of recognition on all three emotions. Our data may present issues for any position maintaining that emotions are represented entirely categorically, or entirely dimensionally, within the brain.
Introduction

Discerning fear, anger or disgust in the face of another person alerts one to the presence of a threat, and the ability to detect facial displays of these emotions is crucial both to normal social interaction and to responding appropriately to the environment. Whilst they are all broadly associated with threat, these three emotions are linked with different triggers and responses. Disgust may be triggered by a potential source of contamination and can activate reflexes, such as gagging (e.g., Koerner & Antony, 2010), associated with avoidance of pathogens (e.g., Curtis, De Barra, & Aunger, 2011; Ekman & Cordaro, 2011). Fear occurs as a response to potential physical or psychological harm and may activate impulses to freeze or flee (e.g., Ekman & Cordaro, 2011). Anger can be stimulated by, for example, obstruction to goal attainment or someone else’s attempt to cause harm (Ekman & Cordaro, 2011) and may be associated with physiological changes compatible with fighting, such as increased blood flow to the arms (Levenson, Ekman, & Friesen, 1990). Thus, observing facial displays of fear, anger or disgust in another person can provide a rich source of information about the mental state of the other, and about the presence of, and forms of, threat in the environment. There may be common neural substrates for processing facial emotion in other people and the self (e.g., Goldman & Sripada, 2005), so (for example) processing the disgusted expression on a friend’s face may activate similar mechanisms to those involved in feeling disgust, and producing the facial expression, oneself (e.g., Wicker et al., 2003).

Despite extensive study over several decades, questions remain about the relationship of the three “threat” emotions (and others) to one another. There is an ongoing debate about whether the emotions displayed on faces (and, indeed, emotions more generally) represent discrete categories (e.g. Ekman et al., 1971) or points along continuous dimensions (e.g., Russell 1980). The categorical hypothesis of emotion representation suggests that fear, anger
and disgust comprise three of a set of six “basic”, qualitatively distinct emotions (e.g., Ekman, 1971; Izard, 1977; Ekman, 1992) – anger, disgust, fear, happiness, sadness and surprise. It is postulated that each of the basic emotions not only has its own evolutionary history and physiology, but corresponds to a relatively specific facial configuration, perceived reliably and similarly across cultures (e.g., Ekman, 1973; Ekman, 1992).

Conversely, the two-dimensional hypothesis (e.g., Schlosberg, 1954; Russell, 1980; Russell, 2003) postulates no qualitative distinction between emotion categories, instead advocating that specific emotional states fall at specific points in a continuous emotional space defined by two orthogonal dimensions: i) valence, the subjective experience of the affect, which varies in its pleasantness, and ii) arousal, the degree to which an emotion is calm or excitatory (Russell, 1980; 2003). Whilst the emotional states linked with labels of fear, anger and disgust are all negative in valence and associated with relatively high arousal, there are differences, such as that lower arousal may be associated with disgust than with fear or anger (e.g., Adolphs, Russell, & Tranel, 1999). Differences in arousal and valence associated with different emotional states may be consistent with, for instance, autonomic arousal differences on viewing faces displaying different emotions (Johnsen, Thayer, & Hugdahl, 1995).

The discrete category and two-dimensional models are associated with different predictions on the localization of emotional processing in the brain. The discrete category hypothesis predicts a qualitative neural dissociation across emotions, with different brain areas associated with different emotional categories. On the other hand, the bi-dimensional account of emotions predicts that similar brain regions will be involved in processing all emotional states, with quantitative differences across emotions. Neuropsychological (as well as neuroimaging) data have to date provided inconclusive evidence to distinguish between these hypotheses. Whilst certain brain regions have been shown consistently to be involved in
emotional processing, their emotional specificity is debated. The amygdala, insula and basal ganglia, as well as areas of frontal and parietal cortex, are among the brain regions which have consistently been linked to the processing of facial anger, disgust or fear. However, whilst in some studies each of these regions has been associated specifically with impairment in the recognition of one or another of the threat emotions, other findings indicate a more general involvement in facial emotion processing. Below, this evidence is discussed with reference to a few key brain regions.

**Amygdala: fear, anger, valence or arousal?**

Patients with bilateral amygdala damage have been found to have relatively specific difficulty in recognising fear (e.g., Adolphs, Tranel, Damasio, & Damasio, 1994; although see Adolphs, Tranel, et al., 1999). Such specific lesion-expression mappings may be taken to support a categorical representation of emotions at the level of brain function, and the role of the amygdala in the processing of fear has been emphasised over the years (e.g., LeDoux, 2003). However, the picture is not simple: some patients with similar lesions have also been found to have deficits in the ability to recognise other facial emotions, including anger (Graham, Devinsky, & Labar, 2007), although this is inconsistent across patients (Adolphs, Tranel, Damasio, & Damasio, 1994; Calder, 1996). Neuroimaging data are also mixed with respect to the specificity of the amygdala’s involvement. A meta-analysis of 105 fMRI papers (Fusar-Poli et al., 2009) confirmed greater sensitivity in the amygdala for fear than for other of the basic facial emotions. However, the authors also note its significant activation during presentation of other emotions, and some neuroimaging data directly suggest a role for the amygdala in processing the valence dimension (e.g., Todorov & Engell, 2008) or the arousal dimension (Lewis, Critchley, Rotshtein, & Dolan, 2007; Rotshtein, Malach, Hadar, Graif, & Hendler, 2001). For Lane et al. (1997), the amygdala forms a part of an emotion processing circuit.
(including various other cortical and subcortical areas) which represents the pleasure dimension of an emotion, with activity in different parts of this circuit said to differ for pleasant and unpleasant emotions. Others (e.g., Adolphs, Russell, & Tranel, 1999) attribute a role to the amygdala for assessing the level of emotional arousal in facial (and other) stimuli. Overall, then, both neuropsychological and neuroimaging data provide mixed support for both the two-dimensional and categorical models of emotion processing with respect to the function of the amygdala.

Insula and Basal Ganglia: disgust, anger, arousal?

