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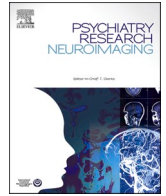
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A functional MRI facial emotion-processing study of autism in individuals with special educational needs.

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ABSTRACT

This study aimed to investigate the functional imaging associations of autism in individuals with special educational needs and demonstrate the feasibility of such research. The study included 18 individuals (3 female, 15 male; mean age 24.3; mean IQ 69.7) with special educational needs (SEN), of whom 9 met criteria for autism. The task examined the Blood-oxygen-level dependent response to fearful and neutral faces. Individuals in the autism group had 2 clusters of significantly reduced activity centred on the left superior frontal gyrus and left angular gyrus compared to those with SEN alone in response to the fearful faces. In the response to neutral faces, individuals in the autism group also had a cluster of significantly greater activity centred on the right precentral gyrus compared to those with SEN alone. We suggest that autistic characteristics in individuals with SEN are associated with changes in fearful facial emotion processing analogous to those previously reported in autistic individuals without SEN, and who are of average or above average cognitive ability. The finding of enhanced response to neutral facial stimuli needs further investigation, although we speculate this may relate to reports of the experience of ‘hyper-mentalisation’ in social situations as reported by some autistic individuals.

1. Introduction

Autism, or autism spectrum disorder (ASD) is a phenotype characterised by a dyad of differences of social communication and social interaction, and restricted, repetitive patterns of behaviour, interests or activities (American Psychiatric Association DSM-5 Task Force, 2013). It is simultaneously a relatively heterogeneous phenotype including those whose autism has a known or suspected aetiology (e.g. when occurring in the context of a specific genetic condition such as fragile X syndrome), as well as those for whom no known aetiology has been identified; and a homogenous group by virtue of the individuals sharing the features requisite for a diagnosis.

The question of whether there is any overarching biological finding that underlies the differences in reciprocal social communication and interaction in autism has been the subject of considerable investigation (Ashwin et al., 2007; Kaiser et al., 2010; Pelphrey and Carter, 2008; Pelphrey et al., 2011). It is almost certain that at the individual level there will be considerable variation, however, within groups of individuals with a common contributory aetiology closer alignment of

underlying biology may be expected. Indeed, previous investigation by the authors has shown that, for example, autistic individuals with fragile X syndrome (FXS) show patterns of neural response that differ from those with FXS alone, with parallels to the patterns found in groups of autistic individuals of average or enhanced intellectual ability (McKechanie et al., 2019). More broadly we would expect that given that autistic individuals share the features requisite for a diagnosis, that there might be some shared features of underlying neurobiology.

Given the centrality of differences in social understanding to autism, much of the prior research has focused on examining and understanding these differences, as well as attempting to examine any underlying differences in neurobiology during tasks that examine these differences. Differences in the perception of facial emotional stimuli have commonly been suggested as a contributory factor, which may impact on downstream differences in social communication, understanding and interaction. Prior studies examining facial emotion recognition in groups of autistic individuals, usually in comparison with neurotypical controls, have notably reported considerable variability in findings; with regions of both increased and decreased activation reported (Di Martino et al.,

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2009; Philip et al., 2012). It is likely that this is at least partially explained by a combination of small sample sizes, heterogeneity of participants and variability in study design. It is also important to consider that the direction of the relationship between the phenotype and the underlying biology is likely to neither be direct nor unidirectional. For example, whilst a difference in underlying biology may contribute to differential facial emotion recognition; so also a primary reduction in social interaction by virtue of a different mechanism will likely provide reduced exposure to facial stimuli and thus contribute to differential development of underlying pathways (Leppanen and Nelson, 2006). Nonetheless, two of the more consistent findings have been differences in activation in temporal structures and the fusiform gyrus, with especial reference to the fusiform face area (FFA). In temporal structures, regions of both increased and decreased activation have been reported in the groups of autistic individuals, most commonly in the region of the superior temporal gyrus and sulcus (Ashwin et al., 2007; Hadjikhani et al., 2007; Humphreys et al., 2008; Pelphrey et al., 2007; Philip et al., 2012). On the other hand, the FFA has more consistently been reported as showing hypo-activation in autistic individuals, with this finding present in approximately 2/3rds of studies, with no difference reported in the remaining studies (Perlman et al., 2011).

