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Abstract

Human cognition can be conceptualized as an axis whereby males tend toward relative strengths in mechanistic ('things'-thinking) cognition and females tend toward relative strengths in mentalistic ('people'-thinking) cognition. Psychiatric conditions are hypothesized to reflect the extreme ends of this axis, with over-developed social cognition underlying the psychotic-affective spectrum in contrast to under-developed social cognition characterizing the autism spectrum. Consistent with this hypothesis, I found a diametric relationship between autistic and schizotypal features based on questionnaire data drawn from a large non-clinical sample of undergraduates. I also conducted two literature reviews asking: 1) Is mentalistic cognition enhanced in borderline personality disorder (BPD)? and 2) are BPD and depression associated with extreme female phenotypes? Both conditions involved elevated mentalistic cognition, a female-bias in their prevalence, and associations with female-typical hormonal profiles. These findings provide evidence that psychological variation is organized along an axis shaped by sex differences and that extreme expressions of evolved cognitive systems mediate a suite of psychiatric conditions.

Keywords: autism; schizotypy, borderline personality disorder; depression; empathy; evolutionary medicine
for the pulse that moves us
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1. Introduction

Humans are vulnerable to a wide range of psychiatric perturbations, which poses a paradox when behaviour is examined through an evolutionary lens – given the significantly-reduced fitness associated with psychological dysfunction, why has our species evolved with susceptibility to high rates and diversity of psychiatric conditions? Most psychiatric research focuses on describing the psychological, neurological, and genetic mechanisms underlying psychiatric disorders, but a complete account of human behaviour requires an integration of proximate and ultimate causation (Nesse & Stein 2012). Examining relationships between normal and abnormal behaviour can help identify evolutionary causes of psychiatric conditions by revealing sources of variation that create and maintain susceptibility to psychiatric disorders. My thesis reviews variation in empathic functioning and examines relationships between autistic and schizotypal phenotypes to test a series of hypotheses for why the human lineage has evolved with a liability to autism spectrum conditions (ASCs) and psychotic-affective spectrum conditions (PACs).

Autism is diagnosed by the presence of language deficits, impaired social reciprocity, and restricted interests and repetitive behaviours (Happé 1994; APA 2012). These features vary along a spectrum within healthy populations and therefore subtle manifestations of autistic features, such as preference for aloneness or mental rigidity, can also be conceptualized as variants of personality or cognitive style, in addition to, or instead of, psychiatric illness (Happé 1999; Baron-Cohen 2002). The psychotic-affective spectrum includes schizophrenia, schizoaffective disorder, depression, bipolar disorder, and borderline personality disorder (BPD); these conditions overlap in their genetic underpinnings and core phenotypes, which centrally involve dysregulated emotional functioning and altered reality perception (Craddock & Owen 2010; Crespi 2011). Like autism, features comprising conditions of the psychotic-affective spectrum grade more or less smoothly into normality in healthy populations, suggesting that these conditions
represent extreme manifestations of naturally occurring variation in human affect and cognition.

There are two main theories for the evolutionary bases of ASCs and PACs and both posit strong effects of evolved cognitive variation in contributing to psychiatric risk. Under the empathizing-systemizing (E-S) theory humans have evolved with two fundamental and parallel cognitive systems, *empathizing* involves predicting and responding to the behaviour of others with an appropriate emotion and systemizing is the capacity to predict and respond to the behaviour of rule-governed systems (Baron-Cohen 2002; Baron-Cohen et al. 2005). Sex differences in psychological functioning at the population level are explained by the relative balance between empathizing and systemizing, on average, females tend toward relative strengths in empathizing and males tend toward relative strengths in systemizing (Baron-Cohen et al. 2003; Baron-Cohen & Wheelright 2004). That individuals with ASCs demonstrate enhanced systemizing and impaired empathizing forms the basis for the 'extreme male brain' (EMB) theory of autism, which postulates that exaggerated sex differences in psychological functioning—due largely to elevated prenatal androgen exposure—play a major aetiological role in the autism spectrum (Baron-Cohen 2002; 2009; Baron-Cohen et al. 2011). Given the usefulness of Baron-Cohen's EMB theory in accounting for some key features of autism, it is useful to extend the framework and investigate the potential role of 'extreme female' phenotypes, such as elevated empathizing abilities, in contributing to psychiatric disorders.

The 'diametric disorders' hypothesis proposes that ASCs and PACs represent two extremes of variation in human social cognition (Crespi & Badcock 2008). Social cognition broadly describes the set of integrated and distributed neural networks that evolved to facilitate the complex social interactions characteristic of our species. Under the diametric disorders hypothesis, social cognition is conceptualized as varying along an axis where under-developed social cognition manifests as ASCs (at one end) and hyper-developed social cognition manifests as schizophrenia and the broader psychotic-affective spectrum (at the opposite end). Therefore, the diametric model predicts that the autism spectrum and the psychotic-affective spectrum will exhibit opposite phenotypes for a range of traits involved in social cognition. Existing evidence from neurological and psychological studies converge in supporting the diametric disorders
hypothesis (reviewed in Crespi & Badcock 2008; Brosnan et al. 2010), but specific and targeted tests are needed to further elucidate the breadth of diametric relationships between autistic and psychotic-affective phenotypes.

The diametric model and the EMB theory of autism are similar in that they both highlight the role of extreme phenotypes in contributing to psychiatric conditions, but the models have slightly different foci. Organization of social-cognitive variation is central to the diametric hypothesis, whereas dysregulation of psychological sex differences is key under Baron-Cohen's EMB theory. Given that social cognition -and psychological abilities more generally- vary as a function of sex, these two models appear to have highlighted two important and interacting axes of variation, social cognition and sex dimorphism, that underlie human susceptibility to psychiatric dysfunction.

My thesis extends the extreme male brain framework and tests predictions from the diametric disorders hypothesis to further elucidate how these naturally occurring variation in the human social brain creates and maintains psychiatric conditions. In Chapter 1, I test predictions from alternative models, including the diametric disorders hypothesis, for the relationship between autistic and schizotypal phenotypes from psychometric data collected from a non-clinical student sample. The next two chapters are literature reviews (with some new data, in Chapter 3) that focus on the links between enhanced social-cognitive abilities and psychiatric conditions: Chapter 2 examines evidence for enhanced empathic functioning in borderline personality disorder (BPD) and Chapter 3 reviews evidence from sex-ratio studies, psychological functioning, and hormonal correlates to evaluate the hypothesis that BPD and depression represent the extreme female brain in contrast to autism as the EMB. Through integrating two key theories, these chapters help develop an evolution-psychiatry framework for understanding the role of variation in sex and social cognition in shaping human susceptibility to major suites of psychiatric illness.
1.1. References


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2.1. Abstract

Both autism spectrum conditions (ASCs) and schizophrenia spectrum conditions (SSCs) involve altered or impaired social and communicative functioning. These overlapping features may indicate common aetiological factors underlying both autism and schizophrenia, or alternatively, the shared phenotypes may manifest similarly but reflect independent, or even diametric causes. We outline three alternative models (overlapping, independent, and diametric) for the possible relationship between ASCs and SSCs, and compare predictions for the expected relationships between autistic and schizotypal phenotypes using the Autism Quotient (Baron-Cohen et al. 2001) and the Schizotypal Personality Questionnaire-Brief Revised (Cohen et al. 2010) from a large non-clinical sample of undergraduate students sampled from two universities. Consistent with previous research, autistic features were positively associated with several schizotypal features, with the most overlap occurring between interpersonal (negative) and disorganized schizotypy with autistic-typal social and communication phenotypes. The first component of a principal components analysis (PCA) reflected these positive correlations and suggested the presence of an axis (PC1) that represents general social interest and aptitude. By contrast, the second principal component (PC2) exhibited a pattern of positive and negative loadings indicative of an axis from autism to positive schizotypy, such that positive schizotypal features, especially magical thinking and unusual perceptions, loaded in the opposite direction to core autistic features. These PCA patterns were replicated in a second data set from Wakabayshi et al. (2012).
To provide validation for our interpretation of the PCA data, we also measured handedness preference and mental rotation ability, as these are well-established correlates of SSCs and ASCs, respectively. PC2 scores were related to hand preference, such that increasingly 'schizotypal' scores predicted reduced strength of handedness, which is consistent with previous research in both schizophrenia and schizotypy. Furthermore, PC1 scores were positively related to performance on the mental rotation task, possibly reflecting trade-offs between social skills and visual-spatial ability. Taken together, these results provide novel evidence for an autism-positive schizotypy axis, and highlight the importance of recognizing that psychological variation involving reductions in general social interest, functioning and skills may have diverse causes.

2.2. Introduction

The relationship between autism spectrum disorders (ASCs) and schizophrenia spectrum disorders (SSCs) has been subject to ongoing, unresolved investigation since Kanner (1943) and Asperger (1944) first defined and characterized autism (Kolvin 1971; Rutter 1996, 1972; Tantam 1988; Rapoport et al. 2009; Crespi 2011; King & Lord 2011). Both spectra involve altered and impaired social and communicative functioning (Pilowsky et al. 2000; Couture et al. 2010; Solomon et al. 2011), which has suggested to some authors that autism and schizophrenia overlap in their aetiologies (Hurst et al. 2007; Tordjman 2008; Craddock & Owen 2010). One approach to addressing the relationship between ASCs and SSCs has been the analysis of psychometric, questionnaire data salient to both conditions, collected from clinical or non-clinical populations. Such data allow inference to be drawn regarding patterns of cognitive-affective similarities and differences between ASCs and SSCs, which can provide insights into phenotypic overlap involving aspects of altered social functioning.

Impairments in social reciprocity, communication, and behavioural flexibility are central features of the autism spectrum (Happé et al. 2006). Social and communication impairments are also characteristic of the schizophrenia spectrum, however these are not central to the schizophrenia diagnosis as they are to autism; symptoms and characteristics comprising SSCs can be understood as belonging to one of three
dimensions: positive, negative, and disorganized. Positive symptoms involve hallucinations, paranoia, thought disorder, referential thinking and delusions in schizophrenia whereas negative symptoms capture social withdrawal, flattened affect, apathy and alogia (Andreasen et al. 1995; Basso et al. 1998). Disorganized symptoms of SSCs include bizarre speech, thoughts and behaviour. Since the delineation of autism from schizophrenia in the DSM-III (APA 1980), it has been recognized that ASCs and SSCs overlap in several cognitive and behavioural features, most notably in the realm of social dysfunction.

For example, Konstantareas and Hewitt (2001) contrasted the presenting characteristics of 14 men with high-functioning autism to 14 men with chronic paranoid schizophrenia using observational data, psychometric evaluations, medical records and comprehensive interviews. Results revealed that no subjects with schizophrenia met the criteria for autism, almost half of the subjects with autism met criteria for disorganized schizophrenia, and the two diagnostic groups did not differ in their expression of negative schizophrenia symptoms including alogia, affective flattening, and attentional impairments, as assessed by the SANS (schedule for negative symptoms; Andreasen 1984).

In a non-clinical sample of college students, Hurst and colleagues (2007) examined relationships between autistic features and schizotypal features using two widely-employed measures (Autism Quotient; Baron-Cohen et al. 2001 & Schizotypy Personality Questionnaire; Raine 1991) and found strong positive associations between total AQ score and total SPQ score. Correlations were especially strong between negative schizotypy and AQ social skills, and between disorganized schizotypy and AQ communication, though positive schizotypy was moderately and positively related to autistic-typal attention to detail and communication as well. The authors interpreted these trait associations as indicating that autism and schizophrenia may overlap on a single spectrum rather than exist as two distinct spectra as currently implied by DSM categories.

Using the same self-report measures as Hurst et al. (2007) but with a clinical sample, Spek and Wouters (2010) compared 21 adult males with autism to 21 adult males with schizophrenia and found that the presence or absence of negative schizophrenia
symptoms could not reliably discriminate between the two conditions. For both diagnostic groups, negative schizophrenia symptoms were strongly and positively associated with autistic-like social and communication characteristics. The authors concluded that positive symptoms are the most useful in predicting presence of schizophrenia, whereas social skills are most predictive of autism.

In a related investigation, Wouters and Spek (2011) assessed the ability of the AQ to differentiate between individuals with high-functioning autism, individuals with schizophrenia, and non-clinical individuals. They found the AQ was 75% accurate in distinguishing subjects with autism from subjects with schizophrenia. The clinical groups did not show differences on attention to detail and imagination, but adults with autism reported a significantly more autistic-like social and communicative style than did the adults with schizophrenia. On a spectrum of autistic features, the authors suggested that healthy individuals and individuals with autism exist at opposing ends, and individuals with schizophrenia lie somewhere in between.

Using the AQ and the SPQ in a group of adolescents with and without ASCs, Barneveld and colleagues (2011) found that subjects with ASCs were more likely to demonstrate schizotypal traits than subjects without an ASC diagnosis; the relationships were strongest for negative symptoms but extended to positive and disorganized symptoms as well. Given that AQ attention switching was related to all three forms of schizotypy, the authors suggested that deficits in attentional and executive functioning might underlie some of the similarities between autistic and schizotypal phenotypes.

Russell-Smith et al. (2011) sampled non-clinical adults using the OLIFE Unusual Experiences scale (Mason et al. 2005) and the AQ, reporting positive correlations between total autism and total schizotypy scores. Positive schizotypy was also positively related to an empirically-derived factor from the AQ that appeared to indicate autistic-typical recognition of pattern and detail. Consistent with Hurst et al. (2007), the authors found the greatest overlap between the social deficits of autism and the interpersonal symptoms of schizotypy. They interpreted their results as consistent with models positing common factors for the social deficits and alterations shared between ASCs and SSCs.
Wakabayashi et al. (2012) studied the relationships between autism, schizotypy, and obsessive-compulsive disorder (OCD) and, like Hurst et al. (2007) and Russell-Smith et al. (2011), found modest, positive correlations between the SPQ and the AQ, with the most overlap between autism and schizotypy in the area of social-affective difficulties. In a multiple regression, however, positive schizotypy did not predict autistic features. Overall, the authors concluded that autism and schizophrenia share more differences than they do similarities.

These previous studies provide empirical support for phenotypic overlap between ASCs and SSCs at the psychometric and behavioural levels in both clinical and non-clinical populations. Some studies have reported overlap of autistic features with manifestations of positive schizotypy (Hurst et al. 2007; Barneveld et al. 2011; Russell-Smith et al 2011), but the strongest overlap between the two spectra consistently appears between the negative symptoms of SSCs and the social-communicative deficits that are central to ASCs (Konstantareas & Hewitt 2001; Spek & Wouters 2010; Hurst et al. 2007; Barneveld et al. 2011; Russell-Smith et al 2011; Wakabayashi et al. 2012). Generalized deficits such as abnormal social functioning comprise a broad range of phenotypes and likely reflect a multitude of complex causal factors, such that phenotypic similarities inferred from psychometric and behavioural data is not sufficient to infer shared aetiologies (Sasson et al. 2011). Given that various perceptual, cognitive, and affective alterations underlie the behavioural abnormalities expressed in ASCs and SSCs, we also measured two well-established correlates of autism and schizophrenia in order to provide some validation of our interpretation of the questionnaire data.

Previous research has demonstrated enhanced visual-spatial abilities, such as superior performance on mental rotation tasks, in individuals with autism and in individuals with autistic features (Happé 1999; Mitchell & Ropar 2004; Caron et al., 2006; Falter et al. 2008; Grinter et al. 2009). These enhanced skills of individuals with autism may reflect a cognitive style that is unique to ASCs, one involving increased local relative to global processing (Happé 1999). More broadly, autistic islets of visual-spatial ability may stem from enhancements in primary perceptual functions in ASCs; importantly, these perceptual alterations may underlie the social and communication features viewed as central to the spectrum (Mottron et al. 2006). Within the schizophrenia spectrum, mental rotation performance appears reduced and strongly affected by sex: on a classic mental
rotation task (Shepard & Metzler 1971), Jiménez et al. (2009) found that males with schizophrenia performed worse than females with schizophrenia and worse than the control groups, whereas females with and without schizophrenia did not differ significantly in their performance. In women only, Thakker and Park (2010) found that low negative schizotypy predicted slower rotation of 2-dimensional letters. In a large sample of adults with schizophrenia, Zhai et al. (2011) found that two SNPs associated with increased schizophrenia risk predicted reduced mental rotation performance in the clinical group. Taken together, enhanced performance on mental rotation tasks is associated with the autism spectrum whereas relatively-reduced performance on similar tasks may, at least somewhat, characterize aspects of the schizophrenia spectrum.

Atypical patterns of cerebral asymmetry likely play a role in schizophrenia aetiology, and several studies have reported decreased cerebral lateralization, as indexed by a handedness preference leaning toward mixed and non-right handedness, in both schizotypy and schizophrenia (Richardson 1994; Claridge et al. 1998; Chapman et al. 2011; Somers et al. 2009; Dragovic et al. 2005; Sommer et al. 2001). Mixed handedness appears to be particularly predictive of positive schizotypal features such as magical thinking and delusional beliefs (Preti et al. 2007; Nicholls et al. 2005; Barnett & Corballis 2002). In previous studies that used the Waterloo Handedness Questionnaire (WHQ; Steenhuis & Bryden, 1989) to examine hand preference in schizotypy and schizophrenia, Upadhyay et al. (2004) found an increased prevalence of mixed handedness in individuals with schizophrenia, and Bryson et al. (2009) reported that mixed handedness predicted magical ideation. In autism, studies have indicated ambiguous (no clear hand preference) handedness (Escalante-Mead et al., 2003); dissociation between hand skill and hand preference (McManus et al., 1992); and differences in handedness patterns as a function of specific autistic subtypes (Soper et al. 1986), but no clear patterns have emerged. Overall, handedness is a well-validated and easily assessed correlate of SSCs, especially for the positive dimensions of schizophrenia.

Most studies comparing ASCs with SSCs using psychometric data have focussed on single, specific predictions, rather than testing a set of alternative hypotheses. Here, we use autism and schizotypy questionnaires in addition to data from mental rotation performance and handedness preference to evaluate three hypotheses for the
relationship between the autism spectrum and the schizophrenia spectrum. This approach allows us to validate our interpretations of the relationship between autistic and schizotypal features in order to build explicit models of how the two disorder spectra may be related to one another at both aetiological and phenotypic levels.

Firstly, observations of distinct developmental trajectories for autism and schizophrenia (Kolvin, 1971) and the absence of evidence for an increased prevalence of schizophrenia in autistic populations (Volkmar & Cohen, 1991) have shaped the view that the aetiologies underlying the two disorders are independent (Rutter 1996). This perspective is implied by DSM IV categories that treat autism and schizophrenia as mutually exclusive diagnoses (APA 1994). Under this ‘independence’ model, we would expect that autistic features, as measured by scores on Baron-Cohen and colleagues (2001) Autism Quotient (AQ), should not be strongly positively associated with scores on aspects of schizotypy. Additionally, we would predict that mental rotation ability predicts autistic features whereas handedness predicts schizotypal features. From this perspective, any similarities between the two spectra may be attributable to different causal factors.

Secondly, shared phenotypes between autism and schizotypy could reflect overlapping aetiologies; as also suggested by recent genetic evidence interpreted as indicating shared risk factors between autism and schizophrenia (e.g. Ousley et al., 2007; Burbach & van der Zwaag 2009). Both spectra involve reduced performance across a range of social-cognitive abilities, including theory of mind and emotion recognition, as well as corresponding impairments in overall social functioning (Abdi & Sharma 2004; Brüne 2005; Sprong et al. 2007; van Rijn et al. 2008). By this ‘overlap’ model, if shared factors underlie the overlapping social alterations and impairments between autism and schizotypy, then autistic features and schizotypal features should show positive associations for those phenotypes specifically related to social interests and social functioning. Furthermore, we may predict that neither mental rotation performance or hand-preference associate uniquely with the questionnaire data.