Calder, Keane, Manes, Antoun, & Young (2000) describe a patient with lesions to the insula and to the basal ganglia with selective deficits in facial disgust recognition, and patients with early Huntingdon’s Disease (HD) – a genetic neurodegenerative condition in which severe basal ganglia degeneration is prominent – have also been found to have particularly impaired recognition of disgust stimuli (Montagne et al., 2006; Sprengelmeyer et al., 1996; Wang, Hoosain, Yang, Meng, & Wang, 2003). Hennenlotter et al (2004) conducted an fMRI study of the processing of emotional stimuli in a group of pre-manifest HD mutation carriers and found reduced activation of the insula and basal ganglia during presentation of disgust stimuli. Under a categorical view of emotion representations, these results may suggest that disgust, as a distinct emotional category (Ekman, 1971), could specifically be subserved by regions of insular cortex and basal ganglia. However, again the evidence is inconsistent. Milders, Crawford, Lamb, & Simpson (2003) did not find impaired disgust recognition in their HD group, instead reporting relatively worse performance for fear stimuli. In addition, Calder, Keane, Lawrence, & Manes (2004) report specific impairment of anger recognition after damage to the ventral striatum, suggesting that this area may specifically subserve anger. Henley et al. (2008) found that reduced striatal volume in people with early and premanifest HD was associated
with impairments in the recognition of disgust, but also of anger, fear and surprise. Johnson et al. (2007) found that recognition of all negative emotions was impaired in people with the HD mutation (potentially more in line with dimensional views of emotion), although this was not related to striatal volume. Some lesion data also directly implicate the insula into dimensional accounts of emotion. Berntson et al. (2011) found that people with lesions to the insula showed attenuated valence ratings of emotional pictures, as well as reporting reduced arousal to both pleasant and unpleasant stimuli.

Neuroimaging data in normal subjects are also mixed. One meta-analysis of 105 studies suggested greatest insula sensitivity for disgust, but also activation in response to anger (Fusar-Poli et al., 2009). Wager, Phan, Liberzon, & Taylor's (2003) meta-analysis of 65 studies indicated a role for the insula in processing the valence of emotions, and some (e.g., Critchley, Corfield, Chandler, Mathias, & Dolan, 2000) have found the insula to be implicated in arousal. For the basal ganglia, a meta-analysis (of 55 fMRI and positron emission tomography (PET) studies; Phan, Wager, Taylor, & Liberzon, 2002) indicated a particular relationship with disgust processing, but also that areas such as the putamen were involved in processing facial emotion more generally. Thus, as for the amygdala, the emotional specificity of both the basal ganglia and the insula with respect to the threat emotions remains unclear.

**Frontal, parietal and temporal cortical regions – categorical or dimensional?**

Several studies have also indicated that disruption to certain frontal and prefrontal regions can be differentially involved in impairment of the detection of different emotional states. For instance, Marinkovic, Trebon, Chauvel, & Halgren (2000) found relatively specific impairments in fear recognition following surgical resection of right prefrontal cortex. Harmer, Thilo, Rothwell, & Goodwin (2001) found that disruption of medial frontal cortex using transcranial magnetic stimulation increased reaction times when identifying morphs of angry, but not
happy, facial expressions (although other threat emotions were not assessed). However, various frontal and prefrontal regions are also thought to have a more general role in emotion processing, including facial emotion recognition (e.g., Fusar-Poli et al., 2009, for a meta-analysis of fMRI data), and some data from brain damaged patients support this. For instance, Keane, Calder, Hodges & Young (2002) report a general impairment in the recognition of emotion in faces and voices in patients with frontal variant frontotemporal dementia. Heberlein, Padon, Gillihan, Farah & Fellows (2008) found that lesions to ventromedial frontal cortex generally impaired facial emotion recognition, which may suggest that these regions represent general aspects of emotion, such as their dimensional properties.

Other cortical regions to which damage has been empirically associated with reduced overall ability to recognise facial emotions include an area of sensory cortex within the frontoparietal cortex (Adolphs, Damasio, Tranel, Cooper, & Damasio, 2000). It has been proposed that observation of emotional states in others activates similar neural circuitry to that when the emotion is experienced by the self (e.g., Wicker et al., 2003), and also that responding to others’ expressions involves activation of the motor programs one would use to produce that expression oneself (Preston & de Waal, 2003). The parietal regions in Adolphs et al.’s (2000) study are thought to be involved in the correspondence between movements in self and other (Iacoboni et al., 1999). Whilst this account perhaps fits most obviously with categorical accounts (with specific categories of emotion corresponding to specific motor programs), it may also be compatible with dimensional accounts, assuming that specific points in a dimensional emotion space correspond in some predictable way with sensorimotor representations.

Finally, areas such as the superior temporal sulcus (STS), are known to respond to changeable aspects of faces, such as facial expressions (e.g., Andrews & Ewbank, 2004). The relationship of
this area with specific facial emotions may be complex, with elements of both categorical and graded representations (e.g., Said, Moore, Norman, Haxby, & Todorov, 2010).

In summary, brain lesion data as well as data from neuroimaging studies, are mixed with respect to the degree of overlap between the processing of (facial) anger, disgust and fear they suggest at a neural level. There is therefore no consensus on whether they support a categorical or dimensional notion of emotion representation in the brain. Many of the lesion studies described above rely on individual patients, or series of patients, selected on the basis of their specific cognitive or emotional deficit, or the anatomical location of their lesions, which makes it difficult to draw more general conclusions. Adolphs et al. (2000) used a technique whereby the visible lesion on each patient’s MRI or CT scan was transferred to a reference brain, and lesions were summed for groups of patients defined by a median split of their overall emotion recognition accuracy. Whilst this study has the advantage of assessing the importance of specific brain areas over a large number of brain-damaged patients with various different types of lesion, it, like many of the other lesion studies previously mentioned, relies on visual delineation of lesions and on a lesion overlap method. It is primarily a descriptive technique which is not statistically based. This also has the disadvantage of not taking into account areas of brain damage not immediately obvious to the naked eye, and/or not part of the perceived “main” lesion of a patient.

A more objective assessment of structure-function mapping can be achieved by use of Voxel-Based Morphometry (VBM) (e.g., Ashburner & Friston, 2000), which was employed in Henley et al.’s, (2008) study of HD. VBM provides an unbiased and comprehensive method of relating differences in behavioural variables to structural brain variation (which may or may not be visible to the naked eye). In essence, for a series of participants’ brain images, each voxel in each brain is assigned (based on scanning data) a value representing the probability that it
represents intact tissue. Behavioural data is obtained for each participant. Then a separate multiple regression is computed for each voxel of the brain to assess the correlation of a specific behavioural measure (e.g., emotion recognition accuracy) with the integrity of the brain tissue in that voxel. Thus, if damage to a specific brain area affects performance on a specific task, a significant association with performance may be expected in the corresponding voxels, whereas if damage in that area does not affect this task, there would be no association.

In Henley et al.’s (2008) paper, regions of interest in the striatum and insula were specified based on the known common neural correlates of HD, but VBM may also be used to assess the whole brain in groups of participants with more varying lesions (e.g., Leff et al., 2009; Chechlacz et al., 2010; Sui, Chechlacz, & Humphreys, 2012; Demeyere, Rotshtein, & Humphreys, 2012).