Despite the fact that a significant proportion of autistic individuals have a co-occurring intellectual disability, very few of the studies investigating autism either include, or focus on, these individuals; with a recent meta-analysis estimating that only 6% of participants in the autism studies they examined had an intellectual disability (Russell et al., 2019). Reports of the proportion of autistic individuals who have an intellectual impairment or disability varies; however, the Centers for Disease Control and Prevention in the United States reported that amongst children with ASD, 44% had an IQ > 85, 25% were in the range of 1–2 s.d. below the mean (IQ 70–84), and 31% had in IQ in the intellectual disability range, i.e. IQ > 2 s.d. below the mean (Baio et al., 2018). When looking at the functional Magnetic Resonance Imaging (fMRI) literature in ASD, Philip et al. (2012) reported in their systematic review that of 90 identified studies, only 5 studies, or 5.5%, (Gervais et al., 2004; Öktem et al., 2001; Pierce et al., 2004, 2001; Wicker et al., 2008) included individuals with a mean IQ in the range of 1–2 s.d. below the mean (IQ 70–84) and none of them included a group of individuals with a mean IQ in the intellectual disability range (IQ < 70). More recently, Gabrielsen et al. (2018) and Reiter et al. (2018) in their functional imaging studies have included groups with low average group mean IQ, with Gabrielsen similarly noting that this is a poorly investigated area.

Of note, other recent reviews of fMRI in autism similarly reveal that the overwhelming majority of studies do not include those with lower cognitive ability. Clements et al. (2018) review of social motivation in autism as measured by fMRI included 13 papers of which none had a group mean IQ of less than 100; and 10 of the 13 papers had group mean IQ of greater than 110. Similarly, in their comprehensive review and meta-analysis of face processing in autism, Aoki et al. (2015) identified 13 papers, of which only one, previously identified, (Wicker et al. (2008)) considered a group with a mean IQ of less than 85 (mean IQ 81.8). Whilst it is noted that fMRI studies often only include those of average, or above average, ability (Hull et al., 2016) and further it is suggested that, “This may be an inherent issue in fMRI studies that require the capacity to understand the instructions related to a cognitive task in an MRI scanner, and to execute the instructions,” (Dickstein et al., 2013); it is noteworthy that in other systematic reviews of cognitive aspects of autism using other techniques (electroencephalography/magnetoencephalography/event-related potentials/pupillary response/reaction time/choice/accuracy/effort) that the groups are similarly of average or above-average cognitive ability (Bottini, 2018; O’Reilly et al., 2017). Thus, whilst there are clearly issues with fMRI that act as barriers to participation for those of lower cognitive ability; many of these same barriers appear to be at play in studies

using other modalities.

In the context of relatively limited use of fMRI with groups of individuals of lower cognitive ability, this study first sought to further demonstrate the feasibility of conducting such research in a group of individuals with special educational needs, who were of lower average cognitive ability. Further, it sought to investigate one of the more robust prior findings; of differential activation to facial stimuli, in a group of individuals with lower average IQ; considering the impact of higher levels of autistic characteristics on the Blood-oxygen-level dependant (BOLD) signal response. In particular, we hypothesised that a subgroup with higher autistic traits would show lower activation to fearful faces, than the comparison subgroup with special educational needs alone.

2. Methods

2.1. Participant recruitment

The participants for this study were individuals who had been previously enrolled in a brain imaging study examining the characteristics of individuals receiving special education needs (SEN) support (Johnstone et al., 2007). For this parent programme of research, all educational boards in Scotland had been approached, with 18 of 19 agreeing to participate. In turn, the schools in those boards were each contacted, with 99 of 273 agreeing to participate. The teachers in each of the schools were asked to identify the children receiving special education support because of presumed low intellectual ability (with an estimated IQ of 50–80, as Intelligence Quotient (IQ) was not routinely measured in schools or SEN services). For the original study, the exclusion criteria had been those with Down syndrome or other syndromal features, major sensory impairments, absence of speech, significant cerebral palsy, and individuals with clear severe or profound intellectual disability. It was by re-contacting participants who completed this parent study that individuals were recruited to the present study.