Thirdly, Crespi and Badcock (2008) forwarded the ‘diametric disorders’ hypothesis, which places autism and schizotypy on opposite ends of an axis of social cognition. By this ‘diametric’ model, the phenotypes of autism spectrum centrally involve under-
developed social cognition, whereas positive schizophrenia spectrum phenotypes involve manifestations of over-developed social cognition, such as 'hyper-developed' theory of mind in paranoia or an exaggerated sense of self and agency in megalomania (Crespi and Badcock 2008). Under the diametric model, social deficits and abnormalities as assayed by psychometric data or psychological tests could manifest similarly (for example, as social withdrawal, disinterest, or skill reductions), but such similarities may reflect highly diverse or diametrically-different causes between ASCs and SSCs. The diametric model predicts that when variation due to general social deficits, alterations and abnormalities is removed, an autism-schizotypy phenotypic axis will emerge where autistic features negatively predict positive schizotypal features. Under the diametric model, we would also expect that the autism-positive schizotypy axis associates with both handedness and mental rotation, such that increasing schizotypy predicts reduced lateralization and increasing autism predicts increased mental rotation performance.

We evaluated predictions from the independent, overlap and diametric models through (1) examining the bivariate correlations between subscales of the AQ and a revised version of Raine and Benishay's (1995) brief Schizotypal Personality Questionnaire (SPQ-BR; Cohen et al. 2010), (2) performing a principal components analysis (PCA) on subscale scores from the AQ and SPQ-BR, and (3) relating the questionnaire data to strength of handedness and performance on a mental rotation task. Together, these analyses provide an unbiased assessment of the phenotypic structures of autism and schizotypy as measured using two of the primary questionnaires deployed in ongoing research, and they allow us to link neuropsychological correlates of either spectra with patterns of overlap between spectra. Additionally, this approach allows us to determine in particular if an autistic-positive schizotypy axis emerges, as predicted under the diametric model.
2.3. Methods

2.3.1. Sample

Data was collected from 605 undergraduate students (380 females and 225 males) at both University of Alberta and Simon Fraser University. As part of a larger collaborative project approved by ethics boards at both universities, data was collected in single sessions held over the course of two semesters at each institution.

2.3.2. Measures

We used the Autism Spectrum Quotient (AQ; Baron-Cohen et al., 2001) to measure the extent to which participants endorsed traits consistent with the autism spectrum. The AQ is a brief self-report questionnaire that provides a quantitative measure of autism-related psychological traits in adults of normal intelligence (Bishop et al. 2004; Woodbury-Smith et al. 2005; Hoekstra et al. 2008). A total of 50 questions assess autistic traits across five areas (10 questions per domain) which include: 1) social skills; 2) communication; 3) attention to detail; 4) attention switching; and 5) imagination. For the social skills and communication domains, either poor social skills and communication or the preference to be in non-social situations increases the participant’s score. Attention shifting tends to be less flexible in autism (Courchesne et al. 1994; Fletcher-Watson et al. 2006), so if participants describe their attention as focused or inflexible, they are scored by the questionnaire as ‘more autistic’. Similarly, individuals with autism tend to demonstrate heightened attention to detail and interest in activities requiring such resources (Shah & Frith 1993; O’Riordan et al. 2001; Baron-Cohen et al. 2009) and therefore, responses endorsing these attributes increase the AQ score. Responses are in a 4-point Likert-scale format ranging from ‘definitely agree’ to ‘definitely disagree’, and whenever participants mildly or strongly endorse a trait in the autistic direction, they score one point for that question (taking into account reverse-scored items) for a possible scoring range of 0 – 50.

Schizotypy was assessed using the Schizotypal Personality Questionnaire-Brief Revised (SPQ-BR; Cohen et al. 2010). This instrument is a revised version of the SPQ-Brief (Raine & Benishay 1995) and includes 32 items in a 5-point Likert-scale format with
response choices ranging from 'strongly disagree' to 'strongly agree'. Scores can range from 0 to 160 with increasing scores reflecting higher levels of schizotypy. Factor analysis on the SPQ-BR has supported seven subscales, which cluster satisfactorily into three or four super-ordinate factors. These three higher-order factors include cognitive-perceptual schizotypy, interpersonal schizotypy, and disorganized schizotypy; these factors map onto the positive, negative, and disorganized dimensions of schizophrenia as described above (Andreasen et al. 1995; Basso et al. 1998; Clark et al. 2010). Under the factor of cognitive-perceptual (positive) schizotypy, there are three subscales: magical thinking; unusual perceptions; and ideas of reference. For interpersonal (negative) schizotypy, the subscales include constricted affect and social anxiety. The disorganized factor includes eccentric behaviour and odd speech. This measure was chosen because it is brief, sensitive, and covers a broad range of schizotypal features.

We also gave subjects the Mental Rotation Test (MRT; Vandenburg & Kuse, 1978) and the Waterloo Handedness Questionnaire (WHQ; Steenhuis & Bryden, 1989) as these measures tap into cognitive and perceptual factors that likely underlie autistic and schizotypal symptomatology. The MRT is a timed 20-item test that requires participants to mentally rotate three-dimensional objects to choose one figure, out of four possible options, that correctly matches the target object. The WHQ is a 32-item questionnaire asking participants to identify which hand they use for a variety of tasks. Response choices range from strongly left to either hand to strongly right with overall scores ranging from -32 to +32. We used absolute values of WHQ scores to measure the strength of handedness irrespective of direction, given that strength is a moderate predictor of schizotypy (e.g. Somers et al., 2009).

2.3.3. Analysis

Data from Wakabayashi et al. (2012) were also included for use as a replication dataset; in this study, the authors gave the AQ and Raine's (1991) original 74-item SPQ to a large sample (n=662) of non-clinical adults. To provide an unbiased assessment of the phenotypic structure of the autism and schizotypy data, we performed a principal component analysis (PCA) on the AQ and the SPQ-BR, for the data collected here in addition to the data from Wakabayashi et al. (2012). Given that the AQ is scored on a different and smaller scale than the SPQ-BR, we a priori chose to use the correlation
matrix rather than the covariance matrix in the PCA; therefore, the factor loadings are expected to be lower and more similar to one another compared to output using covariance matrix and additional rotations. All analyses were performed in R.

2.4. Results

Data were analyzed from 605 participants (380 females and 225 males) with a mean age of 19.4 years. The majority of study subjects identified their ethnicity as Western European descent (87%), and ethnicity did not demonstrate significant effects in any of the following analyses. A summary of descriptive statistics and sex differences for the four measures (AQ, SPQ-BR, MRT, WHQ) is presented in Table 2.1.

Table 2.1. Sex differences in the AQ, SPQ-BR, MRT, and WHQ

<table>
<thead>
<tr>
<th>Measure</th>
<th>Males (n=225)</th>
<th>Females (n=380)</th>
<th>Welch's t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean</td>
<td>S.D.</td>
<td>mean</td>
</tr>
<tr>
<td>AQ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social skills</td>
<td>2.57</td>
<td>1.68</td>
<td>2.44</td>
</tr>
<tr>
<td>Attention switching</td>
<td>4.94</td>
<td>2.10</td>
<td>4.63</td>
</tr>
<tr>
<td>Attention to detail</td>
<td>5.40</td>
<td>2.29</td>
<td>5.38</td>
</tr>
<tr>
<td>Communication</td>
<td>2.52</td>
<td>1.93</td>
<td>2.11</td>
</tr>
<tr>
<td>Imagination</td>
<td>2.51</td>
<td>1.70</td>
<td>2.11</td>
</tr>
<tr>
<td>Total AQ</td>
<td>17.93</td>
<td>5.84</td>
<td>16.66</td>
</tr>
<tr>
<td>Social anxiety</td>
<td>11.17</td>
<td>3.64</td>
<td>10.64</td>
</tr>
<tr>
<td>Constricted affect</td>
<td>15.38</td>
<td>4.87</td>
<td>13.98</td>
</tr>
<tr>
<td>Interpersonal</td>
<td>26.56</td>
<td>7.22</td>
<td>24.62</td>
</tr>
<tr>
<td>Eccentric behaviour</td>
<td>12.45</td>
<td>3.97</td>
<td>11.11</td>
</tr>
<tr>
<td>Odd speech</td>
<td>9.85</td>
<td>2.28</td>
<td>10.22</td>
</tr>
<tr>
<td>Disorganized</td>
<td>22.30</td>
<td>5.27</td>
<td>21.33</td>
</tr>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>----------------------</td>
<td>------</td>
<td>-----</td>
<td>------</td>
</tr>
<tr>
<td>Magical thinking</td>
<td>7.58</td>
<td>3.36</td>
<td>8.23</td>
</tr>
<tr>
<td>Unusual perceptions</td>
<td>10.33</td>
<td>3.21</td>
<td>9.52</td>
</tr>
<tr>
<td>Ideas of references</td>
<td>17.22</td>
<td>4.31</td>
<td>16.60</td>
</tr>
<tr>
<td>Cognitive-perceptual</td>
<td>35.14</td>
<td>7.85</td>
<td>34.35</td>
</tr>
<tr>
<td><strong>Total SPQ-BR</strong></td>
<td>83.99</td>
<td>15.12</td>
<td>80.29</td>
</tr>
<tr>
<td>MRT</td>
<td>12.62</td>
<td>5.00</td>
<td>9.11</td>
</tr>
<tr>
<td>WHQ*</td>
<td>34.08</td>
<td>21.72</td>
<td>36.71</td>
</tr>
</tbody>
</table>

*The WHQ ranges from -64 to +64 with negative values indicating left-handedness and positive values indicating right-handedness. Higher values indicate stronger handedness bias and values closer to 0 indicate mixed handedness.

Total AQ score was positively and significantly correlated with total SPQ-BR score in males, females, and in both sexes when analyzed together (Table 2.2, 2.3, 2.4). This positive relationship between the AQ and the SPQ-BR was consistent for most of the subscales (indicated by grey shaded areas in Tables 2.2, 2.3, & 2.4). Of the AQ scales that deviated from this general pattern, attention to detail was negatively correlated with SPQ-BR odd speech in females only, and imagination was negatively correlated with SPQ-BR magical thinking in males and in both sexes when analyzed together.
Table 2.2. Correlation coefficients between AQ and SPQ-BR in females and males

<table>
<thead>
<tr>
<th>Measures</th>
<th>Social skills</th>
<th>Attention switching</th>
<th>Attention to detail</th>
<th>Communication</th>
<th>Imagination</th>
<th>Total AQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social anxiety</td>
<td>0.50***</td>
<td>0.41***</td>
<td>0</td>
<td>0.42***</td>
<td>0.17***</td>
<td>0.5***</td>
</tr>
<tr>
<td>Constricted affect</td>
<td>0.41***</td>
<td>0.14***</td>
<td>0.03</td>
<td>0.39***</td>
<td>0.15***</td>
<td>0.37***</td>
</tr>
<tr>
<td>Interpersonal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constricted affect</td>
<td>0.53***</td>
<td>0.3***</td>
<td>0.02</td>
<td>0.47***</td>
<td>0.18***</td>
<td>0.5***</td>
</tr>
<tr>
<td>Eccentric behaviour</td>
<td>0.25***</td>
<td>0.13**</td>
<td>0.12**</td>
<td>0.34***</td>
<td>0.04</td>
<td>0.3***</td>
</tr>
<tr>
<td>Odd speech</td>
<td>0.12**</td>
<td>0.17***</td>
<td>-0.04</td>
<td>0.24***</td>
<td>-0.03</td>
<td>0.16***</td>
</tr>
<tr>
<td>Disorganized</td>
<td>0.24***</td>
<td>0.17***</td>
<td>0.07</td>
<td>0.35***</td>
<td>0.01</td>
<td>0.29***</td>
</tr>
<tr>
<td>Magical thinking</td>
<td>-0.04</td>
<td>0</td>
<td>0.1*</td>
<td>0.01</td>
<td>-0.1**</td>
<td>0</td>
</tr>
<tr>
<td>Unusual perceptions</td>
<td>0.07</td>
<td>0.14***</td>
<td>0.11**</td>
<td>0.17***</td>
<td>-0.04</td>
<td>0.16***</td>
</tr>
<tr>
<td>Ideas of reference</td>
<td>0.16***</td>
<td>0.26***</td>
<td>0.09*</td>
<td>0.26***</td>
<td>0.06</td>
<td>0.29***</td>
</tr>
<tr>
<td>Cognitive-perceptual</td>
<td>0.09*</td>
<td>0.19***</td>
<td>0.13***</td>
<td>0.2***</td>
<td>-0.03</td>
<td>0.21***</td>
</tr>
<tr>
<td>Total SPQ-BR</td>
<td>0.36***</td>
<td>0.29***</td>
<td>0.1*</td>
<td>0.43***</td>
<td>0.07</td>
<td>0.43***</td>
</tr>
</tbody>
</table>

*Significance at < 0.05   **< 0.01   ***< 0.001. Grey shaded area indicates significant positive correlations and bold values indicate significant negative correlations.
Table 2.3. Correlation coefficients between AQ and SPQ-BR in males

<table>
<thead>
<tr>
<th>Measures</th>
<th>Social skills</th>
<th>Attention switching</th>
<th>Attention to detail</th>
<th>Communication</th>
<th>Imagination</th>
<th>Total AQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social anxiety</td>
<td>0.55***</td>
<td>0.43***</td>
<td>0.01</td>
<td>0.37***</td>
<td>0.24***</td>
<td>0.51***</td>
</tr>
<tr>
<td>Constricted affect</td>
<td>0.41***</td>
<td>0.14*</td>
<td>0.06</td>
<td>0.33***</td>
<td>0.15*</td>
<td>0.34***</td>
</tr>
<tr>
<td>Interpersonal</td>
<td>0.55***</td>
<td>0.31***</td>
<td>0.04</td>
<td>0.40***</td>
<td>0.22**</td>
<td>0.48***</td>
</tr>
<tr>
<td>Eccentric behaviour</td>
<td>0.24***</td>
<td>0.21**</td>
<td>0.27***</td>
<td>0.37***</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>Odd speech</td>
<td>0.06</td>
<td>0.25***</td>
<td>0.13*</td>
<td>0.21**</td>
<td>-0.02</td>
<td>0.22***</td>
</tr>
<tr>
<td>Disorganized</td>
<td>0.2**</td>
<td>0.27***</td>
<td>0.26***</td>
<td>0.36***</td>
<td>0.02</td>
<td>0.38***</td>
</tr>
<tr>
<td>Magical thinking</td>
<td>-0.12</td>
<td>0</td>
<td>0.12</td>
<td>-0.05</td>
<td>-0.16*</td>
<td>-0.05</td>
</tr>
<tr>
<td>Unusual perceptions</td>
<td>0.03</td>
<td>0.12</td>
<td>0.14*</td>
<td>0.07</td>
<td>-0.05</td>
<td>0.11</td>
</tr>
<tr>
<td>Ideas of reference</td>
<td>0.20**</td>
<td>0.30***</td>
<td>0.11</td>
<td>0.26***</td>
<td>0.01</td>
<td>0.30***</td>
</tr>
<tr>
<td>Cognitive-perceptual</td>
<td>0.08</td>
<td>0.21**</td>
<td>0.17*</td>
<td>0.14*</td>
<td>-0.08</td>
<td>0.19**</td>
</tr>
<tr>
<td>Total SPQ-BR</td>
<td>0.36***</td>
<td>0.34***</td>
<td>0.19**</td>
<td>0.38***</td>
<td>0.07</td>
<td>0.45***</td>
</tr>
</tbody>
</table>

*Significance at < 0.05 **< 0.01 ***< 0.001. Grey shaded area indicates significant positive correlations and bold values indicate significant negative correlations.
Table 2.4. Correlation coefficients between AQ and SPQ-BR in females

<table>
<thead>
<tr>
<th>Measures</th>
<th>Social skills</th>
<th>Attention switching</th>
<th>Attention to detail</th>
<th>Communication</th>
<th>Imagination</th>
<th>Total AQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social anxiety</td>
<td>0.47***</td>
<td>0.40***</td>
<td>0</td>
<td>0.44***</td>
<td>0.11*</td>
<td>0.50***</td>
</tr>
<tr>
<td>Constricted affect</td>
<td>0.41***</td>
<td>0.13*</td>
<td>0.02</td>
<td>0.41***</td>
<td>0.12*</td>
<td>0.37***</td>
</tr>
<tr>
<td>Interpersonal</td>
<td>0.52***</td>
<td>0.29***</td>
<td>0.01</td>
<td>0.50***</td>
<td>0.14**</td>
<td>0.50***</td>
</tr>
<tr>
<td>Eccentric behaviour</td>
<td>0.26***</td>
<td>0.05</td>
<td>0.01</td>
<td>0.30***</td>
<td>0</td>
<td>0.22***</td>
</tr>
<tr>
<td>Odd speech</td>
<td>0.15**</td>
<td>0.14**</td>
<td>-0.14**</td>
<td>0.27***</td>
<td>-0.02</td>
<td>0.14**</td>
</tr>
<tr>
<td>Disorganized</td>
<td>0.26***</td>
<td>0.10*</td>
<td>-0.05</td>
<td>0.34***</td>
<td>0</td>
<td>0.22***</td>
</tr>
<tr>
<td>Magical thinking</td>
<td>0</td>
<td>0</td>
<td>0.09</td>
<td>0.06</td>
<td>-0.06</td>
<td>0.04</td>
</tr>
<tr>
<td>Unusual perceptions</td>
<td>0.09</td>
<td>0.14**</td>
<td>0.09</td>
<td>0.22***</td>
<td>-0.06</td>
<td>0.17***</td>
</tr>
<tr>
<td>Ideas of reference</td>
<td>0.13*</td>
<td>0.24***</td>
<td>0.08</td>
<td>0.25***</td>
<td>-0.07</td>
<td>0.28***</td>
</tr>
<tr>
<td>Cognitive-perceptual</td>
<td>0.1</td>
<td>0.17***</td>
<td>0.11*</td>
<td>0.23***</td>
<td>0</td>
<td>0.22***</td>
</tr>
<tr>
<td>Total SPQ-BR</td>
<td>0.36***</td>
<td>0.25***</td>
<td>0.04</td>
<td>0.45***</td>
<td>0.05</td>
<td>0.41***</td>
</tr>
</tbody>
</table>

*Significance at < 0.05  **< 0.01  ***< 0.001. Grey shaded area indicates significant positive correlations and bold values indicate significant negative correlations.

A principal components analysis (PCA) was performed using the R `prcomp` function on the correlation matrix of scores for the five subscales of the AQ (social skills, attention switching, attention to detail, communication, and imagination) and the seven subscales of the SPQ-BR (social anxiety, constricted affect, eccentric behaviour, magical thinking, unusual perceptions, and ideas of reference). Given that the AQ is scored on a smaller scale than the SPQ-BR, we chose to standardize the data by using the correlation matrix rather than the covariance matrix. We included the seven subscales of the SPQ-BR in the PCA rather than their higher-order factors (positive/cognitive-perceptual, negative/interpersonal, disorganized) because collapsing the subscales together would obscure the contributions of specific subscales (e.g. magical thinking) that demonstrated unique associations with the AQ in the correlation tests; this decision allowed for a finer-grained analysis in addition to providing output that builds upon the factor analysis on AQ and O-LIFE data in Russell-Smith and colleagues (2011).
The patterns and strengths of loadings for principal components 1 (PC1) and 2 (PC2) were directly interpretable, so we chose not to perform any rotations on the components: loadings greater than 0.30 were considered relatively strong. Table 2.5 shows the loadings of each subscale on components 1 and 2 for both sexes combined; we performed sex-specific PCAs as well, but the differences between females and males were minor, so we chose to include and interpret the combined sex PCA only. PC1 demonstrated positive loadings with both AQ and the SPQ-BR domains, and accounted for 29.2% of the variance, whereas PC2 included positive and negative loadings from both questionnaires, and accounted for 14.7% of the variance. Given that each of the remaining components explained a small quantity of the total variation (< 8%) and that we did not make any predictions concerning their interpretation, only PC1 and PC2 are included in Table 2.5 and considered here. Males scored significantly higher than females on PC1 ($x_{\text{males}} = 0.33$, $x_{\text{females}} = -0.14$; $t = 3.15$, df = 472.92, $p = 0.002$). Females scored slightly higher than males on PC2 ($x_{\text{females}} = 0.076$, $x_{\text{males}} = -0.079$) but this difference did not approach statistical significance ($t = -1.37$, df = 454.52, $p = 0.16$).