Our aim in this study was to assess the recognition of the three commonly researched basic “threat” emotions – anger, disgust and fear – in a group of patients with anatomically diverse brain damage, and to relate brain lesions to emotion recognition deficits in an unbiased fashion across the whole brain. In doing so we hoped to clarify the degree to which the lesions causing impairments in the recognition of fear, anger and disgust are overlapping and the degree to which they are distinct. Fear, anger and disgust have been the subject of many studies of facial emotion recognition impairment in brain-damaged patients. These three emotions are also generally placed in similar gross regions of commonly-discussed emotional dimensions – each is unpleasant (negative in valence) and is associated with relatively high arousal. Thus a dimensional model (Lane, 1997; Russell, 1980) (even one in which there is a distinction between the brain areas subserving positive and negative emotions) might predict a high degree of overlap between these three emotions with respect to the regions of the brain.
in which damage is correlated with impaired facial emotion recognition. A categorical account of emotion representation may emphasise distinct brain regions for anger, disgust and fear.

We assessed the ability of a group of 26 chronic neurological patients with anatomically varied, stable brain lesions to recognise facial displays of fear, anger and disgust. Two different experiments were used to assess emotion recognition accuracy, one using static and another using dynamic (moving) facial stimuli. To characterise the overall nature of impairments in the recognition of these three emotions, we compared the accuracy of the 26 patients with that of a group of 29 neurologically intact control participants. We then used Voxel-Based Morphometry (VBM) to conduct a whole-brain assessment of the relationship between brain structure and emotion recognition.

**Behavioural experiments**

**Method**

**Participants**

Twenty-six participants in the patient group (mean age 65.0 years, s.d. 12.9 years, 3 females) were recruited from the long-term panel of neuropsychological volunteers established by the Behavioural Brain Sciences Group and the Birmingham University Cognitive Screen (BUCS, www.bucs.bham.ac.uk) at the School of Psychology, University of Birmingham. Inclusion criteria were that a) the patients had acquired brain damage (various aetiologies, e.g. stroke, carbon monoxide poisoning) and were not in an acute stage (> 12 months post injury), and (b) the patient had a T1 weighted 3T MRI scan. Each participant provided informed consent according to the procedures in agreement with ethics protocols at the School of Psychology and Birmingham University Imaging Centre (BUIC). Twenty-nine healthy control participants
were also recruited (mean age 66.8 years, s.d. 11.4 years, 9 females) by local advertisement. Participants were reimbursed for their time. There was no significant difference between the mean ages of the two groups (t(52) = 0.54; p > 0.1).

**Stimuli, Design and Procedure**

Two facial affect recognition tasks – a “static” task and a “dynamic” task – were used. This was in order to minimise the impact of specific procedural factors. In the patient group, data from the dynamic task were available for 25 participants and data from the static task were available for 23 participants.

In the control group, 22 participants completed the static task and 15 participants completed the dynamic task, with 8 participants completing both tasks.

Participants completed the different tasks in an order independently randomly determined for each participant.

**Dynamic task**

The stimuli and the experimental procedure were adapted from Calder, Young, Rowland, & Perrett (1997) and Phillips et al. (1998).

**Stimuli**

Stimuli were derived from Ekman & Friesen’s (1976) series (Figures 1 and 2). A trial in the dynamic task involved watching a face transform from 100% neutral through 18 morphed intermediate stages (e.g., 90% neutral, 10% expression) to 100% expression over the course of 2 seconds. This resulted in an animation appearing to show an initially expressionless person adopt an emotional expression. Nine facial identities (five female) were used in the experiment proper, with each identity posing two different expressions. An extra identity was used for the
practice trials, posing all six expressions. Models’ hair and background details were masked with grey (see Figure 1).

Each face subtended an approximate visual angle of between 7.7 and 9.4 degrees in the vertical plane and between 4.8 and 6.6 degrees horizontally.

Design and procedure
Each participant completed six practice trials (one for each expression) and thirty-six experimental trials (six for each expression). The experimenter ensured apparent understanding of the task before proceeding from practice to experimental trials. Experimental trials were split into two blocks of eighteen. The stimuli were presented in a pseudo-random order. At the start of each trial, a face with a neutral expression was displayed. The experimenter then pressed the space bar to animate the face, at which point its expression moved from 100% neutral through 18 intermediate images to 100% expression over the course of 2 seconds. The image of the face displaying the full emotional expression then remained on the screen until a response was made. On the left of the experiment window were six “buttons” arranged in a column, each with an emotion word on it: from top to bottom, anger, disgust, happiness, sadness, surprise and fear. When the animation as complete, the experimenter read the six possible response options to the participant, after which the participant gave a verbal response to indicate his or her chosen expression label, or pointed to the chosen label. The experimenter gave the corresponding response by clicking the left mouse button over the button with the chosen label. Once this was complete, the next trial was initiated by the experimenter when the participant was ready.
Figure 2. Example of beginning (a, 100% neutral), end (e, 100% angry) and 3 intermediate (b, c, d) pictures used to create animations of facial expressions in dynamic task. An actual trial involves 18 intermediate consecutive pictures (20 total), one replacing the other, over the course of 1.5 seconds.

Example of each of six “basic” facial expression stimuli (Ekman & Friesen, 1976). Clockwise from top left: fear, anger, disgust, happiness, surprise, sadness.
Static Task

Stimuli

The static task was also a simple categorisation of prototypical, 100% (Ekman and Friesen, 1976) facial expressions (Figure 1). Faces of ten identities (six female) each posed six basic facial expressions. Faces were presented on a grey background with outline features cropped. Each stimulus subtended an approximate visual angle of 10.5 degrees in the vertical plane and 7.5 degrees horizontally.

Procedure

There were 60 trials. The stimulus for each trial was selected pseudorandomly, and there was no time limit for a response. At the start of the experiment, basic instructions appeared on the screen, which were also read aloud by the experimenter. The experimenter ensured apparent comprehension of the experiment before proceeding.

Each emotion name was assigned (randomly, for each participant) a number from 1 to 6. These assignments were displayed across the bottom of the screen on each trial in white writing (e.g., 1 = fearful, 2 = sad, etc.). Participants were instructed to press the number, on a keyboard, of the expression that best described the image. The experimenter ensured understanding of the correspondences and read out the possible responses when appropriate. Also where appropriate, due to motor or other disabilities, the participant instead indicated to the experimenter the number or the expression they wished to select and the experimenter pressed the indicated key (approx. 9 participants). After a response was given, there was a 250ms interval before the commencement of the next trial. No feedback was given.
Results

Correct responses were scored 1 and incorrect responses scored 0. Hence, the score expected by chance is approximately 0.17 (1/6) in both tasks. Figure 3 shows the accuracy for each of the three threat emotions across the two tasks in the patient and control groups.

