Original Article

The 'extreme female brain': increased cognitive empathy as a dimension of psychopathology

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ABSTRACT

Baron-Cohen's 'extreme male brain' theory postulates that autism involves exaggerated male-typical psychology, with reduced empathizing (considered here as social–emotional interest, motivation and abilities) and increased systemizing (non-social, physical-world and rule-based interest, motivation and abilities), in association with its male-biased sex ratio. The concept of an 'extreme female brain', involving some combination of increased empathizing and reduced systemizing, and its possible role in psychiatric conditions, has been considerably less well investigated. Female-biased sex ratios have been described in two conditions, depression and borderline personality disorder (BPD), that also show evidence of increases in aspects of empathy in some studies. We evaluated the hypothesis that BPD and depression can be conceptualized in the context of the 'extreme female brain' by: (1) describing previous conceptualizations of the extreme female brain model, (2) reviewing evidence of female-biased sex ratios in BPD and depression, (3) conducting meta-analyses of performance on the Reading the Mind in the Eyes test (RMET) among individuals with BPD, clinical or sub-clinical depression, and other psychiatric conditions involving altered social cognition and mood (schizophrenia, bipolar disorder, eating disorders, and autism), in relation to disorder sex ratios, and (4) evaluating previous evidence of increased empathic performance in these, and related, psychiatric conditions, and (5) synthesizing these lines of evidence into models for causes and effects of an 'extreme female brain'. Our primary empirical results are that RMET performance is enhanced in sub-clinical depression, preserved in borderline personality disorder, and reduced in other disorders (by meta-analyses), and that across disorders, more male-biased patient sex ratios are strongly associated with worse RMET performance of patients relative to controls. Our findings, in conjunction with previous work, suggest that increased cognitive empathizing mediates risk and expression of some psychiatric conditions with evidence of female biases, especially sub-clinical depression and borderline personality disorder, in association with increased attention to social stimuli, higher levels of social and emotional sensitivity, negative emotion biases, and over-developed mentalist thought. These results link evolved human sex differences with psychiatric vulnerabilities and symptoms, and lead to specific suggestions for future work.

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1. Introduction

Evolved sex differences in psychological and biological traits play important roles in the development, causes, and manifestations of many psychiatric conditions (Rutter, Caspi, & Moffitt, 2003). The 'extreme male brain' (EMB) theory of autism postulates that autism spectrum conditions reflect extreme manifestations of 'male-typical' psychology due in part to high prenatal testosterone (Baron-Cohen, 2002; Baron-Cohen, Knickmeyer, & Belmonte, 2005). This theory can

help to account for several notable features of autism, including its strongly male-biased sex ratio and reduced performance in measures of empathy and theory of mind (Baron-Cohen et al., 2011). Given the usefulness of the EMB theory in generating testable hypotheses and accounting for patterns in data on autism, it is of interest to investigate the other side of the spectrum: if extreme psychological 'maleness' can manifest in autism spectrum traits, what psychological traits and psychiatric conditions might be associated with extreme psychological 'femaleness'?

Consideration of human psychological sex differences in the context of psychiatric conditions requires addressing two central issues at the outset. First, the 'extreme male brain' (EMB) and 'extreme female brain' (EFB) in this context have been defined psychologically and seldom involve neurological studies; the EFB and EMB, thus mainly describe psychological profiles that exist at the extreme ends of normal

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distributions of sexually-dimorphic psychological traits (e.g., Grove, Baillie, Allison, Baron-Cohen, & Hoekstra, 2013). Psychological traits that differ between males and females do so statistically when measured from large samples, meaning that sex differences are small but statistically significant at the population level. Because the distributions of these psychological traits overlap considerably between the sexes, an individual male may exhibit EFB phenotypes, and likewise, an individual female may express EMB traits; however, statistically, an EMB profile is more likely to describe a male and an EFB profile is more likely in a female (Baron-Cohen et al., 2005). Average sex differences are important, however, in that they may result in the extremes of distributions of sex-differential psychological phenotypes exhibiting strong sex biases, depending on the shapes of the distributions.

Second, the extreme development of many normally-distributed traits can mediate the expression of psychiatric conditions, as for personality disorders that explicitly represent maladaptive extremes of psychological personality variation (e.g., Nettle, 2007a; Trull, 2012; Trull & Durrett, 2005; Widiger & Presnall, 2013), and for more-severe psychiatric disorders whose psychological phenotypes grade more or less continuously into those of non-clinical populations (e.g. Constantino, 2011; van Nierop et al., 2012). For psychological and psychiatric phenotypes that are normally distributed as well as sexually dimorphic, extreme developments are thus expected to occur more often within one sex than the other and to contribute to psychological dysfunction.

In this article, we develop and evaluate central aspects of the construct of the 'extreme female brain' in relation to psychiatric conditions. We first briefly explain Baron-Cohen's 'extreme male brain' model of autism spectrum conditions, in the context of his psychological model of low empathizing in combination with high systemizing and the male-biased sex ratios found in association with autism. Second, we describe previous conceptualizations of the 'extreme female brain' construct, and their relationships with empathizing, systemizing, and biased sex ratios, and our model of the EFB as proposed and evaluated here. Third, we evaluate our hypothesis through: (1) review and evaluation of evidence regarding sex ratio biases in BPD and depression, two conditions postulated as reflecting extreme female brain phenotypes that have yet to be analyzed in this context, (2) using meta-analyses to evaluate the prediction that cognitive empathizing ability, as indicated by the Reading the Mind in the Eyes test (RMET) (Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001) is increased or preserved in BPD and clinical or sub-clinical depression, but not in other psychiatric conditions (bipolar disorder, schizophrenia, eating disorders, and autism); and (3) testing for a positive association between higher RMET performance in patients compared to controls, and more female-biased disorder sex ratios, across this set of disorders. Finally, we discuss the implications and limitations of our results, and make suggestions for future research.