**Table 2.5. Principal components 1 and 2 loadings for males and females**

<table>
<thead>
<tr>
<th>Measure</th>
<th>PC1 (29.2%)</th>
<th>PC2 (14.7%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AQ</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social skills</td>
<td>0.334</td>
<td>-0.364</td>
</tr>
<tr>
<td>Attention switching</td>
<td>0.269</td>
<td>-0.205</td>
</tr>
<tr>
<td>Attention to detail</td>
<td>0.040</td>
<td>0.166</td>
</tr>
<tr>
<td>Communication</td>
<td>0.364</td>
<td>-0.242</td>
</tr>
<tr>
<td>Imagination</td>
<td>0.132</td>
<td>-0.349</td>
</tr>
<tr>
<td>Social anxiety</td>
<td>0.390</td>
<td>-0.177</td>
</tr>
<tr>
<td>Constricted affect</td>
<td>0.346</td>
<td>-0.072</td>
</tr>
<tr>
<td>Eccentric behaviour</td>
<td>0.338</td>
<td>0.188</td>
</tr>
<tr>
<td>SPQ-BR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Odd speech</td>
<td>0.273</td>
<td>0.273</td>
</tr>
<tr>
<td>Magical thinking</td>
<td>0.129</td>
<td>0.488</td>
</tr>
<tr>
<td>Unusual perceptions</td>
<td>0.278</td>
<td>0.412</td>
</tr>
<tr>
<td>Ideas of reference</td>
<td>0.331</td>
<td>0.251</td>
</tr>
</tbody>
</table>
PC1 demonstrated relatively strong (> 0.30) positive loadings for two of the AQ subscales (social skills and communication) and for four of the SPQ-BR subscales (social anxiety, constricted affect, eccentric behaviour, and ideas of reference). PC2 included relatively strong negative loadings from two of the AQ subscales (social skills and imagination) and strong (> 0.40) positive loadings from two of the seven SPQ-BR subscales (magical thinking and unusual perceptions). Most of the AQ subscales and SPQ-BR subscales were positively related and a few were negatively related. The positive correlations between several of the AQ and SPQ-BR subscales are reflected in the PCA output; PC1 demonstrated positive loadings from several domains, with the strongest loadings from subscales related to social and communicative functioning (AQ: communication, social skills; SPQ-BR: social anxiety, constricted affect, eccentric behaviour, ideas of reference). These results are inconsistent with independence between autistic and schizotypal features as assayed by these metrics.

For all loadings stronger than 0.30 on PC2, subscales from the AQ loaded negatively and subscales from the SPQ-BR loaded positively. Given that the SPQ-BR subscales that loaded oppositely to AQ subscales were all from the positive/cognitive-perceptual schizotypy factor, the pattern of PC2 loadings could be interpreted as an axis where aspects of positive schizotypy diametrically oppose autistic features. Consistent with this interpretation is the finding that PC2 was negatively associated with total AQ score (r = -0.43, p < 0.0001) and positively associated with total SPQ-BR score (r = 0.32, p < 0.0001). This pattern is captured in Figure 2.1.
Figure 2.1. Plot of AQ scores versus SPQ-BR scores with point size indicating relative PC2 score (point size increases as PC2 score increases).

PCA results for the AQ and SPQ data from Wakabayashi et al. (2012) were similar to our PCA results (Table 2.6). The first component explained 28% of the variance and indicated relatively-strong positive loadings for AQ social skills, attention switching, and communication and for SPQ social anxiety, constricted affect, no close friends. The second component accounted for 16.8% of the variance and demonstrated negative loadings for all AQ subscales (except for attention to detail) though none of these subscales met the 0.30 cut-off for strong loadings. Like our PCA results however, the strongest negative loadings from the AQ on the second component were social skills and imagination, contrasting with strong (> 0.40) and relatively-strong (> 0.30) positive
loadings for subscales belonging to positive/cognitive-perceptual schizotypy (in order of strength: ideas of reference, unusual perceptions, and magical thinking).

<table>
<thead>
<tr>
<th>Measure</th>
<th>PC1 (28%)</th>
<th>PC2 (16.8%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AQ Social skills</td>
<td>0.364</td>
<td>-0.275</td>
</tr>
<tr>
<td>Attention switching</td>
<td>0.326</td>
<td>-0.045</td>
</tr>
<tr>
<td>Attention to detail</td>
<td>0.082</td>
<td>0.286</td>
</tr>
<tr>
<td>Communication</td>
<td>0.371</td>
<td>-0.130</td>
</tr>
<tr>
<td>Imagination</td>
<td>0.268</td>
<td>-0.222</td>
</tr>
<tr>
<td>Social anxiety</td>
<td>0.330</td>
<td>-0.024</td>
</tr>
<tr>
<td>Constricted affect</td>
<td>0.334</td>
<td>-0.127</td>
</tr>
<tr>
<td>No close friends*</td>
<td>0.345</td>
<td>-0.162</td>
</tr>
<tr>
<td>Suspiciousness**</td>
<td>0.262</td>
<td>0.295</td>
</tr>
<tr>
<td>SPQ (Raine 1991)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eccentric behaviour</td>
<td>0.205</td>
<td>0.246</td>
</tr>
<tr>
<td>Odd speech</td>
<td>0.195</td>
<td>0.230</td>
</tr>
<tr>
<td>Magical thinking</td>
<td>-0.031</td>
<td>0.394</td>
</tr>
<tr>
<td>Unusual perceptions</td>
<td>0.146</td>
<td>0.409</td>
</tr>
<tr>
<td>Ideas of reference</td>
<td>0.186</td>
<td>0.456</td>
</tr>
</tbody>
</table>

*Contributes to interpersonal schizotypy. **Contributes to both interpersonal and cognitive-perceptual schizotypy. SPQ (Raine 1991) has 2 more subscales than the SPQ-BR, for a total of 9 subscales.

2.4.1. **Autism, Schizotypy, and Mental Rotation**

The questionnaire results were then tested for association with scores on the mental rotation task (MRT), given that previous research has provided evidence for enhanced MRT performance in individuals with autism and in individuals with autistic features (e.g. Falter et al. 2008). We found that total AQ score, as well as social skills, positively predicted MRT score in both sexes, though the positive correlation between MRT and total AQ score was driven by males (Table 2.7). AQ attention switching and MRT score were also positively associated, in males only. We found positive correlations of MRT
performance with negative/interpersonal and disorganized schizotypy and negative associations of MRT score with ideas of reference (in females) and magical thinking (in males) (Table 2.7). PC1 demonstrated a significant positive correlation with MRT score in both sexes, though males drove this effect. PC2 was not related to MRT performance (Table 2.8).

2.4.2. Autism, Schizotypy, and Strength of Handedness

Mixed or ambiguous handedness predicts schizotypy and schizophrenia, particularly positive schizotypy (e.g. Bryson et al. 2009) and as such, we tested for associations of handedness strength with both SPQ-BR and AQ scores. Because one of the four study cohorts did not complete the Waterloo Handedness Questionnaire (WHQ), the sample size for all analyses using this data is n = 504 (316 females & 188 males). The distribution of WHQ scores was strongly skewed, so we used a Kendall's rank correlation test for all following analyses. Consistent with previous research, total SPQ-BR score, as well as all three subtypes of schizotypy (interpersonal/negative, disorganized, and cognitive-perceptual/positive), were significantly and negatively associated with strength of handedness (Table 2.7). Handedness strength did not demonstrate any correlations with the AQ (Table 2.7). PC2 was negatively associated with strength of handedness (Table 2.8).
### Table 2.7. Correlation coefficients of AQ and SPQ-BR with mental rotation and absolute handedness

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mental Rotation Score</th>
<th>Absolute WHQ Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>males</td>
<td>females</td>
</tr>
<tr>
<td><strong>AQ</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social skills</td>
<td>0.107</td>
<td>0.091</td>
</tr>
<tr>
<td>Attention switching</td>
<td>0.146*</td>
<td>-0.062</td>
</tr>
<tr>
<td>Attention to detail</td>
<td>0.049</td>
<td>0.031</td>
</tr>
<tr>
<td>Communication</td>
<td>0.047</td>
<td>-0.014</td>
</tr>
<tr>
<td>Imagination</td>
<td>-0.020</td>
<td>0.002</td>
</tr>
<tr>
<td><strong>Total AQ</strong></td>
<td>0.112</td>
<td>0.016</td>
</tr>
<tr>
<td><strong>SPQ-BR</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social anxiety</td>
<td>0.112</td>
<td>0.014</td>
</tr>
<tr>
<td>Constricted affect</td>
<td>-0.010</td>
<td>0.032</td>
</tr>
<tr>
<td>Interpersonal</td>
<td>0.052</td>
<td>0.029</td>
</tr>
<tr>
<td>Eccentric behaviour</td>
<td>0.147*</td>
<td>0.131**</td>
</tr>
<tr>
<td>Odd speech</td>
<td>0.041</td>
<td>0.037</td>
</tr>
<tr>
<td>Disorganized</td>
<td>0.127*</td>
<td>0.111*</td>
</tr>
<tr>
<td>Magical thinking</td>
<td>-0.181**</td>
<td>-0.052</td>
</tr>
<tr>
<td>Unusual perceptions</td>
<td>0.073</td>
<td>-0.016</td>
</tr>
<tr>
<td>Ideas of references</td>
<td>0.033</td>
<td>0.114*</td>
</tr>
<tr>
<td>Cognitive-perceptual</td>
<td>-0.028</td>
<td>-0.087</td>
</tr>
<tr>
<td><strong>Total SPQ-BR</strong></td>
<td>0.053</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*Significance at < 0.05 **< 0.01 ***< 0.001. All handedness correlation coefficients are Kendall's tau.
Table 2.8. Correlation coefficients of PC1 and PC2 with mental rotation and absolute handedness

<table>
<thead>
<tr>
<th>Component</th>
<th>Measure</th>
<th>MRT score (n=605)</th>
<th>Absolute WHQ score (n=504)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>males</td>
<td>females</td>
</tr>
<tr>
<td>PC1</td>
<td></td>
<td>0.13*</td>
<td>0.03</td>
</tr>
<tr>
<td>PC2</td>
<td></td>
<td>0.05</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*Significance at < 0.05  **< 0.01. All handedness coefficients are Kendall's tau. Sample sizes differ as not all participants completed WHQ.

2.5. Discussion

This study examined autistic and schizotypal features in relation to each other and to mental rotation performance and handedness strength in a large non-clinical sample to test specific predictions from the independent, overlap, and diametric models for the relationship between ASCs and SSCs. Drawing from correlation tests and PCA results, we found support consistent with both the overlapping and diametric models, and no evidence for the model of independence. Overall, our results are consistent with previous research indicating a large degree of phenotypic overlap between autism and schizotypy, and novel in revealing preliminary support for an autism-positive schizotypy phenotypic axis, but only after the effects of general social alterations and abnormalities are removed.

In accordance with results from several previous studies (Hurst et al. 2007; Russell-Smith et al. 2011), we found evidence indicating considerable overlap between autistic and schizotypal features that are related to interest and aptitude in social and communicative functioning. Autistic-like communication and social skills were most strongly and positively associated with interpersonal (negative) schizotypy, followed by disorganized schizotypy. These positive correlations were evident in PC1: this component included relatively-strong (> 0.30) positive loadings from subscales of both the AQ and the SPQ-BR, and the strongest loadings were found for social skills, communication, social anxiety, constricted affect, eccentric behaviour, and ideas of...
reference. Consistent with both the overlapping and diametric models, we interpreted PC1 as a factor indicating general social-communicative disinterest, impairments and abnormalities. The subscale *attention to detail* demonstrated a different pattern of loadings in comparison to the other AQ subscales (very low and positive on PC1, moderately-low and positive on PC2). According to Baron-Cohen et al. (2001), *attention to detail* measures a person's tendency and preference to focus on and recall local rather than global details (e.g. Item 5: “I notice small sounds when others do not”). Detail-oriented attention may be a separate dimension of autism, relatively independent of general social skills and autistic-typal imagination.

The overlap between autistic and schizotypal features evidenced in PC1 is consistent with the high degree of conceptual, diagnostic, and phenotypic overlap observed between the broader social phenotypes of autism and schizophrenia, especially between Asperger's syndrome and schizoid personality in childhood and/or schizotypal personality disorder (SPD) (Rapoport et al. 2009; Tantam 1988; Wolff 2000). Both Asperger's syndrome and SPD are characterized by reduced social abilities, odd or eccentric social behaviour, mental rigidity, and unusual communication, which has led to questions whether these two higher-functioning forms of disorder represent discrete or overlapping conditions (Wolff 2000). Given that altered social functioning may involve a diversity of complex causes, evidence for shared behavioural phenotypes involving weaknesses or general abnormalities has limited ability to explain how or why such similarities exist (e.g., Sasson et al., 2011). Future research investigating patterns of similarities and differences in the specific nature of social abnormalities between ASCs and SSCs will be useful in further understanding the relationship between these sets of conditions. For example, Konstantareas & Hewitt (2001) observed thought disorder in both high-functioning autism and paranoid schizophrenia, but they described the disordered thoughts of individuals with autism as relatively immature in comparison to the complex and bizarre thoughts of the subjects with schizophrenia. Indeed, the overlap between autistic social-communicative deficits and schizotypal interpersonal features may reflect the insensitivity of psychological questionnaires to pick up on the subtle differences in the nature of the social alterations that may be characteristic of each spectrum. Our findings and these considerations are not inconsistent, however,
with the hypothesis that the presence of social deficits contributes to risk or expression of both autism spectrum and schizophrenia spectrum conditions.

The diametric model and the overlapping model do not diverge in their predictions with respect to PC1, but the models differ in their explanation for the causes underlying the similarity: the overlapping model suggests that shared causal factors underlie the social traits common to both the autism spectrum and schizophrenia spectrum, whereas the diametric model suggests that opposite causal factors lead, to some degree, to general social phenotypes that present similarly enough to show strong correlations. Under the diametric model, the overlap evidenced by the bivariate correlations and PC1 need not reflect shared causal factors, but rather may indicate that autism and schizotypy involve social deficits and abnormalities due to different causes. By this hypothesis, social deficits and abnormalities in autism may represent central, underlying causes of the autism-related traits, whereas social deficits and abnormalities in schizotypy (and, by extension, in schizophrenia) may predominantly represent effects of the neuropsychological alterations that characterize the schizophrenia spectrum, including paranoia, alterations to regulation of affect, social ambivalence, social anhedonia, delusions with social content, and ideas of reference, as well as impaired social cognition due to general cognitive deficits and disorganized thought processes. Some of these psychological alterations, especially paranoia, delusions, and ideas of reference, involve aspects of hyper-mentalizing (Abu-Akel 1999; Badcock 2004) and illustrate how peculiar social behaviour and social withdrawal in schizophrenia may result from causes that are diametric to those underlying autistic social deficits, which are present from early childhood and are associated with other phenotypes (such as resistance to change, detail-focussed attention, and visual-spatial abilities enhanced relative to verbal skills), as described by Kanner (1943) and summarized in Crespi (2011).

Consistent with a prediction specific to the diametric model, we found evidence suggestive of a phenotypic axis of autism-schizotypy (PC2), after removing apparent general social-deficit and abnormality variation measured by both questionnaires and quantified by PC1. Based on the pattern of PC2 loadings, this autism-schizotypy axis appears to reflect a diametric pattern between autistic features and positive aspects of schizotypy, especially magical thinking and unusual perceptions. The presence of such as axis was consistent with the finding that PC2 was negatively associated with absolute
strength of handedness across individuals, such that increased PC2 scores (in the 'schizotypal' direction) predicted reduced lateralization. This effect was very small, with correlation coefficients around 0.08, though this is similar to other findings in handedness research (e.g. Shaw et al. 2001). Additional tests for associations of PC2 scores with variables that are well-established correlates of schizophrenia, schizotypy, and autism will be useful in further evaluating the hypothesis that this score quantifies an axis from autism spectrum, to normality, to positive schizotypy. Also, future studies could perform confirmatory factor approaches on psychometric data to explicitly test the fit of a diametric model versus overlap model on such data.

We compared questionnaire scores to performance on a mental rotation task, and did not find a relationship between MRT score and PC2 scores, as we would expect under the diametric model. However, PC1 was significantly and positively related to MRT score across the entire sample, though analyzing the sexes separately indicated that males drove this effect. Autistic and schizotypal subscales that also positively predicted MRT included: social skills; attention switching (males only); total AQ score (significant in entire sample, though driven by males); interpersonal (negative) schizotypy; and disorganized schizotypy. Taken together, these results suggest that enhanced mental rotation skills are associated with reduced social-communicative functioning; this is an interesting finding that may be explicable in the context of trade-offs between different types of cognitive systems (e.g. empathizing and systemizing; Nettle 2007) or trade-offs between verbal compared to visual-spatial skills more generally (Jarrold et al. 2000; Johnson & Bouchard 2007). This link between altered social skills and enhanced visual-spatial ability warrants further investigation, especially with respect to sex-specific effects.

The primary limitations of our study are the use of undergraduate samples, which may not be characteristic of the population at large, and the relatively low magnitudes of some of the correlation coefficients. Additionally, while high in its utility, self-report data is limited in its ability to provide a detailed picture of the relationship between autism and schizotypy. Given the growing body of evidence from psychometric data that consistently indicates phenotypic overlap between ASCs and SSCs, it will be useful for future research to turn toward genetic and neuropsychological data in order to examine patterns of similarities and differences between the two spectra. However, based on our
results, the degree to which the overlapping social phenotypes of autism spectrum traits and schizotypy stem from diametric or overlapping causes remains an important question for future research. More generally, our results suggest that social-deficit and social-abnormality phenotypes, as assessed by scales such as the AQ and SPQ-BR, may have less usefulness in distinguishing between different psychological and psychiatric conditions than do 'positive' phenotypes, such as magical thinking, local-versus-global processing, or attention to detail (see Spek & Wouters 2010). In accordance with this approach, Russell-Smith and colleagues (2010) found that higher levels of autistic features predicted enhanced performance in local versus global information processing as assessed by the Embedded Figures Test (EFT; Witkin et al. 1971), whereas positive schizotypal features predicted reduced performance. Our results also highlight the value in testing predictions from alternative models for the relationship between autism and schizotypy, rather than focussing on a single model and its predictions.

2.6. References


3. The Borderline Empathy Paradox: Evidence and Conceptual Models for Empathic Enhancements in Borderline Personality Disorder

Natalie L. Dinsdale & Bernard J. Crespi

Journal of Personality Disorders, doi: 10.1521/pedi_2012_26_071

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3.1. Abstract

Empirical evidence and therapeutic interactions have suggested that individuals with borderline personality disorder (BPD) may demonstrate enhancements in aspects of social-emotional cognition. To assess the empirical evidence for this phenomenon, and to comprehensively evaluate alternative hypotheses for its possible role in BPD aetiology and symptoms, the authors systematically searched the literature for investigations of empathy in BPD and reviewed 28 studies assessing a range of empathic abilities. Considered together, these data demonstrated comparable levels of evidence for enhanced, preserved, and reduced empathic skills in individuals with BPD. Evidence for empathic enhancements is thus substantial but inconsistent across studies, being found mainly under more socially-interactive experimental paradigms. Based on the results of the review and previous explanations for BPD symptoms, the authors propose a new model for explaining the borderline paradox: that a combination of increased attention to social stimuli and dysfunctional social information processing may account in part for the specific empathic enhancements and reduced overall social functioning in BPD.
3.2. Introduction

Clinical anecdotes and recent empirical evidence have suggested that individuals with borderline personality disorder (BPD) may demonstrate enhanced empathy in spite of impaired interpersonal functioning, a paradox referred to as “borderline empathy” (Franzen et al., 2011; Krohn, 1974). Drawing from therapeutic interactions with borderline patients, the psychoanalyst Alan Krohn (1974) first identified the paradoxical nature of the diagnosis, describing how some individuals with BPD appear to possess an uncanny sensitivity to other people’s subconscious mental content and states, despite their inability to coherently integrate such information into stable concepts of self and other that are fundamental to healthy interpersonal functioning. Both Krohn (1974) and Carter and Rinsley (1977) proposed that enhanced empathic sensitivity develops in the borderline child in response to confusing or neglectful parenting, which motivates the child toward increased empathic functioning.