For participants who had completed both tasks (22 patients and 8 controls), an ANOVA was conducted with accuracy as the dependent variable, task (2 levels: static and dynamic) and emotion (3 levels: fear, anger, disgust) as within-subject independent variables, and participant type (2 levels: patient and control) as between-subject independent variable. Where necessary, Huynh-Feldt corrections for non-sphericity were used (Howell, 2002). There was a significant overall effect of emotion, $F(2, 56) = 5.42, p < 0.01$. Accuracy for fear (mean 0.48, s.d. 0.25) was significantly lower than that for anger (mean 0.63, s.d.0.22) and disgust (mean 0.64, s.d. 0.28) ($t(29) = 3.48; p < 0.01; t(29) = 3.06, p < 0.01$). Accuracy for anger and disgust did not differ significantly from each other ($p > 0.8$). There was also a significant effect of participant type, $F(1, 28) = 14.25, p = 0.01$, with greater accuracy in the control group (mean 0.77, s.d. 0.08) than the patient group (mean 0.51, s.d. 0.14). However, there was no main effect of task type, although there was a trend for higher mean accuracy in the dynamic than the static task, $F(1, 28) = 2.84, p = 0.10$. No two- or three-way interaction reached significance (max $F < 0.3$).

Overall, patients performed more poorly than controls, but this did not interact with emotion. Fear was more difficult to identify than the other two emotions, for both patients and controls.

Analyses were also separately conducted for the static and dynamic tasks in order that data from the full sample (i.e., not just those who had completed both tasks) could be analysed. In each task, there was a significant effect of emotion (static task $F(2, 86) = 4.96; p < 0.01$;
dynamic task $F(2, 76) = 7.80$, $p < 0.01$) and a significant effect of participant type (static task $F(1, 43) = 18.51$, $p < 0.001$; dynamic task $F(1, 36) = 13.55$, $p < 0.001$), and in neither task was there a significant interaction between emotion and participant type (both tasks $F < 1$). In each task, fear was recognised significantly less accurately than each of the other two emotions (static task fear vs. anger, $t(44) = 2.04$, $p < 0.05$; static task fear vs. disgust, $t(44) = 3.15$, $p < 0.01$. Dynamic task fear vs. anger, $t(39) = 4.01$, $p < 0.001$; dynamic task fear vs. disgust, $t(39) = 3.07$, $p < 0.01$). Accuracy for anger and disgust did not differ significantly from each other in either task (static task $t(44) = 0.91$, dynamic task $t(39) = 0.31$).

These analyses for the two tasks separately thus confirm an effect of emotion (with fear being less easily recognised than anger or disgust), and of participant type (with patients having lower accuracy than controls), but no interaction between the two. They also confirm that a similar pattern of results is found for both the static and dynamic tasks.

**Discussion**

The group of participants with brain damage performed significantly more poorly than the healthy age-matched controls in their identification of anger, disgust and fear in facial stimuli. However, there was no evidence that any one of the three threat emotions was any more affected by brain damage than any other. In one sense this is not a surprising finding given the relatively diverse nature of brain lesions in the patient group. Fear was the emotion which was least accurately identified, with no significant difference between anger and disgust. This is broadly commensurate with previous literature (e.g., Rapcsak et al., 2000).

The pattern of results was the same for the static and dynamic tasks, although there was a non-significant trend for higher accuracy in the dynamic task. Because there were other procedural and presentational differences between the static and dynamic tasks (e.g.,
presentation of response options on the screen, appearance of experiment window, length of experiment), it is not possible to directly assess the impact of using moving as opposed to stationary stimuli. However, there was no indication in our data that the moving or static pictures had a differential effect on the different groups of participants, or on the recognition of different emotions.

**Voxel-Based Morphometry (VBM)**

In this study, we used VBM to assess the statistical relationship between brain structure and recognition accuracy for anger, fear and disgust in the 26 patients.

**Methods**

**Behavioural Data**

*Emotion recognition accuracy*

There was no evidence in the behavioural data (above) that the task type (static or dynamic) interacted with the specific emotion (anger, fear or disgust), and thus for the VBM we combined data for the static and dynamic tasks. Although the means for the static and dynamic tasks did not significantly differ, there was a non-significant trend \( p = 0.10 \) for greater accuracy in the dynamic task. Therefore, before combining the two sets of scores, we converted them to standard scores \( (Z \text{ scores}) \) based on the mean and standard deviation of the data from the control participants (see Table 1). Thus each patient’s \( Z \) score represented the number of standard deviations from the control’s group mean, averaged across the static and dynamic tasks. Where data were missing for either task (4 participants), the score from the other task was used. To ensure that this treatment of missing data was not biasing the results,
we repeated the analyses substituting group means for missing values. This did not notably affect the findings.

<table>
<thead>
<tr>
<th>Task</th>
<th>Control group Mean</th>
<th>Control group Standard Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anger Static</td>
<td>0.68</td>
<td>0.21</td>
</tr>
<tr>
<td>Disgust Static</td>
<td>0.76</td>
<td>0.19</td>
</tr>
<tr>
<td>Fear Static</td>
<td>0.61</td>
<td>0.30</td>
</tr>
<tr>
<td>Anger Dynamic</td>
<td>0.88</td>
<td>0.18</td>
</tr>
<tr>
<td>Disgust Dynamic</td>
<td>0.86</td>
<td>0.21</td>
</tr>
<tr>
<td>Fear Dynamic</td>
<td>0.65</td>
<td>0.33</td>
</tr>
</tbody>
</table>

Table 1. Mean and standard deviation of scores for control group, for calculation of Z scores.

Covariates

The score from a picture naming task from the Birmingham University Cognitive Screen (Humphreys et al., 2012, www.bcos.bham.ac.uk) was included as a covariate. In this task, patients were presented with 14 line drawings of everyday objects, such as an umbrella and bunch of grapes. Each drawing is on a separate piece of paper and the patient has up to fifteen seconds to name it. For analysis we used the number of correct responses (from 0 to 14) for each participant. The mean score on this measure was 8.9 (s.d. 4.6). Score on this picture naming measure did not correlate significantly with any of the emotion accuracies individually or as a mean, or with any of the Z scores for the analysis.

This covariate was included to partially account for the influence of less specific perceptual difficulties in participants.

Age, gender and handedness were also included as covariates in the analysis.
Brain imaging data

Scanning took place at Birmingham University Imaging Centre, using a 3T Philips Achieva MRI system with 8-channel phased array SENSE head coil. A T1-weighted sequence (sagittal orientation, TE/TR= 3.8/8.4ms, voxel size 1x1x1mm) was used to acquire anatomical scans. Scanning time was 5 minutes. We used SPM software (www.fil.ion.ucl.ac.uk/~spm) to analyse the images and the relationship between imaging and behavioural data.