2.2. Ethics procedures and consent

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008. All procedures involving human subjects/patients were approved by Scotland A Research Ethics Committee, Reference 11/AL/0261. Written informed consent was obtained from all subjects/patients or, where appropriate, from their welfare guardian/nearest relative in accordance with section 5.1 of the Adults with Incapacity (Scotland) Act 2000 [as revised].

2.3. Imaging procedure

Prior to their scan, participants were given the opportunity to rehearse the scanning procedure on a mock scanner. On the mock scanner, housed in the Clinical Research Imaging Centre (CRIC), participants were able to rehearse immediately prior to their main scan. The mock scanner was a replica of the main scanner used, with the only difference being that it did not have a main coil. However, the use of earplugs, headphones and an audio recording of the scanning sequences used in the main scanner all helped to simulate the sensory experience. Only when participants were comfortable in the mock scanner did they proceed to the main scan.

All scans were completed on a Siemens MAGNETOM Verio 3T scanner. For the structural imaging, using a Magnetization Prepared - Rapid Gradient Echo (MPRAGE) sequence, a T1 structural image was obtained made up of 160 coronal slices of 1 mm slice thickness and 1 mm x 1 mm x 1 mm voxels. A repetition time (TR) of 2.3 s, an echo time (TE) of 2.98 ms, flip angle of 9° and field of view (FOV) of 256 mm were used. For the functional imaging, 159 vol were acquired; each containing 26, interleaved, 5 mm slices of voxels 3.4 mm x 3.4 mm x 5 mm.

In this case a TR of 1.56 s, a TE of 26 ms, flip angle of 66° and FOV of 220 mm were used.

The functional imaging task used was a block-design task with two main conditions including a series of neutral faces, and a series of fearful faces, the faces being taken from the Pictures of Facial Affect series (Ekman and Friesen, 1976). A visual fixation cross presented at the beginning and end of the sequence, as well as between the conditions of interest, was used as the baseline condition. The complete sequence presented 6 blocks, each of six faces alternating between the blocks of fearful or neutral faces. Within each block, each face was shown for 3.5 s with an inter-stimulus interval of 0.5 s. In between each block was an interval of 12.5 s during which the fixation cross was shown. There were two variations of the sequence, with one starting with a block of neutral faces and the other starting with a block of fearful faces; these sequences being balanced across the groups. The task was modified to remove written instructions on-screen during the task. Instead, participants were spoken with via the in-scanner speaker and microphone to confirm their happiness to proceed and as a reminder of instructions prior to each of the localizer, structural and functional imaging sequences. As had been rehearsed in the mock scanner, participants were asked to depress a trigger button each time they saw an image. This was principally used as an in-scan method for ensuring participants were attending to the task.

2.4. Imaging analysis

Images were analysed using the Statistical Parametric Mapping (SPM) program (version 12, Functional Imaging Laboratory, Wellcome Trust Centre for Human Neuroimaging, University College London; fil.ion.ucl.ac.uk/spm/) running within Matlab (R2011b (version 7.13.0.564), MathWorks, Natick, MA, USA). Data were initially reconstructed using the DICOM Import function within SPM for further processing within SPM.

Prior to pre-processing, the first 7 vol of the functional scans were discarded to reduce the impact of T1 equilibrium effects. Images were initially realigned to the mean Echo Planar Imaging (EPI) image using the Realign (realign and unwarp) module of SPM. The T1 structural image was coregistered to the mean EPI image. The T1 structural image was segmented before both structural and functional images were normalised using the normalisation parameters arising from the T1 image segmentation. Finally, the functional images were smoothed using a Gaussian smoothing kernel of 8 mm full width at half maximum (FWHM) in each of the x, y, and z axes. Figure S1 shows the full pre-processing and analysis pipeline.