Aside from the models based on Krohn (1974), there have been few attempts to explain the causes underlying borderline empathy or its role in BPD aetiology and symptoms. This general lack of study may be attributable in part to the questions of whether or not the phenomenon actually exists, and furthermore, if it can be clearly and reliably documented and explained. Recent studies have reported both enhanced (e.g. Fertuck et al., 2009; Franzen et al., 2011; Frick et al. 2012) and impaired (e.g. Preißler, Dziobek, Ritter, Heekeren, & Roepke, 2010) social cognition in BPD, but the evidence for borderline empathy has yet to be comprehensively reviewed and evaluated in the context of alternative hypotheses for causation. In this article, we evaluate the existing evidence for enhanced empathy in BPD by systematically searching the literature and providing an overview of the relevant studies with consideration of their varying methodological approaches. We synthesize these findings in the context of current theories that address the roles of empathy in psychiatric illness, develop a new, testable hypothesis based on increased attention to social stimuli, and suggest directions for future research in BPD based on our findings and model.
3.3. Methods

Literature was reviewed using the online databases Web of Science and PubMed. For the purposes of this article, the term empathy refers to a range of skills that include both emotional and cognitive components (Gallup, 1979; Rankin, Kramer, & Miller, 2005; Singer, 2006; Smith, 2006). It is important to distinguish this definition of empathy and empathic skills from conceptualizations of empathy as positive social-emotional mental connections that foster cooperation, altruism, and wellbeing of the recipient (e.g. Baron-Cohen, 2011). Given the numerous definitions for describing empathizing and mentalizing in the literature, several search terms were used to ensure that all studies examining any domain of empathic skill were included. The following terms were chosen a priori and were searched in conjunction with “borderline personality disorder”: empathy; theory of mind; mentalizing; borderline empathy; and emotion recognition. All references and cited articles from the selected studies were reviewed to check for additional relevant articles. For inclusion, articles needed to empirically assess an interpersonal empathic skill (e.g. facial emotion recognition, mental state attribution, using the definition of empathy described above) or self-reported empathy in a borderline population compared to appropriate controls, or as a function of borderline features in a nonclinical sample. Because affective instability is a diagnostic criterion for BPD (American Psychiatric Association [APA], 2000), articles that assessed only affective regulation skills were excluded. Only peer-reviewed empirical studies were included; reviews, supplementary materials, and meeting abstracts were not.

3.4. Results

The literature search yielded 131 articles, of which 28 met the criteria for inclusion. These articles assessed various aspects of empathy and were organized into categories based on the ability under study and the methodological approach. The six categories included: (1) nonverbal sensitivity; (2) emotion recognition; (3) self-reported empathic skills; (4) emotional intelligence; (5) inferring mental states from passive stimuli such as photographs, movies, cartoons, and stories; and (6) mentalizing in interactions with active stimuli. One study (Harari et al. 2010) investigated both self-reported empathic
skills and mental state attribution from stimuli and was therefore included in both categories.

Table 3.1 summarizes the articles in each empathic category and the number of findings reporting enhanced, reduced, or comparable performance of borderline individuals relative to controls. Overall, the 28 studies employed 19 different empathic tests and reported 41 relevant findings: 14 reported enhanced skills, 13 reported reduced skills, and 14 reported similar skills. Evaluating the patterns and causes of variation among studies of empathy in BPD requires consideration of the procedures deployed and their findings in each category.

**Table 3.1. Evidence for Enhanced, Reduced, and Comparable Empathic Skills in BPD**

<table>
<thead>
<tr>
<th>Empathic Category</th>
<th>Study</th>
<th>Task</th>
<th>Subjects</th>
<th>BPD Performance Relative to Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Enhanced</td>
</tr>
<tr>
<td>Nonverbal sensitivity</td>
<td>n = 1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frank &amp; Hoffman, 1986</td>
<td>PONS²</td>
<td>10 BPD patients &amp; 14 non-BPD clinical controls (100% female)</td>
<td>$p &lt; .02$</td>
</tr>
<tr>
<td></td>
<td>Levine et al., 1997</td>
<td>PFA⁶</td>
<td>30 BPD patients (67% female) &amp; 30 nonclinical controls (50% females)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Wagner &amp; Linehan, 1999</td>
<td>JACFEE⁶</td>
<td>21 BPD subjects with history of sexual abuse &amp; 41 non-BPD subjects with and without history of abuse (100% female)</td>
<td></td>
</tr>
<tr>
<td>Emotion recognition</td>
<td>n = 11</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Bland et al., 2004</td>
<td>PFA</td>
<td>35 BPD patients &amp; 35 nonclinical controls (100% female)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Lynch et al., 2006</td>
<td>PFA</td>
<td>20 BPD patients (85% female) &amp; 20 nonclinical controls (85% female)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Minzenberg et al., 2006</td>
<td>PFA, BLERT⁴</td>
<td>43 BPD patients (88% female) &amp; 26 nonclinical controls (89% female)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Domes et al., 2008</td>
<td>PFA</td>
<td>25 BPD patients &amp; 25 nonclinical controls</td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Measure</td>
<td>BPD Sample</td>
<td>Nonclinical Controls</td>
<td>Comparison</td>
</tr>
<tr>
<td>-------</td>
<td>---------</td>
<td>------------</td>
<td>----------------------</td>
<td>------------</td>
</tr>
<tr>
<td>Dyck et al., 2009</td>
<td>FAN test&lt;sup&gt;a&lt;/sup&gt; ER Test&lt;sup&gt;f&lt;/sup&gt;</td>
<td>19 BPD patients (89% female) &amp; 19 nonclinical controls (89% female)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guitart-Masip et al., 2009</td>
<td>PFA</td>
<td>10 BPD patients (50% female) &amp; 10 nonclinical controls (50% female)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Merkl et al., 2010</td>
<td>PFA</td>
<td>11 BPD patients and 9 nonclinical controls (100% female)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gardner et al., 2010</td>
<td>PDQ-4-BPD&lt;sup&gt;3&lt;/sup&gt;, ATQ&lt;sup&gt;h&lt;/sup&gt;, PFA</td>
<td>150 nonclinical adults (70% females)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unoka et al., 2011</td>
<td>Ekman 60 Faces</td>
<td>33 BPD patients (88% female) &amp; 32 nonclinical controls (94% female)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Guttman &amp; Laporte, 2000</td>
<td>IRI&lt;sup&gt;i&lt;/sup&gt;</td>
<td>27 BPD patients &amp; 28 clinical controls &amp; 27 nonclinical controls (100% female)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Harari et al., 2010</td>
<td>IRI</td>
<td>20 BPD patients (90% female) &amp; 22 nonclinical controls (86% female)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Park et al., 1992</td>
<td>Derived from Gardner (1983)</td>
<td>23 BPD patients (78% female) &amp; 38 outpatients with other PD diagnoses (61% female)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hertel et al., 2009</td>
<td>MSCEIT&lt;sup&gt;j&lt;/sup&gt;</td>
<td>19 BPD female patients &amp; 66 clinical control (45% female) &amp; 94 nonclinical controls (67% female)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gardner &amp; Qualter, 2009</td>
<td>Multiple BPD measures, MSCEIT, SEIS&lt;sup&gt;k&lt;/sup&gt;</td>
<td>523 nonclinical adults (78% female)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study</td>
<td>Measure</td>
<td>Participants</td>
<td>p-value</td>
<td></td>
</tr>
<tr>
<td>-----------------------</td>
<td>------------------</td>
<td>------------------------------------------------------------------------------</td>
<td>--------------------</td>
<td></td>
</tr>
<tr>
<td>Beblo et al., 2010</td>
<td>MSCEIT, TEMINT</td>
<td>19 BPD patients (84% female) &amp; 20 nonclinical controls (85% female)</td>
<td>p = .264</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p = .10</td>
<td></td>
</tr>
<tr>
<td>Arntz et al., 2009</td>
<td>Advanced ToM</td>
<td>16 BPD patients &amp; 16 cluster-C PD subjects and 28 nonclinical controls (100% female)</td>
<td>p &lt; .07</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(Happé 1994)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fertuck et al., 2009</td>
<td>RMETn</td>
<td>30 BPD patients (87% female) &amp; 25 nonclinical controls (60% females)</td>
<td>p &lt; .001</td>
<td></td>
</tr>
<tr>
<td>Frick et al., 2012</td>
<td>RMET</td>
<td>21 BPD female patients &amp; 20 nonclinical female controls</td>
<td>p &lt; 0.01</td>
<td></td>
</tr>
<tr>
<td>Ghiassi et al., 2010</td>
<td>MSATn</td>
<td>50 BPD patients (92% female) &amp; 20 nonclinical controls (85% females)</td>
<td>p = ns</td>
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<tr>
<td>Harari et al., 2010</td>
<td>Faux-Pas Task</td>
<td>20 BPD patients (90% female) and nonclinical controls</td>
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<td>Preißler et al., 2010</td>
<td>MASC, RMET</td>
<td>64 BPD patients &amp; 38 nonclinical subjects (100% female)</td>
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<td>Scott et al., 2011</td>
<td>MSI-BPD, RMET</td>
<td>46 undergraduate students (76% females)</td>
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<td>Ladisch &amp; Fell, 1988</td>
<td>Gieben Test,</td>
<td>20 BPD patients &amp; 39 non-BPD psychiatric patients (sex composition not reported)</td>
<td>p &lt; .05</td>
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<td></td>
<td>Unpleasant Person</td>
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<td>Hierarchy Test</td>
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<td>Flury et al., 2008</td>
<td>Infer states</td>
<td>76 undergraduate students (61% female)</td>
<td>High BPD group more accurate, p &lt; .01</td>
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<td></td>
<td>of partner in</td>
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<td>dyadic interactions</td>
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<tr>
<td>Franzen et al., 2011</td>
<td>Simulated</td>
<td>30 BPD patients &amp; 30 non-clinical controls (73% female)</td>
<td>p &lt; 0.003</td>
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<td>monetary exchange</td>
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3.4.1. Non-verbal sensitivity

In the first study to explicitly investigate the borderline empathy phenomenon, Frank and Hoffman (1986) used the Profile of Nonverbal Sensitivity (PONS; Depaulo & Rosenthal, 1979) in a sample of 10 female borderline patients and 14 sex- and education-matched neurotic control subjects and reported that individuals with BPD demonstrated a heightened sensitivity to nonverbal cues relative to the clinical controls in the study.

3.4.2. Emotion recognition

Emotion recognition has received the most empirical attention of all empathic skills in borderline populations. Based on a review of six studies, Domes, Schulze, and Herpertz (2009) concluded that individuals diagnosed with BPD demonstrate subtle impairments in basic emotion recognition, a heightened sensitivity to detecting negative emotions, and a negativity bias when appraising ambiguous stimuli. Five of these six studies used similar facial stimuli (Pictures of Facial Affect; Ekman, 1993; Ekman & Friesen, 1976, 1979), so although the results may be reliable, they may not be generalizable to studies that employ tasks and stimuli more closely resembling realistic social interactions.

Dyck et al. (2009) assessed facial emotion recognition abilities in 19 borderline personality patients (17 females) with and without comorbid posttraumatic stress disorder and in sex-matched healthy controls using two different tasks with coloured facial stimuli (from Gur et al., 2002). The Fear Anger Neutral (FAN) test asks subjects to rapidly discriminate between negative and neutral facial expressions, and the Emotion Recognition (ER) test involves the precise identification of an emotion out of five possibilities (sadness, happiness, anger, fear, and neutral) with no time limits. When time was constrained, borderline subjects performed more poorly than did the control
group, misinterpreting neutral faces as negative significantly more often. In the absence of time limits, the borderline subjects performed as well as the controls, suggesting that individuals with BPD may process complexly integrated emotional stimuli more slowly than healthy controls; a similar conclusion was supported by Minzenberg, Poole, and Vinogradov (2006; reviewed in Domes et al., 2009).

Guitart-Masip et al. (2009) compared the emotion discrimination abilities of 10 patients with BPD (5 females) and 10 nonclinical sex-matched controls by presenting pairs of neutral and emotional faces (happiness, fear, disgust, anger) from the Ekman and Friesen (1979) series. Stimuli were presented for 700 ms and subjects were instructed to press a button corresponding to the emotional face. Patients demonstrated a reduced performance relative to controls when identifying fear and disgust but performed as well as control subjects for happy and angry faces. Similarly, Unoka, Fogd, Füzy, and Csukly (2011) investigated patterns of accuracy and error in emotion recognition using the Ekman 60 Faces test in 33 BPD inpatients (29 females) and 32 (30 females) matched healthy controls; BPD individuals did not demonstrate impairments in recognizing happy emotions, but did show reduced accuracy in discriminating negative emotions as well as a tendency to over-attribute surprise and disgust and under-attribute fear, compared with the control subjects. Conversely, in a sample of 11 females with BPD and 9 nonclinical female controls, Merkl et al. (2010) assessed facial expression recognition using Ekman's (1993) stimuli set and reported superior performance of borderline subjects in identifying fear.

Two of the articles investigating emotion recognition studied the relationship of these skills to borderline personality features in nonclinical populations; this kind of sampling method is particularly useful in revealing the skills and deficits associated with a borderline personality profile in the absence of significant interpersonal impairment. In a sample of 150 adults sampled from university students and the wider community (70% female), Gardner, Qualter, Stylianou, and Robinson (2010) reported a significant interaction between borderline features and executive control with respect to decoding angry facial expressions, such that high borderline features combined with low executive control predicted poor recognition of angry faces while high borderline features and high executive control predicted enhanced recognition of angry faces. Executive control describes the ability to regulate attentional resources and is often impaired in psychiatric
patients, including individuals with a BPD diagnosis (Ayduk et al., 2008). The interaction of borderline features with decreased attentional resources may thus be responsible for mediating deficits in emotion recognition in BPD.

3.4.3. **Self-reported empathy**

Two studies examined self-reported empathy in individuals with BPD using the Interpersonal Reactivity Index (IRI; Davis, 1980, 1983). Employed extensively in personality research, the IRI is a multidimensional self-report measure of empathy assessing the related but dissociable cognitive and affective components of empathic skill across four subscales: perspective taking; fantasy; empathic concern; and personal distress. Using this instrument, Guttman and Laporte (2000) reported reduced cognitive empathy and increased affective empathy in 27 females with BPD relative to clinical and nonclinical control subjects. In a sample of 20 individuals with BPD (18 females), Harari et al. (2010) found significantly reduced cognitive empathy but comparable levels of affective empathy in individuals with BPD relative to nonclinical controls.

3.4.4. **Emotional intelligence**

Four studies have measured emotional or personal intelligence in BPD; in these studies, the definitions of personal and emotional intelligence describe essentially identical skills. For example, emotional intelligence describes the capacity to perceive, understand, and regulate emotion in addition to using emotions to facilitate mental processes (Mayer & Salovey, 1997). Personal intelligence involves the ability to access one's emotions as well as the ability to perceive and distinguish among another person's motivations and intentions (Gardner, 1983).

Prompted by clinical accounts of the borderline empathy paradox, Park, Imboden, Park, Hulse, and Unger (1992) hypothesized that borderline individuals are endowed with enhanced personal intelligence that could interact with abusive childhood environments to play a key causal role in the development of BPD. To test this idea, the authors evaluated the personal intelligence and history of past abuse of 23 borderline patients (18 females) from their own clinical work and 38 outpatients with other personality disorder diagnoses. For the purpose of this study, Park et al. (1992) derived a rough
scale of personal intelligence from Gardner's (1983) research. Patients were categorized as "gifted" in the domain of personal intelligence if they clearly demonstrated at least three of the following: (1) intense preoccupation with and/or access to feelings of self and others; (2) at least three perceptive observations about other people as expressed during therapy sessions; (3) evidence of empathic concern; and (4) the absence of pervasive envy, grandiosity, or devaluation of others. Preoccupation with feelings was included because the authors reasoned that if individuals with BPD are indeed endowed with emotional giftedness, but these abilities are not realized due to poor environments, the giftedness may manifest as a drive to access and understand emotions. The authors reported that 74% of the borderline patients demonstrated both enhanced personal intelligence and a history of abuse, significantly greater than the 13% of the nonborderline controls. Though intriguing, these results must be interpreted cautiously because of the lack of independent validation for their method of assessing personal intelligence and the potential for clinician bias.

Beblo et al. (2010) assessed emotional intelligence in a sample of 19 borderline patients (16 females) and 20 nonclinical control subjects (17 females) using the Mayer-Salovey-Caruso emotional intelligence test (MSCEIT; Mayer, Salovey, & Caruso, 2002) and the Test of Emotional Intelligence (TEMINT; Schmidt-Atzert & Buehner, 2002). These tests assess performance in four domains of emotional intelligence (perceiving, understanding, and regulating emotion, and applying emotions to mental processes) across a variety of tasks. No difference between BPD individuals and control subjects was found for any domain of emotional intelligence. Using only the MSCEIT, Hertel, Shütz, and Lammers (2009) assessed emotional intelligence performance in 19 female borderline patients as well as other clinical and nonclinical individuals and reported a reduced overall emotional intelligence score of the borderline group relative to the nonclinical control group. Specifically, the borderline patients were reduced in their ability to understand emotional information and to regulate emotions, but they performed as well as the nonclinical controls in perceiving emotions and using emotions to facilitate thought. In contrast to Beblo et al. (2010), Hertel et al. (2009) did not control for general intelligence and therefore the reduced emotional intelligence performance of the BPD patients may be attributable to group differences in cognitive ability. Variation in
borderline symptom severity may also differentially affect emotional intelligence ability in these two studies, but there is insufficient data to evaluate this claim.

In a nonclinical sample of 523 adults (78% female), Gardner and Qualter (2009) studied the relationship of borderline personality features to both trait and ability emotional intelligence using the Schutte Emotional Intelligence Scale (SEIS; Schutte et al., 1998) and the MSCEIT, respectively. Most of the assessed borderline personality features negatively predicted MSCEIT scores for the abilities of understanding, managing, and facilitating emotions. The ability to perceive emotions was not related to BPD features. The overall SEIS score, which measures the trait-based ability to manage, perceive, and utilize emotions, was negatively related to borderline features.

3.4.5. Mentalization using passive stimuli

Given the recent interest in mentalization-based approaches to treating BPD (Fonagy & Luyten, 2009) and the availability of instruments from autism research for assessing theory of mind skills, recent work has begun to assess “mindreading” skills in borderline populations. Results from these five studies are mixed. For example, using Happé’s Advanced Theory of Mind Test, Arntz, Bernstein, Oorschot, and Schobre (2009) assessed mentalizing skills in 16 female patients with BPD, 16 female patients with cluster-C personality disorder diagnoses, and 28 female nonclinical control subjects; study participants were matched for both age and intelligence. The test was translated into Dutch for the purpose of the Arntz et al. study and included stories involving white lies, persuasion, bluffs, and mistakes in addition to non-mental stories for control purposes. After hearing the stories, individuals were asked questions about the characters’ mental states. Patients with BPD performed significantly better than the healthy controls, although cluster-C patients had the highest scores overall.

Ghiassi, Dimaggio, and Brune (2010) studied mentalizing and parent-rearing behaviour in 50 borderline patients (46 females) and 20 nonclinical control subjects (13 females) using two mental state attribution tasks that have been employed in psychoses research: the Mental State Attribution Task-Sequencing and the Mental State Attribution Task-Questionnaire (MSAT-S and MSAT-Q; Brüne, 2005). Individuals were asked to logically sequence a variety of cartoon pictures into coherent stories and then answer first,
second, and third order mentalizing questions about the characters’ beliefs and intentions. The authors did not control for intellectual functioning, and the control group had a significantly higher proportion of males than did the patient group. Performance on the mentalizing tasks did not differ between the patients and the controls, and sex showed no effects on mentalizing ability; however, the authors did find that higher levels of maternal rearing behaviour that involved rejection and punishment were associated with lower mentalizing ability in the BPD patients only.