Image pre-processing

Procedures for image pre-processing are as used by Chechalcz et al. (2010) and Sui, Chechłacz & Humphreys (2012).

MRICro (Chris Rorder, Georgia Tech, Atlanta, GA, USA) was first used to convert and reorient T1 scans from the 26 patients. SPM8 (Statistical Parametric Mapping, Welcome Department of Cognitive Neurology, London UK) was used to process the T1 scans. Scans were transformed to standard MNI space by use of the unified-segmentation procedure (Ashburner & Friston, 2005) as adapted by Seghier et al.(2008). This modified segmentation procedure was used to aid spatial normalisation and tissue classification in lesioned brains, by adding an extra tissue class accounting for abnormal tissue (Seghier et al., 2008). The resultant grey matter and white matter probability maps were smoothed with 12mm FWHM Gausian filter (necessary due to the assumption of random field theory used for reliability tests, Worsley, 2003). Each image was visually inspected to assess whether the segmentation and normalisation procedures were successful. The grey matter maps were then used to carry out a voxel-by-voxel analysis of the relationship between brain damage and our measures of emotion-labelling ability (see below).
For descriptive proposes we created an overlap map that represents the distribution of lesions across the entire patients sample. For each patient a binary map was computed, representing the acquired lesion area, following the procedure specified by Seghier et al. (2008). These binary maps were summed using SPM to produce a lesion overlap map (Figure 4).

**VBM analyses**

Function-lesion mapping was computed using grey matter maps derived from the pre-processed scans of the 26 patients. For each participant, each brain voxel has been assigned a number between 0 and 1 representing the probability it is composed of intact grey matter (see above). Each participant also has accuracy scores between 0 and 1 for emotion recognition (see below). For each voxel, we asked whether a given accuracy score is a significant predictor of the probability that the voxel is composed of intact grey matter. We report results based on a combination of peak height and cluster size (Poline, Worsley, Evans, & Friston, 1997), considering reliable clusters larger than 60 voxels (480mm$^3$), in which every voxel showed a reliable effect of $Z > 2.86$ ($p < 0.005$). A VBM analysis was conducted including accuracy for anger, disgust and fear, as well as age, gender, handedness and Picture Naming score (see above) as covariates.

Within this analysis, different sets of contrasts were performed. First, to assess for dissociative neural correlates, the contributions of each emotion within the model were assessed. Clusters of voxels are reported in which each emotion makes a statistically significant contribution to predictions of tissue integrity (e.g., for fear, contrast weights (1,0,0) for (fear> 0, anger, disgust)). These analyses detect areas in which there is a reliable correlation between accuracy (for a given emotion) and tissue integrity. Subsequently, we used exclusive masking to test whether the observed correlations were specific for the assessed emotion and were not
observed with the other two, using an interaction contrast (e.g., for fear, interaction contrast mask weights \( (1,-0.5,-0.5) \) for \( (\text{fear} > (\text{anger} + \text{disgust})) \)). The interaction contrast used for the mask was thresholded at \( p < 0.05 \), as accustomed in SPM. These contrast analyses detect areas in which the lesion-behaviour correlation (for a given emotion) differs significantly from 0 and this effect is also significantly greater than for the other two emotions.

To test for common neural correlates across all three expressions, a contrast was also performed (“overall analysis”, contrast weights \( (1,1,1) \) for the three emotions) to assess the combined contribution of anger, disgust and fear accuracies in the prediction of voxel status.

Anatomical labels for clusters were obtained using the SPM Anatomy Toolbox (www.fil.ion.ucl.ac.uk/~spm).

**Results**

**Lesion overlap map (Figure 4)**

This demonstrates the spread and the location of the acquired lesions in the sample of neurological patients. Overall, the lesions covered all regions of particular interest excluding the medial part and the most anterior parts of the frontal cortex. The population did not include acquired lesions in the most superior parts of the brain. Finally, lesions appear more frequent in the right than in the left hemisphere (brighter colours).
Figure 3. Accuracy of recognition of threat emotions on static (top) and dynamic (bottom) tasks for patients and controls.
Figure 4. Lesion overlap map. Brighter colours indicate more patients with a lesion to that area. Coronal slices through the brain at $Z = -35, -15, 5, 25, 45$ and $65$. 
Evidence for the discrete categorical models of Emotions

Figures 5 to 7 show the areas correlated with (respectively) accuracy for disgusted, fearful and angry faces, both before and after contrast masking. For each area specifically associated with an emotion (after contrast masking), the beta value for the three emotions is plotted, with 95% confidence intervals. Essentially, if the 95% confidence interval for an emotion falls entirely above 0, accuracy on the emotion makes a significant contribution to prediction of grey matter integrity at this location.

Disgust

Reduced accuracy in recognition of disgust was associated with damage to an area extending over parts of the right middle orbital gyrus, the right middle frontal gyrus and the right inferior frontal gyrus (p. orbitalis), into the right anterior insula (619 voxels; peak coordinates 38, 44, -14; Z = 3.12) (see Figure 5a).

After contrasting out the effects of the other two emotions, it was found that a portion of this cluster (Figure 5b) in the right middle orbital gyrus and right inferior frontal gyrus (p. orbitalis) was uniquely associated with accuracy of disgust recognition (201 voxels; coordinates at peak 33, 44, -14; Z = 3.12).

Fear

Damage to three areas was associated with accuracy of fear recognition. This included the left thalamus (79 voxels; coordinates at peak -10, -20, 4; Z = 2.96), the left paracentral lobule extending into the left supplementary motor area (SMA) (200 voxels; coordinates at peak -8, -28, 66; Z = 2.99), and the right middle cingulate cortex extending into right supplementary motor area (SMA) (65 voxels; peak coordinates 14, -14, 46; Z = 3.01). These areas are displayed in Figure 6.
Each of these three clusters was uniquely associated with reduced accuracy in fear perception, remaining unchanged after partialling out the effects of accuracy on the other two emotions.

**Anger**

Lesions involving a region in the left inferior temporal gyrus (139 voxels; coordinates at peak -50, -16, -36; $Z = 3.03$), superior and middle frontal gyri (95 voxels; coordinates at peak 48, 28, 46; $Z = 3.39$) and the middle frontal gyrus (73 voxels; coordinates at peak 24, 60, 34; $Z = 3.03$) were associated with reduced accuracy in recognition of anger (Figure 7).

