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fMRI of parents of children with Asperger Syndrome: A pilot study

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Abstract

Background: People with autism or Asperger Syndrome (AS) show altered patterns of brain activity during visual search and emotion recognition tasks. Autism and AS are genetic conditions and parents may show the 'broader autism phenotype.'

Aims: (1) To test if parents of children with AS show atypical brain activity during a visual search and an empathy task; (2) to test for sex differences during these tasks at the neural level; (3) to test if parents of children with autism are hyper-masculinized, as might be predicted by the 'extreme male brain' theory.

Method: We used fMRI during a visual search task (the Embedded Figures Test (EFT)) and an emotion recognition test (the 'Reading the Mind in the Eyes' (or Eyes) test).

Sample: Twelve parents of children with AS, vs. 12 sex-matched controls.

Design: Factorial analysis was used to map main effects of sex, group (parents vs. controls), and sex × group interaction on brain function. An ordinal ANOVA also tested for regions of brain activity where females > males > fathers = mothers, to test for parental hyper-masculinization.

Results on EFT task: Female controls showed more activity in extrastriate cortex than male controls, and both mothers and fathers showed even less activity in this area than sex-matched controls. There were no differences in group activation between mothers and fathers of children with AS. The ordinal ANOVA identified two specific regions in visual cortex (right and left, respectively) that showed the pattern Females > Males > Fathers = Mothers, both in BA 19.

Results on Eyes task: Male controls showed more activity in the left inferior frontal gyrus than female controls, and both mothers and fathers showed even more activity in this area compared to sex-matched controls. Female controls showed greater bilateral inferior frontal activation than males. This was not seen when comparing mothers to males, or mothers to fathers. The ordinal ANOVA identified two specific regions that showed the pattern Females > Males > Mothers = Fathers: left medial temporal gyrus (BA 21) and left dorsolateral prefrontal cortex (BA 44).

Conclusions: Parents of children with AS show atypical brain function during both visual search and emotion recognition, in the direction of hyper-masculinization of the brain. Because of the small sample size, and lack of age-matching between parents and controls, such results constitute a pilot study that needs replicating with larger samples.

Keywords: Autism; Asperger Syndrome; fMRI parents; Sex differences

1. Introduction

The genetic theory of autism (Bailey, Bolton, & Rutter, 1998; Bailey et al., 1995) proposes that autism is strongly heritable, and that first-degree relatives of children with

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autism possess the 'broader autism phenotype' (BAP). Heritability of autism has been estimated to be above 90%, and the BAP has been confirmed among parents of children with autism. For example, parents of children with autism score higher on some of the subscales of the Autism Spectrum Quotient (AQ), compared to controls (Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001; Bishop et al., 2004).

To date there have been no fMRI studies of parents of children with autism or AS to test for the BAP at the neural level. Since people with autism and AS show atypical brain function during fMRI, using tasks such as the Embedded Figures Test (EFT) (a visual search task) (Ring et al., 1999) and the 'Reading the Mind in the Eyes' (or Eyes) task (an advanced emotion recognition task) (Baron-Cohen et al., 1999), it is important to see if on the same tasks, first-degree relatives of children with autism or AS also show atypical brain function. Such a result would implicate these measures as assays for neurocognitive endophenotypes.

The use of the EFT and Eyes tests during fMRI is also relevant to the question of sex differences in brain function, since males in the general population often score higher than females on the EFT (Jolliffe & Baron-Cohen, 1997; Witkin, Dyk, Faterson, Goodenough, & Karp, 1962) and females in the general population often score higher than males on the Eyes test (Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997; Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001). The study below is a preliminary exploration testing for sex differences in brain function during these two tasks. It is preliminary because only six males are tested, against six females.

1.1. The extreme male brain theory of autism

If sex differences are found, then these tasks also allow a preliminary test of the 'extreme male brain' (EMB) theory of autism (Baron-Cohen, 2002). It has been shown that people with AS are faster than sex-matched controls on the EFT (Jolliffe & Baron-Cohen, 1997), and score below average on the Eyes test. In the study below, we also test if parents of people with AS show such hyper-masculinization. The fact that parents score in a hyper-masculinized direction on both of these tasks in terms of performance is consistent with the EMB theory. Thus, parents of children with autism spectrum conditions (ASC) are faster than sex-matched controls on the EFT, and show lower scores on the Eyes test (Baron-Cohen & Hammer, 1997). In the study reported here we test if parents of children with AS show atypical brain function whilst performing these two tests. A preliminary clue that hyper-masculinization might be found in such parents is that mothers of children with ASC show a masculinized second-to-fourth digit (2D:4D) ratio (Manning, Baron-Cohen, Wheelwright, & Sanders, 2001). Here, we report a pilot test of the EMB theory at the level of the brain. Again, this is a pilot study simply because only six mothers and six fathers are included.

In the earlier behavioural studies, sex differences were detected when the sample size comprised 25 males and 25 females (Baron-Cohen & Hammer, 1997). It is unclear if sex differences in brain activity would be revealed in a relatively small sample as reported below. It is, however, possible that, even if at the behavioural level sex differences in performance are not apparent with just six males and six females, it may be at the neural level that sex differences will be seen. This is because in behavioural studies what is being measured is performance (speed or accuracy) and the effect size may be quite small. At the neural level, sex differences may exist in how the brain approaches the task. If the two sexes (on average) are employing very different neural strategies to solve the tasks, this may be detectable even with small samples. On this view, the power to detect sex differences may be greater using fMRI than when using behavioural measures. The same arguments apply to comparing parents of children with AS with sex-matched controls. Even if performance differences are not seen at the level of behaviour, differences may be detectable at the level of brain function.

1.2. Predictions

In the present study, we tested three predictions: (1) parents of children with autism would show atypical brain activity during both the EFT and the Eyes tasks. (2) Male and female controls would show different patterns of brain activity on each of these tasks. (3) On both of these tasks, parents of children with AS would show hyper-masculinized brain activation.

2. The experiment

2.1. Sample

Twelve adult controls (six males, six females) from the general population and 12 parents (six mothers, six fathers) of children with AS took part. The latter were recruited from the volunteer database held by the Autism Research Centre in Cambridge University. All participants were right-handed and came from a mix of occupations and social classes. All were free of any medication use, and had no history of neurological or psychiatric conditions. All gave written consent to participate in scanning. Exclusion criteria for subject selection were myopia (the tasks involved being able to see a screen without the option of wearing spectacles in the scanner), claustrophobia (the procedure required staying still in the scanner for up to 1 h), and metal implants in the body (due to the force of the magnetic field in MRI). The two groups were equated for socio-economic status (ascertained by years in education and occupation), and IQ (as measured by the Weschsler Abbreviated Scale of Intelligence [WASI]). They were not equated for age, which is why this study can only be considered preliminary.