The realignment parameters giving the estimates of translations and rotations of the participant's head during the functional scan were examined with the intent of excluding scans showing more than 1 mm or 1 degree of movement. However, none of the scans exceeded these parameters and thus no scans had to be excluded.

For each contrast examined, a design matrix was created incorporating weightings for the neutral and fear conditions. A 128 s high-pass filter was used to remove slow signal drifts. Second-level analyses were generated using these first level contrast images for each participant to consider differences in activation on contrasts of fear vs baseline, neutral vs baseline fear vs neutral and neutral vs fear.

The initial height threshold was set at $p < 0.001$ uncorrected with results considered significant at $p < 0.05$ at cluster level after family-wise error correction. Regions annotated were identified using the Automated Anatomical labeling Atlas 3 toolbox (Rolls et al., 2019) running in SPM12.

2.5. Measures of cognitive ability

As part of the parent study, all participants had previously completed either the Wechsler Intelligence Scale for Children (WISC) (Wechsler, 1992) or the Wechsler Adult Intelligence Scale (WAIS) (Wechsler, 1999) as appropriate to the individual's age at the time to assess their IQ.

2.6. Measure of autistic traits

The Autism Diagnostic Observation Schedule-2 (ADOS-2, henceforth simply referred to as 'ADOS') was used to directly measure autistic traits. The ADOS is a semi-structured assessment that uses a set of prescribed 'presses' to elicit, demonstrate or create the space in which autistic features may be assessed either by the presence or absence of features which are useful in helping to establish an autism diagnosis (Lord et al., 2000). This format allows for the assessment of autistic and associated features including 31 items across 5 domains. The 5 domains include the domains considered in autism diagnosis (social, communication, and stereotyped behaviours and restricted interests) plus the related domains of creativity and associated features.

For each participant, we used the usual cutoff from the manual of a combined social and communication total of ≥ 10 to divide the group into 'SEN' and 'SEN + autism' groups for the between-group analyses. Using the cut-off of ≥ 7 for autism spectrum from the manual would have resulted in the same group composition, given the range of scores on the ADOS. In the case of two participants, it was not possible to complete an ADOS. However, their scores on the social communication questionnaire (SCQ) which had been completed by their primary caregiver in the previous study were used to categorise them into the ASD or non-ASD subgrouping, using the commonly used cut-off of ≥ 15 .

3. Results

Foremost, we were able to undertake functional MRI scans of individuals with special educational needs, who have traditionally not been included in much of the prior research. This was likely made easier by virtue of the fact that all participants in this study had previously successfully completed structural scans and thus the environment was not entirely novel to them. Nonetheless, we consider the successful completion of the task as a significant result in and of itself. During the functional imaging task all participants depressed the trigger successfully in response to the images; with mean correct responses of 35.7 out of 36, (range 31–36).

To consider the relative effect of autistic traits on facial emotion processing, the participants were divided into two groups: those meeting the ADOS threshold for autism (social and communication total ≥ 10) and those not (social and communication total < 10). Using these groups, contrasts were examined in SPM comparing the groups on their response to each of fearful faces vs baseline, neutral faces vs baseline and fearful faces vs neutral faces. The makeup of the two subgroups is shown in Table 1.

3.1. Response to fearful faces

In the analysis comparing response to fearful faces versus baseline,

Table 1
Baseline details of participants included in the imaging analyses.

	Autism group	Non-autism group
<i>n</i>	9	9
Male: female	8:1	7:2
Age	25.2 (1.7)	23.2 (1.1)
Full-scale IQ	68 (10.9, 46–87)	71 (16.0, 52–99)
Verbal IQ	67 (11.1, 48–87)	72 (18.2, 55–103)
Performance IQ	75 (11.5, 50–89)	74 (12.2, 62–97)
ADOS Total*	13 (10–16)	2 (0–5)
ADOS CSS*	7 (5–9)	1 (1–2)

Note. Results show group means (s.d.) for age, mean (s.d., range) for IQ; and median (range) for the ADOS scores. The groups were not significantly different on gender ($p = 0.527$), age ($p = 0.215$), full-scale IQ ($p = 0.313$), verbal IQ ($p = 0.382$) or performance IQ ($p = 0.263$).