Preißler et al. (2010) assessed social-cognitive skills in 64 females with BPD and 38 nonclinical female subjects using two tasks: the “Movie for Social Cognition” (MASC; Dziobek et al., 2006) and the “Reading the Mind in the Eyes” Test (RMET; Baron-Cohen, Wheelwright, Hill, Raste, & Plumb, 2001). The MASC involves watching a film and then assessing the emotions, thoughts, and mental states of the characters, providing multidimensional social-cognitive stimuli that can detect subtle difficulties in mentalizing abilities. The RMET asks individuals to infer mental states from the eye regions of photographed faces, and it has been shown to reliably discriminate between people with and without high-functioning autism. For the MASC, Preißler et al. (2010) found that borderline patients demonstrated reduced skill relative to healthy controls, while the RMET results suggested comparable skills in both groups. Consistent with some of the facial expression recognition research, Preißler et al. (2010) argued that the higher sensitivity of the MASC reveals a reduction in the ability of individuals with BPD to integrate complex social information, especially when time is constrained. In contrast, Fertuck et al. (2009) reported higher RMET scores in 30 individuals with BPD (26 females) relative to 25 control subjects (15 females), and Frick et al. (2012) reported higher RMET scores in 21 females with BPD compared with 20 control females. These divergent findings cannot easily be attributed to differences in intellectual functioning, because Preißler et al. (2010) matched the controls and borderline individuals on fluid IQ, and Fertuck et al. (2009) and Frick et al. (2012) matched their control and borderline groups by education level. Preißler et al. (2010) pointed out, however, that the increased proportion of males in the Fertuck et al. (2009) control group may have reduced control scores to a lower end of the range than is normally reported in control subjects, and therefore increased the probability of detecting group differences.
Scott, Levy, Adams, and Stevenson (2011) assessed mental state attribution as a function of borderline traits using the RMET in a nonclinical sample of undergraduate students. Based on a modified version of the Mclean Screening Instrument for BPD (MSI-BPD; Zanarini et al., 2003), 46 subjects (31 females) were assigned to the low-borderline condition and 38 subjects (25 females) were assigned to the high-borderline condition. The authors reported no difference in mental state decoding ability between the two groups for positive or neutral RMET stimuli, but for negative stimuli, the high-BPD group performed better than the low-BPD group. This difference was not attributable to group differences in response bias or affective state.

In addition to the empathy data discussed in the previous section, Harari et al. (2010) studied cognitive and affective components of theory of mind skills in the same study using the Faux-Pas Task (Baron-Cohen, O’Riordan, Stone, Jones, & Plaisted, 1999). In this task, cognitive theory of mind represents the understanding that within an interaction, a speaker and listener have different mental states. The affective component taps into a participant's appreciation of the emotional impact of a speaker's statement on a listener. Individuals listen to 20 stories and then answer questions that are designed to test their ability to detect a faux pas. The borderline patients were impaired in their detection and cognitive understanding of a faux pas relative to the control subjects, but performed equally well in their affective understanding. Based on the combined results of both the Faux-Pas Task and the IRI, Harari et al. (2010) concluded that control subjects demonstrate higher cognitive empathy relative to affective empathy while patients with BPD show the reverse pattern.

### 3.4.6. Mentalization using interactive stimuli

Two studies have assessed borderline empathy in real social interactions between individuals with and without BPD. In a clinical setting, Ladisich and Feil (1988) had 20 borderline patients and 39 nonborderline psychiatric patients interact with one another and subsequently report on the feelings and qualities of themselves and other group members, using the Gieben Test (GT; Beckmann & Richter, 1972) and the Unpleasant Person Hierarchy Test (UPHT), a task designed specifically for this study. The composition of sex in the study groups was not reported. Empathic accuracy was assessed by comparing how closely perceivers could predict the self-ratings of other
group members. Patients with BPD were more accurate in inferring the feelings of other patients than all other study subjects, including the participating psychiatrist.

Flury, Ickes, and Schweinle (2008) assessed the association between borderline personality features and empathic accuracy in a sample of 76 undergraduate students (46 females) recruited from a larger sample of students who completed the Borderline Syndrome Index (BSI; Conte, Plutchik, Karasu, & Jerrett, 1980); only those individuals scoring in the upper and lower quartiles were included. Using a paradigm developed by Ickes (1993) and similar to Ladisich and Feil's study, Flury et al. (2008) estimated empathic accuracy by measuring each subject's ability to infer the thoughts and feelings of a partner in dyadic interactions between one high-borderline individual and one low-borderline individual. The authors reported significantly increased accuracy in ratings of the high-borderline group relative to the low-borderline group. To test for alternative explanations for this difference, the authors statistically controlled for stereotypical responding style and found that the borderline advantage disappeared, although there was no significant difference in stereotypical responding between the two groups. After further analyses, the authors concluded that low-borderline participants tended to project their own personality characteristics onto those of their interaction partner, resulting in higher error rates due to the more unusual personality profile of the high-borderline subjects. Conversely, the high-borderline participants accurately assumed that their more atypical personality was not generalizable to their partner, and were therefore more accurate in their ratings. The authors concluded that the borderline advantage was attributable to differences in partner “readability” and not empathic skill. These novel results provide an alternative interpretation of borderline empathy and also indicate the possibility of enhanced self-insight in individuals with borderline personality features.

In a third study using interactive stimuli, Franzen et al. (2011) compared the mentalizing processes of 30 BPD patients (22 females) with 30 nonpatients in a simulated social interaction game developed for research in behavioural economics and decision making. In a multiround virtual trust game involving monetary unit exchanges between human and virtual (computer-screen) players, the researchers were able to experimentally manipulate the fairness and emotional cues exhibited by virtual players as well as the congruency between cues and actual behaviour. For some rounds of the game, players’
emotional cues signalled fair behaviour (i.e., smiles) while in other rounds the cues were inconsistent with level of fairness. The authors found that participants with BPD adjusted their playing strategy according to the objective fairness rather than the emotional cues of the virtual players. This finding could not be explained by group differences in emotion recognition or perceived fairness because both borderline patients and control subjects assessed these elements comparably. These authors concluded that individuals with BPD may thus process social information in a more controlled and deliberate manner, whereas control individuals may process emotional cues, especially salient facial expressions, more automatically.

3.5. Discussion

This review and synthesis has assessed the evidence for the borderline empathy phenomenon across a range of empathic skills. The degree to which empathic abilities are enhanced, comparable, or reduced among individuals with BPD compared to controls was highly variable across studies. However, a sufficient number of studies (14) and different tests (8) showed enhanced empathic skills in BPD to indicate that this phenomenon is worthy of further attention, and additional research effort designed to explain both the causes of borderline empathy and the among-study variation in results.

One possible cause of variation in results among studies is the nature of the empathic test deployed. Thus, in all three studies where empathic skills were examined in interactive social environments, individuals with BPD demonstrated increased abilities to accurately infer mental states and respond appropriately to the behaviour of others, relative to control subjects (Flury et al., 2008; Franzen et al., 2011; Ladisich & Feil, 1988). By contrast, in tasks requiring mental state attributions from passive stimuli, individuals with BPD demonstrated enhanced skills in three tests from four studies (Happé’s Advanced ToM test, Arntz et al., 2009; RMET for negative emotions only, Scott et al., 2011; overall RMET score, Fertuck et al., 2009 and Frick et al. 2012), conserved skills for three tests from four studies (MSAT, Ghiassi et al., 2010; affective understanding of faux pas, Harari et al., 2010; RMET, Preißler et al., 2010; RMET for positive and neutral emotions, Scott et al., 2011), and reduced skills for two tests from two studies (cognitive understanding of faux pas, Harari et al., 2010; MASC, Preißler et
This apparent contrast in results between studies using interactive and passive stimuli suggests that interactive stimuli may be relatively more sensitive in demonstrating the skills of individuals with BPD, and therefore highlights the need for future research to examine borderline social cognition through interactive study environments and relatively realistic social interactions.

For other categories of empathic skills, results were notably mixed. Assays of emotional intelligence suggested enhanced, reduced, or conserved abilities in borderline subjects (Beblo et al., 2010; Hertel et al., 2009; Park et al., 1992). This variation in reported emotional intelligence may vary, in part, as a function of borderline symptom severity or overall cognitive ability. Taken together, findings from facial expression recognition studies suggest that borderline individuals may have an increased sensitivity to negatively-valenced emotional stimuli, and that factors such as reduced executive control may impair performance, especially in tasks requiring quick responses. Given that psychopathology is almost always associated with reduced performance in facial affect recognition (for one exception in schizophrenia research, see Davis & Gibson, 2000), the observation of enhanced borderline performance in four studies is especially noteworthy.

Studies comparing cognitive and affective empathic skills in BPD revealed a consistent and interesting pattern. Harari et al. (2010) reported reduced cognitive empathy but conserved affective empathy among individuals with BPD for measures assessing both empathizing and mentalizing abilities. Control subjects were characterized by higher cognitive empathy relative to affective empathy, whereas individuals with BPD demonstrated the reverse pattern; given that the groups were matched for intellectual functioning, this pattern could not be attributed to group differences in intelligence. Similarly, Guttman and Laporte (2000) reported reduced cognitive empathy and enhanced affective empathy in individuals with BPD relative to control subjects. These studies are limited in that the ability of borderline subjects to accurately rate their own empathic skills is unknown, so results warrant a conservative interpretation. Given that both studies reported reduced cognitive empathy and either normal or enhanced affective empathy, it is possible that borderline empathy is characterized by a dissociation or asymmetry between these different facets of empathic skill (Harari et al., 2010).
Empathic deficits are often implicated as aetiologically central to psychopathology, due to the impaired social functioning characteristic of individuals with psychiatric diagnoses (Cameron, 2009). Indeed, a substantial body of literature indicates reduced social competency for individuals with the Axis I disorders that share psychotic-affective symptoms with BPD, including major depression, bipolar disorder, and schizophrenia (e.g. Barnow et al., 2010; Glaser, Van Os, Thewissen, & Myin-Germeys, 2010; Hooley, 2010; Lieb, Zanarini, Schmahl, Linehan, & Bohus, 2004; Perugi, Fornaro, & Akiskal, 2011). Although it is reasonable to assume that social interactions are facilitated through the effective use of both basic empathic skills such as emotion recognition and more complex skills such as mental state attribution, impairments to overall social functioning may, in principle, result from either reductions or increases in specific abilities from normative levels (Crespi & Badcock, 2008; Montag et al., 2010; Sharp et al., 2011). For example, Langdon, Corner, McLaren, Coltheart, and Ward (2006) studied attentional orienting as a function of gaze shifting in people with and without schizophrenia and found that individuals with schizophrenia were hyper-responsive to gaze, reflexively shifting their attention in the direction indicated by another's gaze at a lower threshold than did subjects without schizophrenia. This automatic and increased sensitivity to gaze may be linked to the tendency of individuals with schizophrenia to over-perceive intentionality and experience paranoia, both of which may contribute to the social difficulties observed in schizophrenia. Similarly, excessive levels of empathy may potentiate or exacerbate depression, anxiety, and borderline features, especially among females (Dammann, 2003; O'Connor et al., 2007; Zahn-Waxler, Crick, Shirtcliff, & Woods, 2006; Zahn-Wexler, Shirtcliff, & Marceau, 2008). The observation of general social deficits in individuals with psychotic-affective conditions is thus not necessarily sufficient to indicate reductions in the empathic skills that underlie social functioning, because such deficits could result from qualitatively distinct alterations. Whether alterations involve reductions or enhancements in specific empathic domains may thus be useful in forming hypotheses for the causes of these conditions. But how might enhanced empathic abilities be related to severe deficits in interpersonal functioning in BPD?
3.5.1. Resolving the borderline empathy paradox

Psychoanalytic accounts attribute borderline empathy to environmental causes, such that in response to inconsistent or neglectful parenting and in an effort to maintain a constant view of the caregiver object, the borderline individual develops enhanced sensitivity to the subtle, subconscious cues indicating the mental states of the parent (Carter & Rinsley, 1977; Krohn, 1974). The tendency to perceive and respond to subconscious drives, combined with a learned distrust of conscious behaviour, thus disrupts the ability of the borderline individual to develop enduring and stable experiences of others in interpersonal contexts, which leads to lasting social dysfunction. This model is supported by evidence suggesting a relationship between maternal neglect and enhanced nonverbal decoding abilities, whereby increased reports of maternal neglect positively predicted scores on the PONS in borderline subjects (Frank & Hoffman, 1986). Linehan (1993) similarly proposed that BPD is characterized by a heightened sensitivity to, and keen awareness of, emotional cues, especially negative cues signalling rejection or abandonment, in the social environment. The origins of this enhanced sensitivity are suggested to be biological in nature, although emotionally invalidating environments—such as the childhood abuse and neglect that is often reported in BPD cases—are expected to exacerbate innate empathic sensitivity. Under this hypothesis, the social difficulties characteristic of BPD result from low thresholds of emotional reactivity and insecure appraisals of emotional events based on accurate perceptions of social cues (Wagner & Linehan, 1999).

Park et al. (1992) also attributed borderline empathy and its role in BPD development to interacting biological and environmental factors, although these researchers emphasized the positive aspects of enhanced empathic skills and referred to them as cognitive “gifts” involving the desire and ability to understand the thoughts and feelings of others, which, in the absence of abuse, would contribute to an individual's wellbeing and not result in BPD. Fertuck et al. (2009) suggested that enhanced mentalizing in BPD engenders reduced interpersonal functioning through a combination of negative expectations upon entering social interactions and reduced executive cognitive control, resulting in the inability to modify incorrect appraisals of social situations. Similarly, Arntz et al. (2009) suggested that impulsivity, emotional reactivity, and working memory deficits observed in
BPD may inhibit the borderline individual's ability to apply intact mentalizing skills in emotionally charged situations, therefore contributing to social dysfunction.

Drawing from the reviewed studies, we suggest that the borderline empathy paradox may be attributable in part to a combination of enhanced attention to, and perception of, social stimuli with dysfunctional processing. Under this model, many individuals with BPD may exhibit increased attention to social stimuli, and thus develop an enhanced ability to perceive social information. Such enhanced attention and perception may become pathological if they interact with deficits in other domains such as attentional control, emotion regulation, and regulation of the attachment system, such that the inferences drawn from social information become amplified and distorted toward negative, self-referential emotional states. This model is consistent with previous evidence of hypersensitivity to the social environment in BPD (Goodman & Siever, 2011; Gunderson & Lyons-Ruth, 2008; Lynch et al., 2006), which involves constant vigilance to anticipated rejection (Fertuck et al., 2009) and difficulties in regulating emotion due to low thresholds for stress-related activation of the attachment system and deactivation of controlled mentalization (Fonagy, Luyten, & Strathearn, 2011). Such stress- and emotion-mediated deactivation of controlled mentalization should be unlikely to reduce performance on the laboratory-based empathic-skill tests analyzed here, which could help to explain preservation of empathic abilities in individuals with BPD but cannot explain enhancements. High sensitivity and attention to social cues may also engender hypermentalizing (overly complex inferences based on social cues), which can interact in a vicious cycle with dysregulated emotionality through anxious, uncontrolled rumination (Sharp et al., 2011). Finally, to the extent that conscious or unconscious mental states of social interactants indeed reflect negatively upon individuals with BPD but remain verbally unexpressed, highly sensitive and accurate empathic inferences that reveal such states may also exacerbate BPD symptoms by instigating emotional dysregulation and dysfunctional interactions. This model based on enhanced attention to, and perception of, social stimuli in BPD is conceptually analogous to models of autism spectrum conditions, where increases have been observed in attention to, and perception of, nonsocial compared to social stimuli (Baron-Cohen, Ashwin, Ashwin, Tavassoli, & Chakrabarti, 2009; Klin, Lin, Gorrindo, Ramsay, & Jones, 2009; Mottron &
Findings from Gardner et al. (2010) and Lynch et al. (2006) are also consistent with this general model for helping to explain the borderline paradox. Thus, in the former study, BPD traits predicted enhanced recognition of anger, but only when executive control was also high; in the latter study, individuals with BPD correctly identified the emotion of morphing facial expressions earlier than did healthy controls, suggesting enhanced perception of emotional cues. The dissociation between cognitive and affective empathy observed by Harari et al. (2010) and Guttman and Laporte (2000) may also be concordant with the model, in that affective empathy may be more closely linked to the automatic and immediate perception of social-emotional cues and accompanying physiological responses, whereas cognitive empathy involves higher order cognitive functions (Shamay-Tsoory, 2011). Borderline empathy may thus involve dysregulation to the integrated social cognitive-affective system, resulting in a characteristic asymmetry or splintering of empathic skills (Fonagy et al., 2011). Gaining an understanding of the specific pattern of cognitive-affective enhancements and reductions in individuals with BPD, and their interactions with social attention and perception, attentional control, and emotion regulation, should clarify the relationship between borderline and normal social cognition, as well as elucidate the role of enhanced empathy in BPD aetiology and symptoms.

Also salient to a model of BPD involving, in part, a maladaptive enhancement of attention to social stimuli is evidence for enhanced performance of individuals with BPD on tasks that typically demonstrate female superiority in nonclinical populations (Table 3.2). It is important to note that most tasks in Table 3.2 are linked to a female advantage, given that overall females appear to outperform males in the general domain of social cognition (i.e., Geary, 2010). Females thus outperform males in facial emotion recognition for a variety of tasks and stimuli (reviewed in Geary, 2010); four studies reported superior performance of borderline subjects in this domain (Gardner et al., 2010; Lynch et al., 2006; Merkl et al., 2010; Wagner & Linehan, 1999). For self-reported affective empathy assessed by the IRI (Davis, 1980, 1993), Guttman and Laporte (2000) reported enhanced scores for borderline patients relative to controls while Harari et al. (2010) reported no difference. Studies using the IRI in nonclinical samples of both
adolescents and adults have found a female advantage in the subscales composing the affective empathy score (Berthoz, Wessa, Kedia, Wicker, & Grezes, 2008; Mestre, Samper, Frias, & Tur., 2009). Females also outperform males on tasks requiring the attribution of mental states from photographs of the eyes (RMET; Baron-Cohen, Jolliffe, Mortimore, & Robertson, 1997; Baron-Cohen et al., 2001). For this task, Preißler et al. (2010) found no group differences whereas Fertuck et al. (2009) and Frick et al. (2012) reported enhanced performance of the borderline subjects relative to non-BPD controls. Scott et al. (2011) reported higher RMET scores for negative emotional stimuli in healthy adults with borderline personality features compared to adults without borderline personality features.