After accounting for (contrasting out) the effects of accuracy on the other two emotions, it was found that the lesion in the right superior and middle frontal gyri (73 voxels; coordinates at peak 24, 60, 34; $Z = 3.03$) was specifically associated with accuracy for recognition of anger expression.

**Overall**

To test for common effects across the three expressions, the main effect of accuracy on tissue integrity was computed. Two brain regions were associated with the combined accuracies for fear, anger and disgust. These regions were in the left inferior temporal gyrus (280 voxels; coordinates at peak -34, -8, -40; $Z = 3.41$), and the superior right frontal gyrus (95 voxels; coordinates at peak 50, 24, 48; $Z = 3.57$). Thus lesions affecting these regions led to overall reduced ability in accurately inferring threat expressions from a face (Figure 8).
Figure 5a and 5b. Areas correlated with accuracy for disgust (a) and after specifically contrasting out the effects of fear and anger (b).

Figure 5c. Beta for different emotions at peak of right orbitofrontal “blob” (b) (38, 44, -14) associated specifically with disgust. Red bars indicate 95% confidence intervals.
Figure 6a, 6b, 6c. Areas correlated with accuracy for fear (unchanged by contrast masking to partial out other two emotions).

a. Area in left paracentral lobule and SMA
b. Area in left thalamus (part of blob a. also visible)
c. Area in right cingulate cortex.
Figure 6d. Beta for different emotions at peak of left paracentral lobule/SMA “blob” (-8, -28, 66) associated specifically with fear. Red bars indicate 95% confidence intervals.

Figure 6e (above). Beta for different emotions at peak of left thalamus “blob” (-10, -20, 4) associated specifically with fear. Red bars indicate 95% confidence intervals.

Figure 6f. Beta for different emotions at peak of right cingulate “blob” (14, -14, 46) associated specifically with fear. Red bars indicate 95% confidence intervals.
Figure 7 a, b and c. Areas whose integrity correlates with accuracy of anger recognition. Blob b also specifically associated with accuracy for anger after contrasting out the effects of other emotions. Figure 7d. Beta (predictive contribution) for different emotions at peak of right frontal “blob” (b) (24, 60, 34) associated specifically with anger. Red bars indicate 95% confidence intervals.
Figure 8. 8a & 8b. Areas associated with overall accuracy on all three emotions. Figure 8c. Beta for different emotions at peak of left temporal “blob” (-34, -8, 40) associated with overall accuracy. Figure 8d. Beta for different emotions at peak of right frontal “blob” (50, 24, 48) associated with overall accuracy. Red bars indicate 95% confidence intervals.
General Discussion

Our data indicate that participants with brain damage of diverse anatomical locations (Figure 4) performed more poorly than age-matched healthy controls in their recognition of facial anger, disgust and fear. There was no evidence that any of the three emotions was disproportionately impaired in the patient group, with a similar pattern of accuracy displayed across patients and controls. This may be related to the diversity of the lesions within the patients’ brains.

The VBM analysis suggested that, within our sample of brain-damaged patients, distinct areas of damage were associated with reduced accuracy for anger, fear and disgust. However, there were also brain areas in which damage was associated with reduced ability across all three emotions. These findings suggest both common and unique areas which are required for identification of the different “threat” emotions, providing support for both the categorical and dimensional models of emotion processing.

Possible emotion-specific areas

For each of the three emotions, brain regions were found in which damage was associated with emotion recognition accuracy. Interestingly, there was no overlap between the regions for the three separate emotion contrasts (although some areas were found to be associated with accuracy across all three; see below). In each case, at least some areas remained significantly associated with accuracy after specifically contrasting out the effects of the other emotions. For disgust, an area of right orbital frontal cortex (Figures 5b and 5c) was specifically associated with accuracy. Regions within the left thalamus, left paracentral cortex and right cingulate
correlated specifically with the ability to detect fear (Figure 6). An area of right superior frontal
cortex correlated specifically with accuracy on anger (Figures 7c and 7d).

The location of these areas might be broadly understood in terms of previous research.

Given the frequent association in the literature of insular cortex with disgust (e.g., Calder et al.,
2000), it is interesting that we found that damage to this area was correlated with poorer
disgust recognition but there was no statistical evidence that this was specific to disgust. Only
the right orbital frontal area survived contrast masking.

Accuracy of fear recognition was specifically associated with damage to areas of possible
sensory and motor function (around the central sulcus). This is interesting in relation to the
simulation theory of emotion (see, e.g., Goldman and Sripada, 2005). Damage to similar areas
was found to associate with emotion recognition impairment in all six “basic” emotions by
Adolphs et al. (2000), who concluded that we may recognise others’ emotional states by
“internally generating somatosensory representations that simulate how the other individual
would feel when displaying a certain facial expression”. It is intriguing that we found such
lesions to specifically impair accuracy on fearful faces, which might suggest that sensory motor
representations are particularly crucial for fear recognition. Our data also suggest that damage
to cingulate cortex and the left thalamus correlated specifically with poorer fear recognition. It
has been suggested that middle cingulate cortex plays a role in processing negative emotions,
as well as pain (see Shackman et al., 2011, for a review), so it is interesting that our results
specifically implicate the region in fear processing. The thalamus – also found in our study to
be specifically linked with fear recognition – has been found to be active during emotion
processing (e.g., Petrini, Crabbe, Sheridan, & Pollick, 2011), and has an established role in
arousal generally (e.g., Schiff, 2008). Parts of the thalamus are also anatomically linked with
the amygdala and have been implicated in fear perception in neuroimaging studies (e.g., Das et al., 2005). Our data support a position in which there is a specific relationship between parts of the thalamus and the recognition of fear, rather than this region having a generically crucial role in emotion recognition.

A small area of superior right frontal cortex was specifically associated with accuracy on angry faces. Lesions to a number of areas of frontal cortex have been associated with reduced facial emotion recognition (e.g., Dal Monte et al., 2012; Keane et al., 2002), and our findings are consistent with the notion that there may be regions in which damage differentially affects recognition of anger (see also, e.g., Murphy, Nimmo-Smith, & Lawrence, 2003).

**Possible common areas**

We also found evidence of areas in which combined accuracy across all three threat emotions was significantly related to the integrity of grey matter tissue. Damage to areas of the left inferior temporal and right superior frontal cortices correlated significantly with combined accuracy for fear, anger and disgust. Whilst a similar left temporal area was also associated with anger accuracy (prior to masking out the effects of the other emotions), this disappeared after contrast masking, suggesting that the association for anger at this location was not reliably greater than for the other two emotions. The contributions of both anger and fear (although not disgust) are reliably above zero at the peak of this cluster (Figure 8c).