*Ratings and scores based on scores for 8 individuals in each group.

ADOS, Autism Diagnostic Observation Schedule; CSS, Calibrated Severity Score.

there were two regions of significantly different activity between the groups; one centred on the left superior frontal gyrus (SFG) ($-12, 56, 30$ (x,y,z), kE 282, $Z \equiv 3.97$, $p = 0.006$), and the other centred on the left angular gyrus ($-50, -54, 32$ (x,y,z), kE 231, $Z \equiv 4.09$, $p = 0.017$). In both cases, there was significantly greater activation in the non-autism group. These clusters are shown in Fig. 1.

3.2. Response to neutral faces

This contrast examined the response to neutral faces versus baseline between the two groups. The non-autism group showed no clusters of significantly greater activation than the autism group in this contrast. However, the autism group showed one cluster of significantly greater activation than the non-autism group in the same contrast; with a peak co-ordinate in the right precentral gyrus and extending to the post-central gyrus and the rolandic operculum (part of the insula cortex) ($56, 8, 18$ (x,y,z), kE 385, $Z \equiv 4.15$, $p = 0.001$). The cluster is shown in Fig. 2.

3.3. Differential response to fearful and neutral faces

On the between group analyses there were no clusters of significant difference between the groups when considering the more subtle contrast of fearful faces vs neutral faces. However, within the autism group alone, considering neutral faces versus fearful faces, this revealed a region in the superior frontal gyrus ($-26, 6, 62$ (x,y,z), kE 125, $Z \equiv 3.91$, $p = 0.022$) of significantly greater activation to the neutral faces. The cluster is shown in Fig. 3.

4. Discussion

This study set out to examine the question of whether, in a group with low average cognitive ability, individuals with high autistic traits showed different patterns of brain activation on a functional imaging paradigm exploring response to processing emotional facial stimuli.

Foremost, whilst all the participants had previous structural scans, this was their first functional scan. That the experience and task was acceptable to the participants and that BOLD signal responses were seen in the within-group analyses (Supplementary Results) validates the use of the task in this population previously largely excluded from imaging research. To the authors' knowledge this study considers the effect of autistic traits on functional imaging in a group of participants with one of the lowest average IQs in the existing literature.

In keeping with the hypothesis, a number of differences were found between the non-autism group and the autism group; some of which

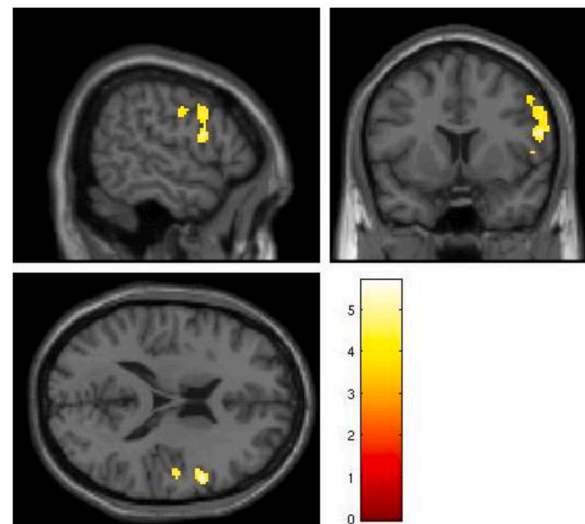


Fig. 2. Cluster of significantly greater brain activation in the autism group compared to the non-autism group during the neutral faces versus baseline contrast. *Note.* Cluster with peak voxel in the right precentral gyrus ($56, 8, 18$ (x,y,z), kE 385, $Z \equiv 4.15$, $p = 0.001$). Cluster is projected on the canonical single subject T1 image from SPM12.

overlapped the findings of a previous meta-analysis of functional imaging in autism. It had been hypothesised that the principal finding would be of a reduced neural response to emotional (fearful) faces in the autistic group; and indeed this was borne out in the between-group comparison of response to fearful faces versus baseline. However, perhaps the more interesting finding was that of enhanced response in the autistic group to neutral facial stimuli.