2. Empathizing, systemizing, and the extreme male brain

A powerful framework for understanding patterns of psychological sex differences is the empathizing–systemizing (E–S) theory, which suggests that humans have evolved two parallel and complementary cognitive-affective systems (Baron-Cohen, 2002; Baron-Cohen, Richler, Bisarya, Gurunathan, & Wheelwright, 2003, 2005, 2011, Baron-Cohen & Wheelwright, 2004; Baron-Cohen et al., 2005, 2011; Chakrabarti & Baron-Cohen, 2006). By this theory, 'empathizing' involves the motivation and skills required to understand and interact appropriately with the social world, and 'systemizing' describes the drive to analyze, understand and manipulate the physical world (Baron-Cohen, 2002, 2009; Baron-Cohen et al., 2005; Lawson, Baron-Cohen, & Wheelwright, 2004; Nettle, 2007b). Crespi and Badcock (2008) and Badcock (2009) use the terms 'mentalistic' and 'mechanistic' in place of empathizing and systemizing, to capture a somewhat wider breadth of cognitive and affective systems; the terms 'mentalizing' and 'mentalization'

have likewise been used extensively in clinical psychology (e. g, Choi-Kain & Gunderson, 2008; Bateman & Fonagy, 2010). Social, empathizing, and mentalistic or mentalizing cognition, and systemizing and mechanistic cognition (which are non-social), are each basically synonymous for our purposes, and these two systems are subserved by different networks of distributed regions of the brain, with activation patterns that tend to be inversely related (Jack, 2014; Jack et al., 2012). Both sets of constructs can be quantified using ether self-report or task-based metrics of the relevant interacts and abilities. Given that higher fetal testosterone mediates both decreased social and empathic interest and abilities, and increased scores on metrics of systemizing (review in Baron-Cohen et al., 2011), and that their neural bases are inversely associated, empathizing and systemizing might be expected to be negatively correlated with one another, as found in some studies (e.g., Grove et al., 2013; Nettle, 2007b). However, the psychological and neurological bases of the relation of empathizing with systemizing remain to be studied in detail.

A primary sex difference in cognition, Baron-Cohen (2002, 2009) postulates, is represented by the balance of empathizing with systemizing, such that on average, males demonstrate a stronger drive to systemize, and females, on average, tend toward empathizing (Baron-Cohen, 2002; Baron-Cohen et al., 2005; Chakrabarti & Baron-Cohen, 2006; Wakabayashi et al., 2007). Under the E–S model, autism represents an extreme expression of male-typical cognition involving a strongly skewed profile of enhanced systemizing and reduced empathizing (extreme Type S in Baron-Cohen et al., 2005). This pattern of exaggerated psychological 'maleness' is consistent with the strong male bias in autism spectrum disorder prevalence (especially among individuals with less-severe autism), as well as with evidence linking autistic phenotypes with elevated exposure to prenatal androgens, hormones that play important roles in 'masculinizing' the developing brain (Baron-Cohen, 2002; Baron-Cohen et al., 2011; Lutchmaya, Baron-Cohen, & Raggat, 2002a, 2002b; Manning, Baron-Cohen, Wheelwright, & Sanders, 2001; Wu & Shah, 2011).

Together, the E–S and EMB theories predict that a primarily-female proportion of the population will exhibit an E–S profile opposite to that observed in autism, one that is skewed toward increased empathizing and reduced systemizing (extreme Type E in Baron-Cohen et al., 2005). Consistent with this prediction, Goldenfeld, Baron-Cohen, and Wheelwright (2005) reported that, based on distributions of scores from the Empathy Quotient and Systemizing Quotient drawn from individuals with and without high-functioning autism, a small and all-female proportion of the sample (7%, and none with autism) exhibited this 'extreme female' profile of high empathizing and low systemizing. Similarly, data from Baron-Cohen et al. (2014) showed that 'extreme type E' individuals (those in the lowest 2.5th percentile for SQ and highest 2.5th percentile for EQ) demonstrated a strong female bias (with 59 of 60 individuals being female, from a total population of 2562 females and 1344 males; $\chi^2 = 28.9$, $P < 0.0001$); similar results are also described in Wheelwright et al. (2006). However, the question of whether or not an EFB, defined in this manner, manifests in aspects or diagnoses of psychiatric conditions has been addressed by only a small number of previous studies.

3. Previous accounts of the 'extreme female brain'

Baron-Cohen (2002, 2012) suggested that increased empathizing drive and abilities need not negatively impact social functioning and engender psychiatric illness, and that low systemizing would be unlikely to cause impairment in psychological functioning. However, in these articles he did not explicitly consider extreme high levels of empathizing or combinations of high empathizing with low systemizing in the context of psychopathologies. A suite of researchers (Abu-Akel, 1999; Abu-Akel & Bailey, 2000; Crespi & Badcock, 2008; Dammann, 2003; Dinsdale & Crespi, 2013; Frith, 2004; O'Connor, Berry, Lewis, Mulherin, & Crisostomo, 2007; Sharp & Venta, 2012; Sharp et al., 2013; Zahn-