A similar area of right superior frontal gyrus, significant for the mean overall analysis, was also found to be correlated with accuracy for anger. However, this again did not remain after contrast masking, suggesting that the association was not significantly greater than for the other two emotions. As shown in Figure 8d, the predictive contribution of both disgust and anger (but not fear) were reliably above zero at the peak of this cluster.
Thus, there were brain areas in which damage was associated with accuracy for at least two of the three emotions. Again, the anatomical location of these areas may be broadly commensurate with certain previous research. Lesions to numerous frontal regions have been associated with impaired ability to recognise facial emotion (e.g., Keane et al., 2002). The inferior temporal cortex has long been associated with representations of visual stimuli (e.g., Gauthier et al., 1996), and the anterior temporal lobe has been thought to have a role in various emotional capacities (see, e.g., Olson, Plotzker & Ezzyat, 2007). The fusiform gyrus has a well-established link with the processing of faces, although is generally less implicated in varying aspects such as expression (e.g., Haxby, Hoffman, & Gobbini, 2000). It is interesting that our data indicate an association between left temporal lobe abnormalities and emotion recognition deficits – it has frequently been the right side which has been associated with linking higher-level visual representations (such as faces) with emotions, and the left more with semantic knowledge (e.g., Snowden, Thompson, & Neary, 2004).

Overall, the data from this study add to a position that recognition of the three “threat” emotions – anger, disgust and fear – may involve both shared and separate neural substrates. The existence of distinct areas which are specifically important to the recognition of each of these three emotions is consistent with distinct representations of these emotions in the brain. This may then support the existence of separate categories of emotion (e.g., Ekman, 1972; 1992). The areas in which damage correlates with more than one emotion challenge the discrete category model. However, a categorical account may allow for some overlap in the (also partially distinct) neural substrates. It should also be noted that the common areas in our study may correspond to any stage in the process of facial emotion recognition. Whilst we include picture naming as a covariate, to partially control for lower-level perception and higher-level linguistic processes, there may still be processing stages not accounted for in the
design which are not specific to facial emotion recognition. It is conceivable, for example, that the common areas in temporal cortex correspond to areas particularly crucial to the perception of (even non-emotional) faces (see, e.g., Haxby et al., 2003). Inclusion of non-emotional face-processing tasks (e.g., identity-based tasks) as covariates may provide a better control for these factors in future studies.

A strictly dimensional position, on the other hand, would easily account for the presence of shared areas. However, it may struggle to explain the existence of distinct regions to which damage specifically impacts on the detection of fear, anger and disgust. The degree to which our data may be consistent with a dimensional view of emotion representation is worth brief exploration. Emotions may be considered dimensional or categorical at different levels. Arguably, it does not necessarily follow that people’s behaviour being consistent with categories of emotion (e.g., categorical perception effects, Young et al., 1997) means that these categories are represented by anatomically distinct substrates. Similarly, a dimensional representation at some level may not preclude the possibility of partially distinct neural circuitry for prototypical disgust, anger and fear: there is no consensus on the manner in which psychological dimensions such as valence or arousal (e.g., Russell, 2003) may be represented neurally (although see, e.g., Adolphs et al., 1999; Anders, Lotze, Erb, Grodd, & Birbaumer, 2004; Killgore & Yurgelun-Todd, 2007). However, in addition, specific impairment of the recognition of different emotions may be possible even under a dimensional view which assumes that the same brain areas subserve perception of all emotions. If the same neural circuitry recognises all emotions, one might still expect activation differences in response to different emotions on functional brain imaging (different levels on a dimension perhaps being represented by different patterns of activation across the same brain regions) (e.g., Grimm et al., 2006). Would this allow that damage to specific regions specifically impairs perception of
different emotions (as our data suggest)? Imagine that an area crucial to the assessment of a dimension, say arousal, is removed. There might then be an impairment of the ability to assess arousal in all emotional stimuli; at its most extreme this would essentially remove the dimension from emotion descriptions, reducing the dimensionality of emotion space. It might be difficult to identify many emotions, but especially those which have close neighbours on the remaining dimension(s) (e.g., valence). Among the six linguistic categories represented by the “basic” emotions, recognition of prototypical happiness may be relatively preserved due to its relative isolation in highly positive valence. But in the absence of this area, what might be assumed by the rest of the brain? Suppose that this loss leads to a state commensurate with constantly low arousal. In this case, fear (high arousal) may be difficult to detect whereas sadness (low arousal) may be identified accurately (perhaps over-identified). Under this (hypothetical) model, it’s also possible that removal of a different area of the arousal detection circuit would lead to the dimension becoming “stuck” at a different level; high arousal, say. Then the opposite pattern may occur – fear could be more frequently correctly recognised than sadness. As discussed in the introduction, there have been suggestions that damage to different areas specifically impairs the recognition of unpleasant or pleasant emotions (e.g., Adolphs et al., 2001; Dal Monte et al., 2012). However, for a dimensional account to accommodate our data – differences in the brain regions required for the accurate identification of anger, disgust and fear (all negative in valence, and relatively high in arousal) – more fine-grained distinctions between levels on the dimensions may be required at the level of brain circuitry. For some, this may raise questions about the level at which emotion could be said to be a dimensional construct.

It is worth noting that, when using techniques such as VBM, the power to detect a region which is important to a behavioural outcome is entirely dependent on variation in voxel
integrity in this region. If there are no participants with lesions to an area (and thus no
variance in voxel values), there will be no correlations to this area, no matter how crucial to the
particular task. Within our study, whilst there is reasonable variation in lesion location, the
sample is fairly small. In addition, some of the regions highlighted by our analysis were small,
and are in need of replication. Use of a larger sample would allow more confident delineation
of which specific areas are and are not necessary for recognition of the different emotions.

Tissue integrity of certain areas which have frequently been associated with fear, anger or
disgust recognition in previous studies (e.g., the amygdala; basal ganglia; see introduction) was
not found to correlate with accuracy in the current study. Of these, perhaps the lack of
association of amygdala damage with fear (or general threat emotion) recognition (despite
lesions covering the amygdala bilaterally) is most striking. It has been found (e.g., Rotshtein et
al., 2010) that unilateral amygdala damage may not cause impairment in explicit fear
recognition, and it may be that bilateral damage is not a feature of our sample. It is, of course,
also difficult to conclude much from a null result such as this, particularly in a relatively small
sample.

Another assumption of VBM is that of a linear relationship between tissue integrity and
assessed behavioural impairment severity. Implications of this may be particularly complex in
the context of the neural representation of psychological dimensions (see above): there may
be many different (and potentially non-linear) ways in which removal of part of a “dimension”
circuit could exert effects for the different emotions. In addition, a one-to-one mapping
between lesions and functions is assumed by VBM, and it is assumed that across individuals,
similar brain structures subserve the same function. Inconsistencies between VBM results and
those found when assessing specific patients may reflect fallacies in this latter assumption.