4.1. Response to fearful facial stimuli

In the fearful faces versus baseline contrast both groups showed significant clusters of activation around bilateral calcarine sulci, extending to fusiform and lingual gyri, and cuneus. As with the previous contrast examining response to neutral faces, the activation in the autistic group appeared to have a more diffuse pattern, albeit that this difference was again not significant.

Considering the between-group analysis on the fearful faces to baseline contrast, the autistic group showed no clusters of increased

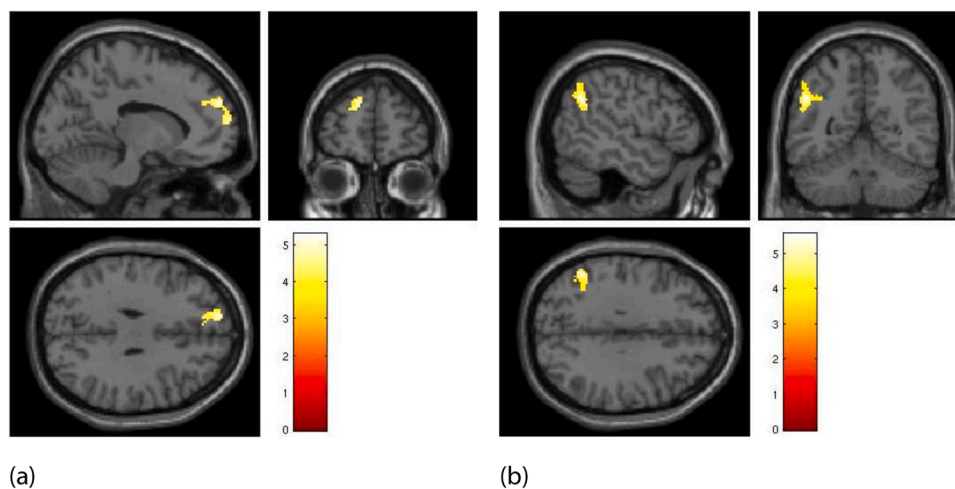


Fig. 1. Clusters of significantly greater brain activation in the non-autism group compared to the autism group during the fearful faces versus baseline contrast. *Note.* (a) Cluster with peak voxel in the left superior frontal gyrus ($-12, 56, 30$ (x,y,z), kE 282, $Z \equiv 3.97$, $p = 0.006$). (b) Cluster with peak voxel in the left angular gyrus ($-50, -54, 32$ (x,y,z), kE 231, $Z \equiv 4.09$, $p = 0.017$). Clusters are projected on the canonical single subject T1 image from SPM12.

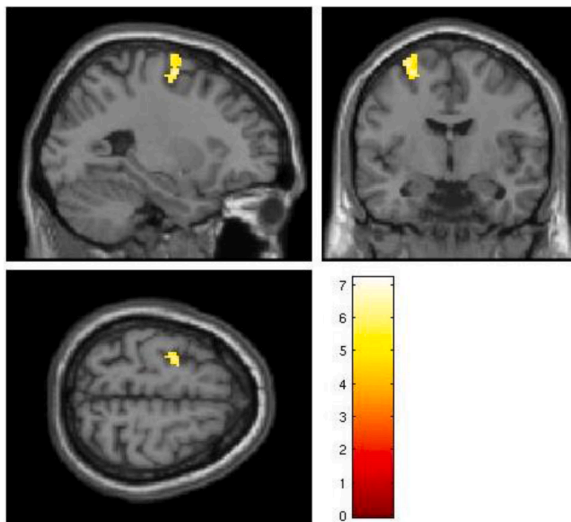


Fig. 3. Cluster of significantly greater brain activation in the autism group during the neutral faces versus fearful faces contrast. *Note.* Cluster with peak voxel in the left superior frontal gyrus ($-26, 6, 62$ (x,y,z), $kE 125, Z \bar{=} 3.91, p = 0.022$). Cluster is projected on the canonical single subject T1 image from SPM12.