**Table 3.2. Sex differences in non-clinical populations for empathic tasks**

<table>
<thead>
<tr>
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<th>Empathic Task</th>
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<td>Levine et al., 1997</td>
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<td>JACFEE</td>
<td>Female advantage (1)</td>
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<td></td>
<td>Bland et al., 2004</td>
<td>PFA</td>
<td>Female advantage (1)</td>
</tr>
<tr>
<td></td>
<td>Lynch et al., 2006</td>
<td>PFA</td>
<td>Female advantage (1)</td>
</tr>
<tr>
<td></td>
<td>Minzenberg et al., 2006</td>
<td>PFA, BLERT</td>
<td>Female advantage (1)</td>
</tr>
<tr>
<td></td>
<td>Domes et al., 2008</td>
<td>PFA</td>
<td>Female advantage (1)</td>
</tr>
<tr>
<td>Facial emotion recognition</td>
<td>Dyck et al., 2009</td>
<td>FAN test, ER Test</td>
<td>Female advantage (1)</td>
</tr>
<tr>
<td></td>
<td>Guitart-Masip et al., 2009</td>
<td>PFA</td>
<td>Female advantage (1)</td>
</tr>
<tr>
<td></td>
<td>Merkl et al., 2010</td>
<td>PFA</td>
<td>Female advantage (1)</td>
</tr>
<tr>
<td></td>
<td>Gardner et al., 2010</td>
<td>PFA</td>
<td>Female advantage (1)</td>
</tr>
<tr>
<td></td>
<td>Unoka et al., 2011</td>
<td>Ekman 60 Faces</td>
<td>Female advantage (1)</td>
</tr>
<tr>
<td>Self-reported empathy</td>
<td>Guttman &amp; Laporte, 2000</td>
<td>IRI</td>
<td>Female advantage (2, 3)</td>
</tr>
<tr>
<td></td>
<td>Harari et al., 2010</td>
<td>IRI</td>
<td>Female advantage (2, 3)</td>
</tr>
<tr>
<td>Emotional intelligence</td>
<td>Park et al., 1992</td>
<td>Derived from Gardner’s personal intelligence concept</td>
<td>Unknown; task designed specifically for this study</td>
</tr>
<tr>
<td></td>
<td>Hertel et al., 2009</td>
<td>MSCEIT</td>
<td>Female advantage (4)</td>
</tr>
<tr>
<td></td>
<td>Gardner &amp; Qualter, 2009</td>
<td>MSCEIT SEIS</td>
<td>Female advantage (4, 5)</td>
</tr>
<tr>
<td>Source</td>
<td>Task Description</td>
<td>Results</td>
<td></td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-------------------------------------------------------</td>
<td>-----------------</td>
<td></td>
</tr>
<tr>
<td>Beblo et al., 2010</td>
<td>MSCEIT, TEMINT</td>
<td>Female advantage (4, 6)</td>
<td></td>
</tr>
<tr>
<td>Arntz et al., 2009</td>
<td>Advanced ToM</td>
<td>Mixed (7, 8)</td>
<td></td>
</tr>
<tr>
<td>Fertuck et al., 2009</td>
<td>RMET</td>
<td>Female advantage (9)</td>
<td></td>
</tr>
<tr>
<td>Frick et al., 2012</td>
<td>RMET</td>
<td>Female advantage (9)</td>
<td></td>
</tr>
<tr>
<td>Ghiassi et al., 2010</td>
<td>MSAT</td>
<td>Unknown for this particular task</td>
<td></td>
</tr>
<tr>
<td>Harari et al., 2010</td>
<td>Faux-Pas Task</td>
<td>Female advantage (10)</td>
<td></td>
</tr>
<tr>
<td>Preibler et al., 2010</td>
<td>MASC</td>
<td>Females = males (11) Female advantage (9)</td>
<td></td>
</tr>
<tr>
<td>Scott et al., 2011</td>
<td>RMET</td>
<td>Female advantage (9)</td>
<td></td>
</tr>
<tr>
<td>Ladisich &amp; Feil, 1988</td>
<td>Gieben Test Unpleasant Person Hierarchy Test</td>
<td>Unknown, Task designed specifically for this study</td>
<td></td>
</tr>
<tr>
<td>Flury et al., 2008</td>
<td>Infer states of partner in dyadic interactions</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>Franzen et al., 2011</td>
<td>Simulated interaction game with monetary exchange</td>
<td>Unknown</td>
<td></td>
</tr>
</tbody>
</table>

(1) Geary, 2010; (2) Mestre et al., 2009; (3) Berthoz et al., 2008; (4) Day & Carroll, 2004; (5) Schutte et al., 1998; (6) Amelang & Steinmayr, 2006; (7) Bosacki, 2000; (8) Russell et al., 2007; (9) Baron-Cohen et al., 2001; (10) Baron-Cohen et al., 1999; (11) Smeets et al., 2009.

*Table has been modified from JPD version due to formatting considerations.

For higher order theory of mind tasks, female superiority is often assumed, although performance of the sexes is dependent on the specific task employed. For example, Russell, Tchanturia, Rahman, and Schmidt (2007) reported a male advantage for Happé’s cartoon task, but Bosacki (2000) reported female superiority on a similar task in healthy preadolescents. With respect to BPD, Arntz et al. (2009) found enhanced performance of the borderline group relative to nonclinical control subjects on Happé’s (1994) Advanced ToM task. Interpretation of these results is severely limited by the relative lack, or absence, of male subjects in most studies of BPD. Future research would benefit from comparing male and female performance in both borderline and nonclinical populations in order to advance understanding of borderline phenotypes in the context of sex differences in social cognition.
3.5.2. Conclusions

By critically examining the evidence bearing on enhanced empathic skills in borderline populations, we have provided the groundwork for future tests of hypotheses concerning both the causes of borderline empathy and the role of empathic enhancements in BPD aetiology, symptoms, and therapy. Given the evidence regarding the borderline empathy phenomenon, we have suggested that the causal bases underlying BPD may involve, in part, a pathological and selective enhancement of normally adaptive empathic abilities, especially with regard to increased attention to social stimuli. More generally, increased understanding of the role that social brain adaptations play in mediating human psychiatric disease risk may help to explain maladaptations of human social interactions, especially for conditions such as borderline personality disorder that centrally involve interpersonal relationships.

3.6. References


4. Developing an ‘Extreme Female Brain’ Theory of Psychotic-Affective Conditions: Insights from Depression and Borderline Personality Disorder

4.1. Abstract

Dissecting the aetiology of female- and male-preponderant psychiatric conditions benefits from an understanding of normal sex differences in cognitive and social-affective phenotypes, as these sex differences precede the expression of psychiatric symptoms and thus mediate sex-specific disease risk. On average, women tend toward relative strengths in mentalistic cognition (or empathizing) whereas men tend toward relative strengths in mechanistic cognition (systemizing). Baron-Cohen's (2002, 2009) 'extreme male brain' (EMB) theory postulates that conditions on the autism spectrum represent extreme variants of male-typical psychology involving enhanced mechanistic cognition and reduced mentalistic cognition. The concept of the 'extreme female brain' (EFB) and its possible role in psychiatric conditions is relatively less explored. Following Baron-Cohen's EMB framework, we review and synthesize evidence from disorder prevalence, studies in mentalistic cognition, and hormonal correlates to evaluate the hypothesis that depression and borderline personality disorder (BPD) represent, in part, expressions of EFB traits. Both conditions demonstrate female-biased sex-ratios and show associations with elevated 2D:4D digit ratio. Individuals with BPD and sub-clinical depression also demonstrate well-replicated evidence for enhanced empathic abilities and sensitivity, which plausibly play an important role in the development of these conditions. Therefore, we propose that depression and BPD, and possibly other conditions of the psychotic-affective spectrum, involve the exaggerated expression of 'female-typical' phenotypes, with a significant aetiologial role of elevated mentalistic cognition. Whether or not reduced mechanistic cognition also contributes to female-preponderant psychiatric conditions is an important question for future research.
4.2. Introduction

Sex differences in psychological and biological traits play important roles in the aetiology, development, and manifestation of psychiatric conditions. The ‘extreme male brain’ (EMB) theory of autism postulates that autism spectrum conditions (ASCs) reflect, in part, extreme manifestations of ‘male-typical’ psychology. This theory can account for several notable features of autism (Baron-Cohen 2002; Baron-Cohen et al. 2005), including its male-biased sex ratio and low levels of empathizing relative to systemizing (Baron-Cohen et al. 2011). Given the usefulness of the EMB theory in generating testable hypotheses and accounting for patterns in data on ASCs, it is of interest to investigate the other side of the spectrum: if extreme psychological 'maleness' manifests as autism spectrum traits, what psychological traits, and psychiatric conditions, should be associated with extreme psychological ‘femaleness’?

Consideration of human psychological sex differences in the context of psychiatric conditions requires several caveats at the outset. Firstly, the ‘extreme male brain’ (EMB) and ‘extreme female brain’ (EFB) in this context are defined psychologically and do not directly involve studies of brains; rather, the EFB and EMB describe psychological profiles that exist at the extreme ends of a normal distribution of sexually-dimorphic psychological traits. 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 could exhibit an EFB, 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 of a female (Baron-Cohen et al. 2005). Secondly, sex differences in psychological functioning do not imply genetic causation or biological determinism, as all psychological traits and behaviour develop and manifest through complex interactions of genetic and environmental influences. Finally, the ‘extreme’ development of many normally distributed traits can manifest as psychiatric conditions, so in the case of traits that are normally distributed and sexually dimorphic, extreme development is expected to occur within one sex more often than the other.
Two psychiatric conditions, depression and borderline personality disorder (BPD), demonstrate apparent female biases in their prevalence (Kessler et al. 1993; Widiger & Trull 1993) and show evidence for enhanced empathy and mentalizing skills, in some previous studies (e.g. Thorma et al. 2011; Harkness et al. 2010; Dinsdale & Crespi 2012). Major depressive disorder (MDD) involves the persistent presence of depressed mood, low self-esteem, and loss of pleasure (APA 2000) and affects up to 16% of North Americans in their lifetime (Kessler et al. 1993). Borderline personality disorder (BPD) may affect up to 6% of the population (Grant et al. 2008, but see Paris 2010) and is characterized by emotional dysregulation, impulsiveness, pervasive instability in mood, behaviour, self identity and interpersonal relationships, as well as the tendency toward black-or-white thinking (Gunderson 1984). BPD and MDD are closely associated: up to 83% of individuals with BPD have a comorbid diagnosis of depression (Lieb et al. 2004; Zimmerman & Mattia 1999); borderline personality features positively predict levels of depression across non-clinical individuals (Fonseca-Pedrero et al. 2011); and individuals with either BPD or MDD exhibit similar temperamental characteristics such as harm avoidance and low self-directedness (reviewed in Luca et al. 2012). In parallel with the development and testing of Baron-Cohen's EMB theory, we synthesized findings from studies examining prevalence, salient psychological correlates, and hormonal correlates of depression and BPD, to develop and evaluate the hypothesis that these conditions represent, in part, expressions of the EFB.

4.2.1. **Sex Differences in the 'Neurotypical' Brain: Empathizing & Systemizing**

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 systems (Baron-Cohen 2002). By this theory, empathizing involves the motivation and skills required to understand and interact 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 et al. 2004). Badcock (2009) uses mentalistic and mechanistic in place of empathizing and systemizing, to capture a wider breadth of cognitive and affective systems.
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. 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 ASC prevalence, as well with evidence linking autism and autistic features with elevated exposure to prenatal androgens, hormones that play key roles in 'masculinizing' the developing brain (Baron-Cohen 2002; Lutchmaya et al. 2002a; Lutchmaya et al. 2002b; Manning et al. 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 strongly skewed toward enhanced empathizing and reduced systemizing (extreme Type E in Baron-Cohen et al. 2005). Consistent with this prediction, Goldenfeld and colleagues (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 all-female proportion of the sample (7%) exhibited this 'extreme female' profile of high empathizing and reduced systemizing. However, the question of whether or not the EFB manifests in psychiatric conditions remains unresolved, and largely unstudied.

4.2.2. Previous Accounts of the EFB

Baron-Cohen (2002) suggested that increased empathizing abilities would positively impact social functioning and thus not engender psychiatric illness. Conversely, several different researchers have implicated an aetiological role of hyper-sensitive empathy or enhanced mentalistic cognition in conditions belonging to the psychotic-affective spectrum (Dammam 2003; O’Connor et al. 2007; Crespi & Badcock 2008; Zahn-Waxler et al. 2008; Dinsdale & Crespi 2012). The psychotic-affective spectrum includes several psychiatric conditions (including schizophrenia, major depressive disorder, bipolar disorder and borderline personality disorder) that overlap in their genetic bases, phenotypes, and correlates (Perugi et al. 2011; Blackwood et al. 2007; Kendler 2005;
Crespi 2011); milder manifestations of symptoms comprising psychotic-affective diagnoses (e.g. magical thinking, paranoia, social withdrawal) are more or less part of normal personality variation in healthy populations (Verdoux & van Os 2002; Bentall 2005).

In an evolutionary hypothesis of BPD, Dammam (2003) postulated that female-preponderant mentalization disorders involve a pathological hyper-sensitivity to empathy, in contrast to the reduced empathy observed in autism. Similarly, excessive levels of empathy may create a liability to, or exacerbate, existing depression and anxiety, especially among females (Zahn-Waxler et al. 2006; Zahn-Wexler et al. 2008; O'Connor et al. 2007). Zahn-Waxler and Van Hulle (2012) put forth a developmental model of depression describing how high levels of empathy and pro-social behaviour in young children can interact with parental depression and marital discord to cause feelings of guilt and responsibility in the child over not being able to 'fix' their parent's unhappiness. This over-involvement of a young child in their parent's emotions can prevent the child from developing healthy interpersonal functioning, and, given the tendency of girls to be more emotionally involved with caregivers than boys, girls appear to be especially affected by dysfunctional home environments and therefore are expected to be more prone to later depression under this model.

Crespi and Badcock (2008) hypothesized that psychotic-affective conditions, with a focus on the schizophrenia spectrum, are diametric to the autism spectrum on an axis of human social cognition with neurotypicals at the centre; autism is associated with under-developed social cognition and schizophrenia with over-developed social cognition. Over-developed social cognition by this hypothesis describes features of psychoses - such as paranoia or delusions of conspiracy - in terms of 'hyper-mentalizing' rather than in terms of mentalizing deficits. To link Crespi and Badcock's (2008) hypothesis with Baron-Cohen's E-S framework, we can understand the social-cognitive impairments and generally-reduced interpersonal functioning characteristic of schizophrenia as centrally involving extreme empathizing, or at least involving aspects of extreme empathizing in combination with other cognitive-affective alterations known to underlie schizophrenia pathology, such as affective dysregulation and reduced working memory. In a test of Crespi and Badcock's hypothesis, Brosnan et al. (2010) studied the relationship between empathizing, systemizing, and psychoses using questionnaires in a non-clinical sample.
of female adults and found that hyper-empathizing predicted reports of increased psychotic symptoms including mania and paranoia. The authors concluded that hyper-empathizing might indeed characterize the EFB, as described under the E-S framework.

In another perspective, Bremser and Gallup (2012) presented a series of findings positing the combination of disordered eating and negative evaluation anxiety as meeting Baron-Cohen's criteria for the EFB. Drawing on the observation that disordered eating is more prevalent among females, as well as being mediated by hormones, the authors surveyed a large sample of undergraduate students to investigate relationships between empathizing, systemizing, disordered eating, and attitudes toward being evaluated by others. A hyper-empathizing profile predicted disordered eating and fear of negative evaluation by others in both sexes and furthermore, the fear of being negatively evaluated was also associated with lower scores in systematic thinking. Findings from objective measures of empathizing and systemizing revealed the same patterns. The EFB profile of high empathizing and low systemizing thus predicted increased risk of eating disorders and social anxiety. Further studies by the same authors found that dysfunctional attitudes towards eating, and fear of negative evaluation, were also associated with higher self-reported scores on schizotypy, including exaggerated suspiciousness, magical thinking and paranoia, which are all features consistent with hyper-mentalizing or extreme empathizing. Therefore, according to Bremser and Gallup (2012), an extreme Type E profile of enhanced empathizing and reduced systemizing accurately describes the combination of dysfunctional attitudes toward eating and fear of negative evaluation anxiety that together comprise disordered eating.

Eating disorders are highly comorbid with Axis I disorders such as depression, and with Axis II diagnoses including schizotypal, borderline, avoidant, and obsessive-compulsive personality disorders (Grilo et al. 2003). Individuals diagnosed with anorexia nervosa (AN) demonstrate schizotypal features (Holliday et al. 2006) and the specific characteristic of weight preoccupation is predicted by both borderline and narcissistic personality features (Davis et al. 1997). Given the considerable overlap of disordered eating with traits and conditions belonging to the broader psychotic-affective spectrum, it is reasonable to hypothesize that other psychotic-affective conditions also demonstrate a psychological profile that is biased toward hyper-empathizing. Of the psychotic-affective spectrum of psychiatric conditions, depression and BPD show the most marked female
preponderance, and thus they form an appropriate starting point: if depression and BPD represent, in part, manifestations of an EFB, then following Baron-Cohen's EMB and E-S frameworks, we predict that these conditions should: (1) exhibit female biases in prevalence; (2) show evidence of enhanced empathic abilities; and (3) demonstrate associations with female-typical digit ratios.

4.3. Methods

To evaluate these predictions, we searched the literature using the databases PubMed and Web of Science, in addition to analyzing data that we collected as part of a larger collaborative project. For prediction (1), we reviewed studies that investigated sex differences in the prevalence of BPD and depression in clinical and community samples, in addition to studies that examined sex differences in the prevalence of depressive and borderline personality features in non-clinical populations. We synthesized these epidemiological findings with results from personality research, focussing on the link between neuroticism and depression. For prediction (2), we drew on our recently published review of empathic functioning in BPD (Dinsdale & Crespi 2012) and then applied similar search criteria for studies investigating empathic functioning in depression. The following terms were searched in conjunction with depression and major depression: empathy; theory of mind; mentalizing; social cognition; and emotion recognition. All references and cited articles from the selected studies were reviewed to check for additional relevant articles. For inclusion, articles needed to empirically assess an empathic skill in a sample of individuals with depression compared to appropriate controls, or assess an empathic skill as a function of depressive personality features. To evaluate prediction (3), we reviewed studies investigating 2D:4D ratio, an indicator of prenatal androgen exposure, in BPD and depression and in relationship to empathizing and systemizing.

We also collected data from a large sample of undergraduates from two universities (n = 282). The measures relevant to this paper include the Borderline Symptom List-23 (BSL-23; Bohus et al. 2009), which is a brief Likert-style self-report instrument that measures the extent to which people endorse traits consistent with BPD. Participants also completed the Reading the Mind in the Eyes test (RMET; Baron-Cohen et al. 2001),
which assesses mental state decoding ability by requiring subjects to identify mental states from pictures of eyes. We analyzed sex differences in BSL-23 scores, sex differences in RMET scores, and the relationship between BSL-23 and RMET scores to evaluate predictions (1) and (2).

4.4. Results

4.4.1. Do depression and BPD demonstrate evidence of female-biased sex-ratios?

The symptoms contributing to both MDD and BPD exist on a spectrum and grade into normal personality variation, sharing particular commonalities and positive associations with the personality trait of neuroticism (Corbitt & Widiger 1995; Widiger et al. 1994). Neuroticism is a normally distributed and multifaceted personality trait that most broadly indicates a person's sensitivity to negative stimuli, and, on average, women exhibit elevated neuroticism relative to men (Nettle 2007). This sex difference in neuroticism becomes especially pronounced in the upper tail of the distribution, where personality pathology manifests; thus, for individuals endorsing extremely high neuroticism, 71% are female (Costa & McCrae 1988; Costa & McCrae 1992; Corbitt & Widiger 1995).

Both BPD and depression appear to demonstrate a female bias in their prevalence and the evidence for a female bias in depression is particularly strong (Table 4.1). From puberty onward, females experience depression more than males and this result holds for depressive symptoms as well as for diagnoses of depression including dysthymia, atypical depression, seasonal depression, and rapid-cycling bipolar disorder (Kessler et al. 1993; Piccinelli & Wilkinson 2000; Lucht et al. 2003). Women are about twice as likely as men to experience a major depressive episode during their lifetime, and each year, 12% of women compared to 7% of men receive a depressive disorder diagnosis; the higher prevalence of females diagnosed with depression each year is also mostly attributable to women having an elevated risk of first onset (Kessler et al. 1993; O'Connor et al. 2007; Shibley Hyde et al. 2008).

It is important to note that the 2:1 female bias primarily comes from samples drawn from European and European-derived nations (Shibley Hyde et al. 2008). For other cultures
and countries, little data are available, but it appears that the female predominance does not exist in the following populations: American Amish (Egeland & Hostetter 1983); African Americans (Brown et al. 1995); Southeast Asians in Canada (Beiser et al. 1993); and Jewish people in USA (Levav et al. 1993). However in a large study drawing subjects from ten countries (USA, Canada, Puerto Rico, France, Germany, Italy, Lebanon, Taiwan, Korea, New Zealand), Weissman et al. (1996) found that even amid variation in overall depression prevalence, females consistently reported higher depression rates than males in every country studied.