However, the considerable advantages of VBM – that it provides a method by which to assess
structure-function correspondence in a relatively unbiased manner across a sample with diverse lesions – mean that such studies have the potential to help address the discrepancies between studies of patients in whom circumscribed lesions have been visually described. In this case, our VBM analysis adds to a position that there are statistical regularities between the anatomical distribution of brain lesions and the detection of the three facial threat emotions, and that both common and distinct regions may characterise this association. This raises questions for any position which holds that emotions are represented entirely dimensionally, or entirely categorically, in the brain.

Understanding the implications of different types of brain damage for the recognition of emotion in other people (and perhaps oneself; e.g., Goldman & Sripada, 2005) has direct applications clinically in brain injured populations. More broadly, though, the manner in which our representations of emotional states relate to one another has potential implications for our understanding of human experience.
References


The ability to recognise the emotions displayed on other people’s faces is crucial to normal social interaction. It can also provide important clues about events in the environment, such as the presence of threats. For instance, to see someone else looked scared might warn us of the approach of a dangerous animal. There are six facial expressions which are often considered “basic”, and which may be recognised similarly across cultures (e.g., Ekman, 1971; Ekman, 1973). These are anger, disgust, fear, happiness, sadness and surprise.

In certain clinical populations, the ability to process facial expression in others is compromised. For example, Harms et al. (2010) reviewed numerous papers on the ability of people with Autism Spectrum Disorders (ASD) to process facial emotions, and confirmed evidence of atypicalities. These atypicalities may relate to some of the clinical features of ASD, such as difficulties with social functioning.

In this thesis, I have considered some clinical populations in which facial emotion processing may be impaired.

In the Literature Review, I assess possible impairments in facial emotion processing in people with genetic syndromes which affect social and/or cognitive development (genetic neurodevelopmental syndromes). Specifically, I looked at the evidence for atypical facial emotion processing in genetic neurodevelopmental syndromes associated with an increased likelihood of diagnosis of ASD (e.g., Moss & Howlin, 2009). The literature review asks what is known about facial emotion processing in these syndromes, and how it might inform us about the relationship of the syndromes with ASD.
A literature search was conducted for papers empirically assessing facial emotion processing in each of the five syndromes most frequently associated with ASD in the research literature (Moss & Howlin, 2009): Fragile X Syndrome (FXS), Tuberous Sclerosis Complex, Rett Syndrome, Down Syndrome (DS) and Phenylketonuria. Of these, studies were found, and reviewed, for DS and FXS. In DS, there is evidence of possible reduced accuracy, in relation to typically developing children of matched intellectual ability, in facial emotion processing tasks (e.g., requiring people to match faces by their emotion). However, this may be subtle, and the nature of the deficit is not clear. In FXS, there is no evidence of reduced accuracy in such tasks, but studies using eye tracking, pupillometry, and functional Magnetic Resonance Imaging (fMRI) indicate atypicalities in emotion processing. Possible implications of these findings for the association of ASD in these syndromes are discussed, along with possible future research directions.

In the empirical paper, we assessed the recognition of basic facial emotions associated with threat – anger, fear and disgust – in 26 people with brain damage from different causes (e.g., stroke, carbon monoxide poisoning). These people’s brain injuries were chronic (happened more than 12 months ago) and stable. We compared the performance of this patient group with that of normal healthy participants of similar ages, on tasks requiring people to identify the expression displayed on photographs of faces (Ekman & Friesen, 1976). We found that the patient group performed more poorly on recognition of all 3 of the “threat” emotions.

For the 26 patients, we also assessed the relationship between emotion recognition accuracy and the anatomical distribution of brain damage. We used these data to inform a debate about how emotions are processed. Whilst fear, anger or disgust in the face of another person all alert the observer to the presence of possible threat, the relationship between the processing
of these emotions is debated: there is no consensus on whether they are represented categorically (e.g., Ekman, 1971) or dimensionally (e.g., Russell, 1980).

Under the categorical model, it is postulated that each of the “basic” emotions not only has its own evolutionary history and physiology, but corresponds to a relatively specific facial configuration, perceived reliably and similarly across cultures (e.g., Ekman, 1973). Conversely, the two-dimensional hypothesis postulates no qualitative distinction between emotion categories, instead advocating that specific emotional states fall at specific points in a continuous emotional space defined by two orthogonal dimensions: i) valence, the subjective experience of the affect, which varies in its pleasantness, and ii) arousal, the degree to which an emotion is calm or excitatory (Russell, 1980). Whilst the emotional states linked with labels of fear, anger and disgust are all negative in valence and associated with relatively high arousal, there are differences, such as that lower arousal may be associated with disgust than with fear or anger (e.g., Adolphs, Russell, & Tranel, 1999). Differences in arousal and valence associated with different emotional states may be consistent with, for instance, autonomic arousal differences on viewing faces displaying different emotions (Johnsen, Thayer, & Hugdahl, 1995).

The discrete category and two-dimensional models are associated with different predictions about the localization of emotional processing in the brain. The discrete category hypothesis predicts a qualitative neural dissociation across emotions, with different brain areas associated with different emotional categories. On the other hand, the bi-dimensional account of emotions predicts that similar brain regions will be involved in processing all emotional states, with quantitative differences across emotions. Neuropsychological (as well as neuroimaging) data have to date provided inconclusive evidence to distinguish between these hypotheses. Whilst certain brain regions have been shown consistently to be involved in emotional processing, their emotional specificity is debated. The amygdala, insula and basal ganglia, as
well as areas of frontal and parietal cortex, are among the brain regions which have consistently been linked to the processing of facial anger, disgust or fear. However, whilst in some studies each of these regions has been associated specifically with impairment in the recognition of one or another of the threat emotions, other findings indicate a more general involvement in facial emotion processing.

In the group of 26 patients, we used voxel-based morphometry (VBM) (Ashburner & Friston, 2000), a statistical technique to assess in an unbiased fashion the relationship between anatomical brain variations and behavioural variables, to relate information from the patients’ brain scans to recognition accuracy for fear, anger and disgust. We found evidence to support both categorical and dimensional hypotheses of emotion representation: some brain areas were associated specifically with recognition of anger, fear or disgust, and some were associated with accuracy of recognition on all three emotions. Our data may present issues for any position maintaining that emotions are represented entirely categorically, or entirely dimensionally, within the brain.

Understanding the implications of different types of brain damage for the recognition of emotion in other people has direct applications clinically in brain injured populations. More broadly, though, the manner in which our representations of emotional states relate to one another has potential implications for our understanding of human experience.
Appendix: Documents confirming ethical clearance