activation compared to the non-autistic group. However, the non-autistic group showed two clusters of significantly greater activation on this contrast; one centred in the left superior frontal gyrus, and one spanning the left angular gyrus, left supramarginal gyrus and left inferior parietal lobule. This result is in keeping with the original hypothesis that the non-autistic group would show increased activations to fearful faces compared to the autistic group. The result in the left angular gyrus is the same region identified by Philip (2009) in their functional imaging study of autistic individuals of average cognitive ability using the same paradigms. In their study, they reported two clusters of significantly greater activation on a fearful faces to neutral faces contrast, with typically-developing controls showing greater activations in the right inferior parietal lobe and the left inferior parietal lobe/angular gyrus. This adds weight to the finding; suggesting that at least in this instance, the finding has some translatability across groups of individuals of different cognitive ability.

4.2. Response to neutral facial stimuli

On the within-group analyses, in both the autistic and non-autistic groups, large clusters of activation were seen in response to the neutral faces versus baseline contrast. These clusters, as expected, included large posterior regions including bilateral lingual gyri and cuneus. Whilst not significantly different, it is interesting to note that as with the response to fearful faces, the patterns of activation appear to be more diffuse in the autistic group than in the non-autistic group; something previously reported in autistic participants of average cognitive ability (Philip, 2009).

In the more subtle contrast comparing differential response to neutral and fearful stimuli, the autistic group showed a cluster in the left superior frontal gyrus of increased activation in the neutral faces > fearful faces contrast. The mechanisms that underlie this result are not clear, however, it has previously been reported that autistic individuals may perform more poorly on discriminating ambiguous stimuli (Law Smith et al., 2010; Wong et al., 2012) and it is possible that this hyper-activation represents either difficulty in interpreting a neutral stimulus, or perhaps a tendency to interpret neutral stimuli as negative (Eack et al., 2015). Interestingly, a similar pattern of increased activation to neutral faces (compared to fearful faces) has also been previously reported in children (Thomas et al., 2001) the significance of which is

not clear.

In the between-group analysis comparing the response to neutral faces versus baseline there were no clusters of significantly greater activation in the non- autistic group; however, the autistic group had one cluster of significantly greater activation than the non-autistic group in the right rolandic operculum/right inferior frontal gyrus (IFG). In general, the IFG has more typically been associated with relative hypo-activation to faces (Malisza et al., 2011) and also specifically to neutral faces in ASD (Bookheimer et al., 2008; Hadjikhani et al., 2007; Koshino et al., 2008). However, hyper- activation in autistic individuals has also been reported, mainly when considering response to non-facial stimuli (e.g. arrows or objects) (Greene et al., 2011; Vaidya et al., 2011). This said, the cluster on the right side overlapped a cluster reported by Philip et al. (2012) in the right rolandic operculum of increased activation in ASD vs controls on basic social tasks. This region has also been previously described as having mirror neurons; differential activation of which has been implicated in both emotion processing and autism. It is of interest that this is a region, in which differential activation appears to be important in autism; is highlighted across individuals of varying cognitive ability.

As with all imaging studies, trying to establish what this hyper-activation represents is far from straightforward. This increased activation could be associated with diminished, similar, or enhanced processing of the neutral stimuli. The finding of generally similar performance of autistic participants on accuracy in identifying neutral faces in previous studies (Kleinhans et al., 2009; Koshino et al., 2008; Pierce et al., 2001; Schultz et al., 2000) potentially supports the idea that this increased activation may occur in the context of similar performance. In this case, it may be that these clusters of increased activation in autistic individuals associated with neutral faces represent excess neural activity in the face of ambiguous stimuli, which ultimately may not be associated with any difference in performance.