Table 4.1. Summary of sex differences in the prevalence and expression of depression

<table>
<thead>
<tr>
<th>Type and Purpose of Study</th>
<th>Authors</th>
<th>Key Finding</th>
<th>Evidence for female bias (Y/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessing prevalence and/or nature of depression in community samples</td>
<td>Kessler et al. 1993</td>
<td>As part of the National Comorbidity Study, structured psychiatric interviews were given to a nationally-representative community sample 8098 adults in the USA. Authors reported that females were 1.7 times more likely than males to meet DSM-III-R criteria for a major depressive episode.</td>
<td>Y</td>
</tr>
<tr>
<td>Assessing prevalence and/or nature of depression in community samples</td>
<td>Weissman et al. 1996</td>
<td>In a sample of 38 000 subjects drawn from 10 countries, overall lifetime prevalence rates for unipolar depression varied across countries but females were consistently twice as likely to meet DSM-III criteria for unipolar depression than males. Bipolar rates were more equal across countries and between sexes.</td>
<td>Y</td>
</tr>
<tr>
<td>Assessing prevalence and/or nature of depression in community samples</td>
<td>Piccinelli &amp; Homen 1997</td>
<td>2:1 ratio of females to males reporting depression in Hong Kong and Korea.</td>
<td>Y</td>
</tr>
<tr>
<td>Assessing prevalence and/or nature of depression in community samples</td>
<td>Angst et al. 2002</td>
<td>In a representative sample of 78 458 subjects drawn from six European countries (Belgium, France, Germany, United Kingdom, Spain, Netherlands), females were 1.96 times as likely than males to meet criteria for major depression. This was consistent in all countries and for all age groups. For minor depression, the female: male ratio reduced to 1.22.</td>
<td>Y</td>
</tr>
<tr>
<td>Assessing prevalence and/or nature of depression in community samples</td>
<td>Lucht et al. 2003</td>
<td>Females were more than twice as likely than males to meet criteria for depression, beginning in adolescence, for both 1-month prevalence and lifetime risk. Prior to puberty, males had slightly higher prevalence rates than females. Females predominated in longer-duration depression. Both male and female risk increased with divorced, separated or widowed status.</td>
<td>Y</td>
</tr>
<tr>
<td>Study</td>
<td>Findings</td>
<td>Relevant?</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
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<td></td>
</tr>
<tr>
<td>Piccinelli &amp; Wilkinson 2000</td>
<td>Some of the gender difference may be artefactual, but increased female prevalence in depression is genuine and attributable to interacting genetic and sociocultural factors.</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>Kuehner 2003</td>
<td>In a systematic literature review, the author reported that recent epidemiological findings concur in an estimate of females being about twice as likely than males to experience unipolar depression.</td>
<td>Y</td>
<td></td>
</tr>
<tr>
<td>Hankin et al. 1998</td>
<td>In a New Zealand sample of 1037 subjects assessed five times over the course of 10 years, authors found that sex differences in depression began to emerge between ages 13-15. The greatest increase occurred between 15 and 18. No sex differences in depression recurrence or depression symptom severity were found.</td>
<td>Y</td>
<td></td>
</tr>
</tbody>
</table>

A compilation of studies examining sex differences in the prevalence of BPD diagnoses and borderline personality features shows that females greatly outnumber males in clinical settings, but the picture is less clear in community samples (Table 4.2). Widiger and Trull (1993) conducted a meta-analysis on demographic data from 75 clinical studies and reported that the female to male ratio for BPD diagnoses was 3:1. This highly female-biased sex ratio contrasts with estimates of the sex ratio in community samples, where several studies suggest comparable rates of BPD in females and males (Table 4.2: Zanarini et al. 2011; Jackson & Burgess 2000; Jane et al. 2007; Grant et al. 2008). Females in the general population do, however, report significantly higher levels of individual borderline personality characteristics (e.g. affective instability, chronic feelings of emptiness, fears of abandonment, and interpersonal challenges) than males (Table 4.2: Aggen et al. 2009; Distel et al. 2008; De Moor et al. 2009; Furnham & Trickey 2011; Fonseca-Pedrero et al. 2011), a pattern that was confirmed by our BSL-23 results, which indicated significantly higher scores in females relative to males (Table 4.2).
<table>
<thead>
<tr>
<th>Type and Purpose of Study</th>
<th>Authors</th>
<th>Key Finding</th>
<th>Evidence for female bias (Y/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meta-analyses of estimates of BPD prevalence drawn from clinical populations</td>
<td>Widiger &amp; Trull (1993)</td>
<td>Average proportion of BPD diagnoses that are female estimated at 76%.</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Lynam &amp; Widiger (2007)</td>
<td>Sex differences in personality traits predicted sex differences in BPD prevalence but male-female differences in BPD prevalence were non-significant.</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>Korzekwa et al. (2008)</td>
<td>In a study of BPD prevalence in a general adult outpatient university clinic, authors found that 75.4% of outpatients meeting DSM-IV criteria for BPD were female.</td>
<td>Y</td>
</tr>
<tr>
<td>Assessing prevalence of people meeting BPD diagnostic criteria in community samples</td>
<td>Jackson &amp; Burgess (2000)</td>
<td>No significant differences between males and females for meeting ICD-10 criteria for BPD equivalent (emotionally unstable).</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>Jane et al. (2007)</td>
<td>No significant difference between males and females for meeting DSM-IV criteria for BPD.</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>Grant et al. (2008)</td>
<td>No significant differences between males and females for meeting DSM-IV criteria for BPD.</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>Zanarini et al (2011)*</td>
<td>No significant sex differences in meeting DSM-IV criteria for BPD.</td>
<td>N</td>
</tr>
<tr>
<td>Assessing prevalence of people endorsing individual BPD features in community samples</td>
<td>Distel et al. (2008)</td>
<td>In three different countries, females scored higher than males on a self-report of BPD features.</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Aggen et al. (2009)</td>
<td>Females scored significantly higher than males on mean BPD factor.</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>De Moor et al. (2009)</td>
<td>Females endorsed the following BPD features significantly more than males: affective instability; identity problems; negative relationships.</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Fonseca-Pedrero et al. (2011)</td>
<td>Females scored higher on affective instability, abandonment, negative relationships.</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Furnham &amp; Trickey (2011)</td>
<td>Females scored higher than males on overall BPD measure.</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Zanarini et al. (2011)*</td>
<td>Females reported mood reactivity and chronic feelings of emptiness significantly more than males.</td>
<td>Y</td>
</tr>
</tbody>
</table>
Dinsdale & Crespi, current data

Females scored significantly higher than males on BSL-23 (females: x=16.12, sd=13.75; males: x=13.06; \( sd=10.25; t=-2.06; df=225.44; p=0.04 \)).

*Included twice

4.4.2. Are BPD and depression associated with enhanced empathizing ability?

Under Baron-Cohen's EMB framework, the 'extreme female brain' involves enhanced empathizing and reduced systemizing. There exist few to no investigations of systemizing ability in depression and BPD, along with no clear hypotheses for how reduced systemizing may engender psychiatric illness, so we provide a partial test of the EFB hypothesis by reviewing evidence of empathizing ability in these conditions. Tests of empathizing ability involve quantification of numerous overlapping but separable social-cognitive processes including affective (e.g. emotion recognition, empathy, imitation) and cognitive components (e.g. Theory of Mind, mentalizing) (Rankin et al. 2005; Singer 2006; Choi-Kain & Gunderson 2008; Davis 1983; Premack & Woodruff 1978). We reviewed studies of theory of mind, empathy, and mentalizing ability in BPD, MDD, and in individuals with sub-clinical manifestations of BPD or depression to evaluate the hypothesis that BPD and depression are associated with increases in empathizing, compared to neurotypicals.

Our literature review of empathic functioning in depression included 14 studies and two reviews which are summarized in Table 4.3; studies involved the assessment of numerous facets of empathizing, including both affective and cognitive components. Studies from Wang and colleagues (2008) and Kettle and colleagues (2008) were excluded because comparison groups included subjects with psychotic features and schizophrenia, respectively. Two reviews of studies of facial emotion recognition in depression agreed that overall, individuals with major depression demonstrate general deficits in emotion recognition, in addition to biased attention and enhanced attention to, and recognition of, negatively-valenced emotional stimuli (Leppänen 2006; Cusi et al. 2011).

Affective empathy, or alternatively, empathic sensitivity, refers to an individual's relative sensitivity to the distress of others; this quality is often assessed by the subscales
personal distress and empathic concern from the Interpersonal Reactivity Index (IRI: Davis 1980, 1983 also see Table 4.4), which is a self-report questionnaire measuring both affective and cognitive empathy. Cognitive empathy as measured by the IRI involves perspective taking and fantasy. Depression appears to be associated with elevated empathic sensitivity (Thorma et al. 2011; O'Connor et al. 2002) but not in individuals with early-onset chronic depression (Wilbertz et al. 2010). Individuals with clinical depression showed reduced emotional awareness in two studies (Berthoz et al. 2000; Donges et al. 2005) whereas for individuals with sub-clinical depression, the severity of depressive symptoms positively predicted emotional awareness (Pasquier & Pedinielli 2010).

Higher-order cognitive empathizing abilities were consistently impaired in individuals with depression. For example, Inoue and colleagues (2004) found that individuals with remitted MDD demonstrated ToM impairments relative to healthy controls on a second-order false belief task and in another study, these ToM impairments predicted risk of future relapse (Inoue et al. 2006). Similarly, Zobel et al. (2010) reported evidence of impaired ToM on cartoon picture story sequencing-task. Findings in major depression starkly contrast with consistent evidence for enhanced mental state decoding skills, in individuals with sub-clinical manifestations of depression (Harkness et al. 2005; Harkness et al. 2010) and in individuals with a maternal history of depression (Harkness et al. 2011). Also, Lane and DePaulo (1999) found that individuals with sub-clinical depressive symptoms (e.g. 'dysphoria') were better than non-dysphoric individuals at detecting phoniness and false reassurances in one experimental paradigm, and more accurate than non-dysphorics at detecting deception intended for an opposite sex target in a second experiment. Overall, the studies indicate general impairments in mentalistic cognition in clinical depression - with the exception of elevated empathic sensitivity - and enhanced mental state decoding skills in sub-clinical depression.
Table 4.3. Summary of key findings for studies in empathic ability in depression

<table>
<thead>
<tr>
<th>Empathizing Ability</th>
<th>Studies</th>
<th>Key Findings</th>
<th>Enhanced (Y/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facial expression recognition</td>
<td>Leppänen 2006, Cusi et al. 2011</td>
<td>Generalized deficits in emotion recognition and enhanced attention to and recognition of negatively-valenced stimuli.</td>
<td>Y/N</td>
</tr>
<tr>
<td></td>
<td>O'Connor et al. 2002</td>
<td>Subjects with depression reported higher levels of empathic concern than subjects without depression.</td>
<td>Y</td>
</tr>
<tr>
<td>Self-reported empathy</td>
<td>Thorma et al. 2011</td>
<td>Subjects with depression reported higher levels of personal distress than subjects without depression.</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Wilbertz et al. 2010</td>
<td>Subjects with early-onset chronic depression reported decreased personal distress and perspective taking.</td>
<td>N</td>
</tr>
<tr>
<td>Emotional awareness</td>
<td>Berthoz et al. 2000</td>
<td>Subjects with depression demonstrated reduced overall emotional awareness.</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>Donges et al 2005</td>
<td>Subjects with depression demonstrated reduced awareness of the emotions of others.</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>Pasquier &amp; Pedinielli 2010</td>
<td>Emotional awareness was positively related to depressive symptoms.</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Harkness et al. 2005</td>
<td>Dysphoric subjects outperformed non-dysphoric subjects on the RMET and levels of dysphoria positively predicted RMET accuracy.</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Lee et al. 2005</td>
<td>Subjects with depression performed worse on the RMET than non-depressed subjects.</td>
<td>N</td>
</tr>
<tr>
<td>Mental state decoding</td>
<td>Harkness et al. 2010</td>
<td>Non-depressed subjects with a previous history of depression outperformed subjects with no depression history on the RMET.</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Harkness et al. 2011</td>
<td>Subjects with maternal history of depression performed better than subjects without maternal history of depression.</td>
<td>Y</td>
</tr>
<tr>
<td></td>
<td>Wolkenstein et al. 2011</td>
<td>No differences in RMET performance between groups.</td>
<td>N</td>
</tr>
<tr>
<td>Theory of Mind</td>
<td>Inoue et al. 2004</td>
<td>Depressed subjects performed poorer than controls on a second-order false belief ToM task.</td>
<td>N</td>
</tr>
<tr>
<td></td>
<td>Lane &amp; DePaulo 1999</td>
<td>Individuals with dysphoria were more accurate than individuals without dysphoria at detecting deception in two experimental paradigms.</td>
<td>Y</td>
</tr>
</tbody>
</table>
Depressed subjects showed impaired performance relative to controls on a cartoon picture sequencing task.

*Shaded areas indicate non-clinical sample

Dinsdale and Crespi (2012) reviewed 28 studies of empathic functioning in BPD and found that about half of the studies reported evidence for enhanced mentalistic cognition in BPD. In dyadic interactions requiring the inference of other subject's intentions and preferences, individuals with BPD outperformed psychiatrists (Ladisich & Feil 1988) and in a virtual monetary-exchange paradigm, individuals with BPD were more successful than healthy controls in perceiving and responding strategically to emotional and behavioural cues indicating fairness (Franzen et al. 2011). BPD and borderline personality features were associated with reduced emotional intelligence by some studies (Hertel et al. 2009; Gardner & Qualter 2009), conserved emotional intelligence in Beblo et al. (2010) and enhanced emotional intelligence in Park (1992). For theory of mind tasks other than the RMET, individuals with BPD demonstrated enhancements relative to non-BPD control subjects for a story task (Arntz et al. 2009), but not for the newly-developed Movie for Assessment of Social Cognition (MASC: Preißler et al. 2010). In the cartoon picture story sequencing-task, individuals with BPD and individuals without BPD performed comparably well (Ghiassi et al. 2010). Overall, for tasks involving active interactions, individuals with BPD consistently demonstrated enhanced mentalistic ability (Dinsdale & Crespi 2012). From the data we collected, we found that borderline personality features as assessed by the BSL-23 did not predict RMET performance in females ($r=-0.09, p=0.23$) or in males ($r=0.15, p=0.17$). However, there was a near-significant interaction between BSL-23 score and sex with respect to RMET performance ($F=3.6, p=0.06$), such that for males, increasing BSL-23 score were associated with relatively-increased RMET scores.

To examine BPD, depression, and mentalistic cognition in the context of the EFB hypothesis, we summarized findings from three measures of empathizing ability in the literature that demonstrate a well-documented female superiority in non-clinical populations and that have also been studied in BPD and depression (*Reading the Mind in the Eyes*, Baron-Cohen et al. 2001; *Interpersonal Reactivity Index*, Davis 1980, 1983; and *Levels of Emotional Awareness*, Lane et al. 1990); these studies provide a strong test of the EFB hypothesis and are summarized in Table 4.4. The RMET assesses
mental state decoding ability and for BPD, two of three studies indicated enhanced RMET performance in individuals with BPD relative to non-BPD control subjects (Table 4.4: Frick et al. 2012; Fertuck et al. 2009). With respect to depression, individuals with sub-clinical depressive symptoms (e.g. 'dysphoria'), maternal history of depression, and previous history of depression all demonstrated enhanced mental state decoding relative to individuals with no depressive symptoms or depressive history (Harkness et al. 2005; 2010; 2011). Individuals with a MDD diagnosis show reduced RMET performance in two studies (Lee et al. 2005; Harkness et al. 2011) and comparable performance to healthy controls in one study (Wolkenstein et al. 2011). Therefore, the difference in RMET performance of individuals with either dysphoria, past depression, maternal history of depression, or BPD, compared to non-depressed or non-BPD individuals, parallels the difference in RMET performance between healthy females and healthy males.

Table 4.4. Empathizing performance in BPD and depression on tasks with documented female advantage in non-clinical populations

<table>
<thead>
<tr>
<th>Task and Evidence of Female Advantage</th>
<th>Study</th>
<th>Sample</th>
<th>Performance in BPD or depression group relative to controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Enhanced</td>
</tr>
<tr>
<td>RMET</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baron-Cohen et al. (1999; 2001)</td>
<td>(1)</td>
<td>30 subjects with BPD (26 females) &amp; 25 non-clinical controls (15 females)</td>
<td>$p &lt; 0.001$</td>
</tr>
<tr>
<td>Our current data: $x_f=28.6, x_m=27.2; t=2.1, p &lt; 0.01$</td>
<td>(2)</td>
<td>21 females with BPD and 21 non-clinical females</td>
<td>$p = 0.009$</td>
</tr>
<tr>
<td></td>
<td>(3)</td>
<td>64 females with BPD &amp; 38 females non-clinical controls</td>
<td>$p = 0.58$</td>
</tr>
<tr>
<td></td>
<td>(4)</td>
<td>46 undergraduate students (31 females)</td>
<td>high-BPD better for negative emotions, $p &lt; 0.05$</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>positive &amp; neutral emotions, $p = n.s.$</td>
</tr>
<tr>
<td></td>
<td>(5)</td>
<td>Study 1: 43 undergraduate females (16 dysphoric &amp; 27 non-dysphoric)</td>
<td>dysphoria + related to RMET, $p &lt; 0.025$</td>
</tr>
<tr>
<td>Reference</td>
<td>Description</td>
<td>Results</td>
<td></td>
</tr>
<tr>
<td>-----------</td>
<td>-------------</td>
<td>---------</td>
<td></td>
</tr>
<tr>
<td>(6)</td>
<td>52 females with MDD &amp; 30 non-depressed control subjects</td>
<td>$p = 0.04$</td>
<td></td>
</tr>
<tr>
<td>(7)</td>
<td>93 undergraduate students (76 females &amp; 17 males; 41 past-depressed &amp; 52 never-depressed)</td>
<td>past-depressed group better, $p &lt; 0.05$</td>
<td></td>
</tr>
<tr>
<td>(8)</td>
<td>91 females (61 depressed &amp; 30 non-depressed) with variation in maternal history of depression</td>
<td>maternal depression + related to RMET, $p = 0.04$; depressed group worse, $p = 0.01$</td>
<td></td>
</tr>
<tr>
<td>(9)</td>
<td>24 MDD patients (13 females) &amp; 20 healthy matched controls</td>
<td>$p = 0.40$</td>
<td></td>
</tr>
<tr>
<td>(10)</td>
<td>30 BPD subjects (20 females &amp; 10 males) &amp; 40 non-BPD controls (20 females &amp; 20 males)</td>
<td>reduced LEAS, $p &lt; 0.001$</td>
<td></td>
</tr>
<tr>
<td>(11)</td>
<td>15 MDD subjects &amp; 15 matched control subjects</td>
<td>reduced LEAS, $p &lt; 0.05$</td>
<td></td>
</tr>
<tr>
<td>(12)</td>
<td>22 MDD subjects (15 females &amp; 7 males) &amp; 22 matched control subjects</td>
<td>LEAS-other score, $p &lt; 0.05$; LEAS-self score, $p &gt; 0.05$</td>
<td></td>
</tr>
<tr>
<td>(13)</td>
<td>107 volunteers from hospital population with sub-clinical anxious and depressive symptoms (13 males &amp; 94 females) with mean age of 43.21 years</td>
<td>LEAS &amp; depressive symptoms + related, $p = 0.003$</td>
<td></td>
</tr>
<tr>
<td>(14)</td>
<td>27 BPD females &amp; 28 clinical control females &amp; 27 non-clinical control females</td>
<td>affective empathy, $p &lt; 0.01$; cognitive empathy, $p &lt; 0.01$</td>
<td></td>
</tr>
<tr>
<td>(15)</td>
<td>20 BPD subjects (18 females) and 22 non-clinical controls (19 females)</td>
<td>cognitive empathy, $p = 0.038$; affective empathy, $p = 0.205$</td>
<td></td>
</tr>
<tr>
<td>(16)</td>
<td>21 patients with severe MDD (13 females) and 21 matched healthy controls</td>
<td>affective empathy, $p &lt; 0.001$; cognitive empathy, $p = 0.288$</td>
<td></td>
</tr>
</tbody>
</table>
For self-reported empathy as assessed by the widely-employed IRI, results were mixed but indicative of a pattern of enhanced or conserved affective empathy combined with reduced or conserved cognitive empathy for both BPD and depression (Table 4.4). Healthy females report higher scores than males for IRI cognitive and affective empathy (Berthoz et al. 2008; Mestre et al. 2009) and thus, under the EFB hypothesis, it appears that depression and BPD are associated with more 'female-typical' affective empathy, but not cognitive empathy.

Results from the LEAS indicated that sub-clinical depressive features positively predict overall emotional awareness (Table 4.4: Pasquier & Pedinielli 2010) whereas BPD and MDD involved reduced emotional awareness, particularly the awareness of the emotions of others (Table 4.4: Levine et al. 1997; Berthoz et al. 2000; Donges et al. 2005). The differences in LEAS scores between individuals with depression or BPD, and individuals without either condition, do not parallel the differences between healthy females and healthy males for this measure.

4.4.3. **Are depression, BPD, and empathizing associated with female-typical digit ratios?**

Hormones play a major role in mediating sexually dimorphic behaviours, firstly through their organizational effects occurring during prenatal development, and secondly, through their activating effects which fluctuate throughout the lifespan as a function of age and reproductive status (Ngun et al. 2011). Digit ratio, specifically the ratio between
the second and fourth digits (2D:4D), is a sexually dimorphic trait that reflects foetal exposure to relative levels of sex steroids in the uterine environment; 2D:4D is negatively related to the ratio of foetal testosterone to foetal estradiol and thus, on average, males demonstrate lower digit ratios than females (Manning et al. 1998; Lutchmaya et al. 2004). In support of the EMB theory of autism, individuals with ASCs as well as their first-degree relatives tend to show smaller, more masculine digit ratios (Manning et al. 2001; Milne et al. 2006, but see Honekopp 2012). We reviewed the small literature of digit ratio in BPD and depression to test the prediction that larger, more feminine digit ratios would be associated with these conditions.

Bailey and Hurd (2005) studied depressive features and digit ratio in a sample of non-clinical undergraduates and found that in males only, more feminine 2D:4D predicted increased scores on Beck's Depression Inventory (BDI: Beck et al. 1996). In contrast, Vermeersch and colleagues (2008) reported that smaller 2D:4D ratios predicted increased depressiveness in adolescent boys, but the traits were not related to each other in adolescent girls. One study investigated digit ratio in relationship to BPD, and consistent with the EFB prediction, more feminine digit ratios predicted increased scores on a borderline personality questionnaire in non-clinical men and women (Evardone et al. 2008).

Also relevant to an EFB model of depression and BPD are relationships of digit ratio to empathizing and systemizing. In a large sample of healthy adults, Voracek and Dressler (2006) found no association of digit ratio with either empathizing or systemizing, as measured by the empathy quotient (EQ: Baron-Cohen & Wheelwright 2004) and the systemizing quotient (SQ: Baron-Cohen et al. 2003). Wakabyashi and Nakazawa (2010) investigated the same variables in a sample of Japanese university students and found that digit ratio negatively predicted SQ scores and positively predicted EQ scores. Similarly, Manning and colleagues (2010) found that 2D:4D was negatively correlated with SQ scores but not related to EQ scores. In another study, von Horn and colleagues (2010) calculated a composite score from EQ and SQ data and found that for males only, feminine digit ratios predicted increased empathizing relative to systemizing. Females but not males showed a positive relationship between affective empathy, as assessed from a self-report Likert scale composed of questions from multiple empathy measures, and left-hand digit ratio (Kempe & Heffernan 2011). Using the RMET to
measure empathizing skill, van Honk et al. (2011) found that digit ratio interacted with testosterone administration to produce differential effects on RMET accuracy of females, such that females with smaller digit ratios demonstrated greater reductions in RMET scores than females with larger digit ratios. Effect sizes in these studies are small, but the overall pattern indicated that decreased ratios of foetal tesoterone to foetal estradiol, as evidenced by 2D:4D, contribute to elevated empathizing in both sexes.

4.5. Discussion

We synthesized evidence from sex-ratio investigations, empathizing research, and digit ratio studies to evaluate the hypothesis that depression and BPD show patterns of association with these traits consistent with an 'extreme female brain' (EFB) hypothesis, in contrast with autism spectrum conditions (ASCs) as the 'extreme male brain' (EMB). Together, the three lines of evidence converge in providing preliminary support for the hypothesis: (1) MDD and BPD, as well as depressive, borderline, and neurotic personality traits, are more prevalent in females (with the exception of community samples indicating an equal sex-ratio of people meeting BPD diagnostic criteria); (2) BPD, borderline and depressive personality features, previous depressive status, and maternal history of depression were related to elevated RMET performance in six out of nine studies (Table 4.4), in addition to BPD and MDD demonstrating associations with elevated self-reported affective empathy relative to control subjects for three of five studies, but reduced emotional awareness in three of four studies; and (3) empathizing is associated with associations with larger, more feminine digit ratios and individuals with depressive and borderline features may also show female-typical digit ratios, though this evidence is sparse and inconsistent. Our review thus indicates that the EMB and E-S frameworks can be usefully extended to investigate the role of female-typical psychological and hormonal phenotypes in contributing to BPD and depression.

Evidence for a female bias in the prevalence of depression and BPD is strong, with the exception of studies that surveyed large community samples and reported no sex differences in the prevalence of individuals meeting DSM or ICD criteria for BPD (Grant et al. 2008; Jackson & Burgess 2000; Jane et al. 2007; Zanarini et al. 2011). To meet DSM-IV-TR criteria for a BPD diagnosis, an individual needs to exhibit any combination
of five symptoms from a nine-item list (APA 2000), thus creating a situation where individuals with very different symptom profiles may receive the same diagnostic label of BPD. Males and females indeed tend to report different kinds of borderline features (Zanarini et al. 2011) and the borderline traits more commonly reported by females (e.g. mood reactivity and chronic feelings of emptiness) may engender clinically significant problems at a lower threshold than those traits more commonly reported by males (e.g. impulsiveness). With respect to the high prevalence estimates of BPD in these community samples (e.g. 5.9% in Grant et al. 2008 and Zanarini et al. 2011), Paris (2010) argued that overly broad definitions of personality disorders in the DSM-IV-TR, unclear distinctions between traits and disorders, and the lack of clinical experience of persons conducting interviews may have inflated prevalence estimates in community samples; together, these factors may also play a role in the discrepancy between sex-ratio estimates drawn from clinical and community samples. Overall, when sex differences in BPD and depression are considered in the context of overlapping features belonging to the broader neuroticism spectrum, with extreme expressions of symptoms manifesting as psychopathology, the evidence generally converges in demonstrating a female-bias for these conditions.

The central feature of the EFB under Baron-Cohen's E-S and EMB theories is an extreme version of the 'female-typical' cognitive profile, one that involves enhanced empathizing and corresponding reductions in systemizing; our review thus constitutes a partial test of the EFB hypothesis. Mentalistic functioning in BPD and depression varies considerably, especially as a function of disorder severity, but the key patterns were elevated empathic sensitivity in depression and BPD, and enhanced mental state decoding skills in sub-clinical depression and in BPD (Table 4.3, 4.4). Both conditions were also associated with reduced emotional awareness and impaired cognitive empathy. Consistent with the EFB hypothesis of depression and BPD, we found that for measures showing elevated empathizing in these conditions (RMET; IRI personal distress & empathic concern), the differences between individuals with either depression or BPD, relative to healthy individuals, paralleled the differences between healthy females and healthy males. Furthermore, the evidence also indicated that increasing levels of depressiveness in individuals without MDD were associated with enhanced mental state decoding ability, as well as elevated emotional awareness (Harkness et al.
Together, these findings are consistent with the hypothesis that social-cognitive features comprising sub-clinical depression may motivate and enable a hypersensitive and analytical framework for solving complex social problems, which becomes compromised during full-blown depression (Allen & Badcock 2003; Forgas 2007; Andrews & Thomson 2009; Harkness et al. 2011). Based on the general female advantage in empathizing, it appears that a ‘complex social-problem-solving’ cognitive style is more characteristic of females than males and therefore, under the EFB hypothesis, enhanced social-cognitive ability and propensity to depression and BPD may be linked.

Clinical depression, among many psychiatric conditions, is associated with impaired executive function, reduced motivation, and working memory deficits (Burt et al. 1995; Fossati et al. 2002; Hasler et al. 2004) and thus it is likely that empathizing performance in severe MDD as well as BPD is confounded by the presence of these global deficits (Lee et al. 2005). For example, Zobel et al. (2010) found that chronic depression predicted poor ToM performance on a cartoon-picture story task, but after controlling for logical memory and working memory, depressive status no longer predicted ToM ability. Similarly, Gardner et al. (2010) reported a significant interaction between borderline features and executive control with respect to decoding emotions from facial expressions, such that high borderline features combined with low executive control predicted poor recognition of angry faces while high borderline features and high executive control predicted enhanced recognition of angry faces. Therefore, several factors common to psychiatric illness, such as general cognitive ability and motivation, may confound the relationship between empathizing ability and specific features of BPD or depression. Disentangling the contributions of depressive and borderline traits and symptoms to specific aspects of mentalistic cognition will require focussed hypotheses and a careful consideration of possible confounding variables.

Given the converging lines of evidence pointing toward a role for enhanced empathizing in psychiatric conditions (Crespi & Badcock 2008; Brosnan et al. 2010; Zahn-Waxler & Van Hulle 2012; Bremer & Gallup 2012; Dinsdale & Crespi 2012), future research needs to develop and test hypotheses for how and why mentalistic enhancements can become maladaptive. As outlined previously, Zahn-Waxler and Van Hulle (2012) forwarded a developmental model of this process, proposing that dysfunctional
childhood environments interact with precocious empathic abilities to engender increased liability to depression and anxiety later in life. A similar model has been proposed for the genesis of BPD (Park et al. 1992). In Dinsdale and Crespi (2012), we suggested that BPD might be caused in part by enhanced attention to, and perception of, social stimuli, interacting with deficits in other domains such as emotion regulation, attentional control, and attachment dysregulation. Understanding how empathizing contributes to depression and BPD, and to the psychotic-affective spectrum of psychiatric conditions more broadly, will require an integration of neurological, developmental, and psychological approaches.

Our EFB hypothesis regarding depression and BPD poses a series of important questions concerning the role of variation along the empathizing-systemizing axes in mediating female-preponderant conditions: is it primarily enhanced empathizing that creates risk of depression and BPD (red area of Figure 4.1) or could enhanced empathizing synergistically interact with reduced systemizing to mediate risk (yellow area of Figure 4.1)? Bremser and Gallup's (2012) research into disordered eating found that decreased performance on a mental rotation task, a correlate of systemizing ability, predicted both dysfunctional attitudes toward eating and fear of negative evaluation anxiety. Other studies have examined neuropsychological functioning in BPD and depression with tasks that belong to the broad domain of systemizing: for example, there is evidence for reduced performance on the Embedded Figures Test (EFT: Witkin et al. 1971) in depression (Calamari et al. 2000) and BPD (Beblo et al. 2006); however, further studies with tests of alternative hypotheses for the role of reduced systemizing, and the role of combined empathizing enhancements and systemizing reductions, in contributing to depressive and borderline pathology are required to further develop the EFB model.

Whether or not these systemizing abilities play a causal role in contributing to risk of depression, BPD, and eating disorder pathologies is unknown, but reduced systemizing ability may, in principle, impair a person's ability to maintain objectivity in social situations. Future research could usefully focus on developing and testing specific hypotheses for how relatively-low systemizing may relate to psychological traits and risk factors, including, for example, negative evaluation anxiety, objective perspective-taking, and tendencies to deploy emotional approaches, more than cognitive ones, to social problem-solving.
Figure 1. Adapted from Baron-Cohen (2002). Variation in psychological functioning illustrated along the axes of empathizing and systemizing. Dark blue region indicates 'extreme male brain' where ASCs manifest. Is depression and/or BPD caused by enhanced empathizing (dark red area) or by an interaction of enhanced empathizing and reduced systemizing (yellow area)?

Of the few studies investigating digit ratio in BPD and depression, findings indicated an association between feminine 2D:4D ratios with borderline characteristics in males and females (Evardone et al. 2008) and with depressive features in adult males (Bailey & Hurd 2005), but not in adolescent males (Vermeersch et al. 2008). Additional studies, particularly of digit ratio in clinical samples of depression and BPD, would be useful. Interestingly, the general pattern of digit ratio studies in schizophrenia and schizotypy reveal evidence for feminization (in contrast to masculinization in autism), though results in the schizophrenia spectrum are more variable (Voracek 2008). Preliminary evidence for positive relationships between more female-typical digit ratio and empathizing in several studies (Wakabyashi & Nakazawa 2010; von Horn et al. 2010; Kempe & Heffernan 2011; van et al. 2011) are also consistent with the EFB model predictions, suggesting a link between reduced prenatal masculinization and elevated empathic functioning, which is congruent with evidence for reduced eye contact and language learning in children that show relatively-elevated levels of amniotic testosterone prenatally (Lutchmaya et al. 2002; Knickmeyer et al. 2005). With research indicating a role of foetal testosterone in shaping sexually dimorphic brain areas (Lombardo et al.
2012), sex differences in hormonal organization are becoming linkable to sex differences in psychological traits, of which the extreme expression appears to underlie sex-related patterns of psychiatric conditions (Figure 4.2).

Figure 4.2. Conceptual model of how the foetal testosterone (fT) to foetal estradiol (fE) ratio (fT/fE) might influence shifts toward relative mentalistic (red arrows) or mechanistic strengths (blue arrows), as well as shifts toward increasing risk of female-preponderant psychotic-affective conditions (PACs), such as depression and BPD, or male-preponderant autism spectrum conditions (ASCs). This model does not imply that fT/fE is the only factor shaping psychological traits and psychiatric conditions, only that it plays an important role in mediating sex differences in mentalistic-mechanistic cognition.

4.6. Conclusions

We extended Baron-Cohen's EMB and E-S frameworks to investigate if BPD and depression are, in contrast to autism, consistent with an EFB model: evidence from digit ratio, sex-ratio, and empathizing studies converge in providing support for conceptualizing these conditions as, in part, expressions of the ‘extreme female brain’. This review in combination with a growing body of research (Bremser & Gallup 2012; Dinsdale & Crespi 2012; Brosnan et al. 2010) implicates an important role for elevated
mentalistic cognition in mediating female-preponderant psychiatric conditions belonging to the broader psychotic-affective spectrum; whether or not reductions in systemizing ability also contribute to these conditions is an important avenue for future research. Understanding the role that sex differences play in shaping variation in mentalistic and mechanistic cognition can help further elucidate the aetiology of female- and male-preponderant psychiatric conditions.

4.7. References


5. Conclusions

Understanding how and why humans are vulnerable to a high rate and diversity of psychological disorders benefits from the grounding of psychiatric research in evolutionary foundations. My thesis tested predictions from Crespi and Badcock's diametric disorders hypothesis in Chapter 1 and extended Baron-Cohen's empathizing-systemizing (E-S) and 'extreme male brain' (EMB) theories to examine an 'extreme female brain' (EFB) model of depression and borderline personality disorder (BPD) in Chapters 2 and 3. Chapter 1 revealed novel psychometric evidence for an autism-positive schizotypy axis and Chapters 2 and 3 implicated an important role for enhanced mentalistic cognition in contributing to psychotic-affective conditions. Together, these chapters help to develop an evolutionary-psychiatry framework for examining how evolved sex differences and variation in the human social brain interact to shape our species' liability to psychiatric conditions.

Consistent with the diametric disorders hypothesis, Chapter 1 reported evidence for a phenotypic axis ranging from autism to positive schizotypy in a non-clinical sample, after the effects of general social functioning were removed. These findings support the hypothesis that variation along a social-cognitive axis diametrically mediates the autism and psychotic-affective spectra. The results also provide some of the first psychometric evidence for an autism-schizotypy axis and highlight the importance of examining relationships between constellations of traits and features when inferring aetiology, rather than just comparing deficit phenotypes. Deficits in general abilities like social functioning are characteristic of both autism and schizophrenia, and reflect highly diverse causes, so it is more informative to examine relationships between 'positive' phenotypes, such as magical thinking in schizotypy and enhanced perceptual functioning in autism, as these features should be more likely to illuminate specific aetiological pathways (Crespi 2011).
The literature reviews in Chapters 2 and 3 revealed evidence for enhanced mentalistic cognition in BPD and depression, and outlined plausible models for how empathic enhancements may contribute to these psychiatric conditions. Furthermore, Chapter 3 indicated that key features of BPD and depression are consistent with an EFB model, given that in addition to demonstrating elevated aspects of empathizing ability, both of these conditions are more prevalent in females and show preliminary evidence for associations with feminine 2D:4D ratios. In addition to Bremser and Gallup’s (2012) work on eating disorders, Chapter 3 provides one of the first applications of Baron-Cohen’s framework to female-preponderant psychiatric conditions. Future research could extend the EFB model to investigate the broader psychotic-affective spectrum: females experience relatively higher levels of positive (compared to negative) schizophrenia symptoms than males (Lindamer et al. 1999); positive schizotypy is associated with elevated reports of empathy (Dinn et al. 2002) and; individuals with paranoid schizophrenia may show enhanced recognition of genuine emotion relative to individuals without schizophrenia (LaRusso 1978). Posing a central role for empathic enhancements in contributing to BPD and depression - and possibly other psychotic-affective conditions - usefully links the EMB and E-S theories with the diametric model, indicating important and overlapping effects of both sex dimorphism and social-cognitive variation in shaping patterns of susceptibility to major suites of psychiatric conditions.

Applying a framework of trade-offs from evolutionary theory may further elucidate how these interacting axes of sex and social cognition mediate variation in normal and abnormal psychological functioning. The mind has evolved under multiple competing and interacting selective pressures and as such, social-brain phenotypes, and cognition more generally, reflects compromises at the level of genes, neurology, and physiology (Hills & Hertwig 2011). Indeed, some evidence suggests that empathizing and systemizing trade off with one another: empathizing is negatively correlated with systemizing across individuals (Nettle 2007); visual-spatial abilities within the broad domain of systemizing negatively predict social and verbal skills belonging to the broad empathizing domain (Pellicano et al. 2006; Cook & Saucier 2010; Johnson & Bouchard 2007); and performance on the RMET negatively predicts performance on the Embedded Figures Test, which is a measure of local versus global processing (Baron-Cohen & Hammer 1997; Baron-Cohen et al. 1997). These performance-based
observations of trade-offs between mechanistic and mentalistic cognition are also evident at the level of brain organization: for example, anatomical evidence indicates that adjusting for overall size, as anterior prefrontal cortex size increases, the size of primary sensory cortices decreases (Song et al. 2011).

The female advantage in mentalistic cognition at the population level suggests that through evolutionary time, females may have conferred greater benefits than males by tending toward the mentalistic end of the mentalistic-mechanistic trade-off. While the distributions of mentalistic ability for females and males overlap considerably, more females than males will exhibit relatively-enhanced mentalistic abilities and thus be at increased risk of psychiatric disorders involving aspects of hyper-empathizing. Pathology increases in likelihood as one moves toward the tails of the distribution of empathizing and systemizing abilities, where enhancements may confer advantages but are also more prone to disruption (e.g. enhanced empathic sensitivity and dysfunctional home environments in childhood contributing to later depression outlined in Zahn-Waxler & Van Hulle 2012). Alternatively, enhancements themselves may contribute more directly to dysfunction, such may be the case in autism where enhanced perceptual functioning in infancy appears to disrupt joint attention systems, thus causing downstream effects which prevent normal development and in turn cause the social and language impairments characteristic of the autism spectrum (Mottron et al. 2006). Under the diametric model, autism and psychotic-affective conditions can be conceptualized as representing contrasting outcomes of dysregulation to the mechanistic/systemizing-mentalistic/empathizing systems.

Examining psychiatric conditions within a trade-off framework, with a focus on evolved sex differences in the balance between mechanistic and mentalistic cognition, can help link proximate and ultimate causation as well as contextualize psychiatric conditions as extremes of naturally-occurring variation in human personality- as 'cognitive styles’- that in some cases, extend into pathology. This approach could potentially lead to novel sex- and symptom-specific therapeutic developments. For example, if future research found that empathizing enhancements synergistically interact with systemizing impairments to mediate depression and BPD (a question posed in Chapter 3, see Figure 4.1), then perhaps psychological interventions that specifically focussed on increasing systemizing skills may be useful in managing certain kinds of depressive or borderline symptoms.
My thesis findings contribute to a developing evolutionary-psychiatry framework that highlights both important and interesting considerations for future research into psychiatric disorders: both over- and under-developed cognitive and affective features can engender psychological dysfunction; altered organization of sex differences in psychological functioning underlie major suites of psychiatric illness; and social brain adaptations have evolved through numerous competing and interacting selective forces, thus creating specific patterns of psychiatric dysfunction that extend from normal variation in personality and behaviour. These considerations can motivate novel hypotheses into the causes and symptoms of psychological dysfunction and also have the potential to inform current diagnostic and treatment paradigms of psychiatric disorder.

5.1. References