In qualitative descriptions of social interactions, some autistic individuals describe the effort that social interactions can take; and how it can be, “very draining trying to figure out everything all the time” (Bargiela et al., 2016). It is far from clear that the finding of increased activation to neutral stimuli in the autistic group is linked to this phenomenon; however, there are potential interesting parallels to be drawn. If common social situations are experienced as potentially ambiguous and necessitate conscious effort to understand as described, then it’s possible that the neutral faces paradigm studied here may represent a model for this phenomenon. Whilst autistic individuals have typically been described as having diminished theory of mind or ability to mentalise; some of the narratives of autistic individuals suggest that whilst there may be difficulties in some of these skills, it is perhaps underpinned by an experience of what the authors consider to be ‘hyper-mentalising’ with increased effort being brought to bear in thinking about and trying to understand a given social situation. Potentially, the less ambiguous fearful facial stimuli require less resource to process; explaining the lack of the same effect in that contrast.

4.3. Limitations

This study has a number of potential limitations, which need to be considered when considering what it adds to the field. These mainly include issues relating to the participants, the measures used and the imaging sequence, and are considered in turn below.

4.3.1. Selection of participants

Firstly, the participants from this study were drawn from a prior study, which had considered structural imaging. It is likely that there was a degree of selection bias in that only those who had been able to successfully undergo the prior structural imaging were even considered for this study. Whilst this made participation easier, it is likely that the participants in this study are not fully representative of the broader group of individuals with special educational needs. One of the main

differences between this study and most of the prior investigations was the use of a comparison group of similarly low cognitive ability as the group with high autistic traits. Whilst this was the entire purpose of the study, the lack of a typically-developing comparison group, or a group with high autistic traits and of average cognitive ability, limits the conclusions that can be drawn. Finally, the study is limited in having a small sample size. However, it remains the case that this is an area of investigation that remains under-researched and that this study shines a light on this area. Having demonstrated the feasibility of such a study, further larger studies should now be possible.

4.3.2. Measures

In this study we chose to use the ADOS-2 as our method for quantifying autistic traits, which as noted in the methods section has the advantage of being a semi-structured assessment for the assessment of autism. Whilst in an ideal situation, a full clinical assessment would have been conducted in order to assess each of the participants for autism, this was beyond the constraints of the study. Nonetheless, as noted previously, the bimodal distribution of ADOS total scores gives greater confidence that the groups appropriately represent groups with relatively high or low autistic traits, which could be reasonably expected for the purposes of this research to represent individuals with or without autism.

4.3.3. Imaging sequence

One of the major limitations of this study was the lack of in-scanner eye-tracking to be able to further interrogate what the results represent. It is entirely possible that some, or indeed all, of the results represent primary differences in patterns of visual attendance to the stimuli. Indeed, given that differences in gaze patterns are frequently seen in autism, it is possible that this may help understand some of the results. Future investigation should incorporate in-scanner eye-tracking to help understand future results at a deeper level.

5. Conclusions

In this study of individuals with special educational needs there were two main findings. Firstly, clusters of significantly greater activation were found in a group of non-autistic individuals compared to an age- and IQ-matched autistic group on an fMRI task examining response to fearful facial stimuli. This finding is in keeping with the literature, showing that groups of autistic and non-autistic individuals do not appear to have the same patterns of response to emotional facial stimuli.

The other finding of the study, which is potentially of greater interest, is that on two different analyses autism was associated with significantly greater activations to neutral facial stimuli. The mechanisms underpinning this are yet to be elucidated, however, the potential that this links in with the descriptions by autistic individuals of increased effort to understand social situations, and that the neutral faces paradigm perhaps is a model for ambiguous social cues, is interesting. Further study could usefully consider this and integrate in-scanner analyses with participant narratives of their experience both of real-life social situations, as well as responses to the paradigms in use to help further interpret this result.

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CRediT authorship contribution statement

Andrew G. McKechnie: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Writing – review &

editing, Project administration. **Stephen M. Lawrie:** Investigation, Writing – review & editing. **Heather C. Whalley:** Methodology, Writing – review & editing. **Andrew C. Stanfield:** Conceptualization, Methodology, Investigation, Writing – review & editing, Funding acquisition.

Declaration of Competing Interest

The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.psychres.2021.111426](https://doi.org/10.1016/j.psychres.2021.111426).

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