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The 2D:4D ratio of the hand and schizotypal personality traits in schizophrenia patients and healthy control persons

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ABSTRACT

Prenatal estrogen/testosterone exposure is known to be involved in early brain development. In this context, the ratio of the index finger to ring finger length (2D:4D) has been put forward as an indicator of the intrauterine sex hormonal level.

A previous study by Collinson et al. (2010) examined 2D:4D ratios in Asian patients with schizophrenia and found an increased 2D:4D pattern in male patients compared to male healthy controls. In the current study, we tried to replicate the result of this study on the 2D:4D ratio in schizophrenia patients and controls in a Chinese sample. Moreover, we investigated the link between 2D:4D ratios and schizotypal personality traits in the participants of the study.

No significant difference between cases and controls in 2D:4D ratios for both hands could be observed. However, a positive association between right 2D:4D ratio and schizotypal personality traits was found in healthy controls (both in the male and female subsamples) suggesting that a high 2D:4D ratio could represent a vulnerability factor for schizophrenia in healthy males and females. Same results were observed for the digit ratio of the left hand and the SPQ in the healthy total and healthy female subsample. Therefore, the inclusion of personality measures to study the link between the digit ratio and schizophrenia might help to provide insights in a potential continuum from healthy to schizophrenic behavior.

1. Introduction

Schizophrenia represents a heavy burden for the patients afflicted and causes great costs for society (Knapp et al., 2004). Therefore, research to better understand schizophrenia represents an important endeavor. As schizophrenia cannot be explained by a single factor, but can be best described as a multi-factorial caused disorder including the influence of both genetics and environment (Cannon et al., 2003; Polan et al., 2007; Tsuang, 2000; Tsuang et al., 2001), diverse approaches are used to investigate the biological underpinnings of schizophrenia.

It has been proposed that neurodevelopmental insults during gestation are associated with the pathogenesis of schizophrenia (Markham, 2012; Mednick et al., 1988; Moldin and Gottesman, 1997). This hints toward antenatal factors being involved in the development of this psychopathological disorder. In this context, mounting evidence indicates a reduction or reversal of hemispheric lateralization, either functional or anatomical, in schizophrenia (Angrilli et al., 2009; Bhojraj et al., 2009; Bleich-Cohen et al., 2009; Crow, 2010; Crow et al., 1996; Mohr et al., 2001; Oertel et al., 2010; Sheng et al., 2013).

On a hormonal level, androgen theories suggest that hemispheric lateralization occurs early in development in response to prenatal estrogen/testosterone exposure (Grimshaw et al., 1995; Witelson and Nowakowski, 1991). However, it is difficult to measure directly the prenatal estrogen/testosterone concentrations in humans because of ethical problems. The ratio of index finger to ring finger length (2D:4D) is a sexually dimorphic anatomic feature determined by the thirteenth week of pregnancy (Manning, 2009). It remains relatively stable throughout adult stage, and has been put forward as an indicator of intrauterine sex hormonal levels (Brown et al., 2002; Manning et al., 1998;

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McIntyre et al., 2005). A low 2D:4D ratio indicates a more 'male' hand mirroring a stronger influence of prenatal testosterone on the bodily (brain) development while gestation. The strong line of evidence from a large number of studies showing a link between individual differences in the 2D:4D ratio and prenatal testosterone levels, but not the level of testosterone or other sexual hormones in adulthood has been summarized in a seminal work by Honekopp et al., 2007. Supporting these observations, numerous studies have demonstrated that males tend to display lower values of 2D:4D ratio than females (Daly et al., 2008; Manning, 2009; Walder et al., 2006; Yang et al., 2009).

Some of the variations in behavioral tendencies and personality have been reported to be associated with 2D:4D ratio (the pattern of early exposure to sex hormones). For example, autistic features such as deficits in communication and social interactions were thought to be related to a low 2D:4D ratio in children with autism (Bejerot et al., 2012; De Bruin et al., 2009; Manning et al., 2001; Milne et al., 2006). A recent study by Leow and Davis (2012) provided evidence that 2D:4D ratio predicts adult face perception skills. Moreover, it was reported that a more masculinized (low) 2D:4D ratio was correlated with attention-deficit/hyperactivity disorder (ADHD) symptoms (Martel, 2009), but there was also an inconsistent finding (Lemiere et al., 2010). Low 2D:4D ratio was also found to be linked to physical aggression (Bailey and Hurd, 2005; Benderlioglu and Nelson, 2004; van der Meij et al., 2012) and alcohol dependence (Kornhuber et al., 2011). Recently, a study by Wacker et al. (2013) demonstrated a link between impulsive sensation seeking and a low 2D:4D ratio in males. Older studies by Fink et al. (2004) and Lippa (2006) revealed inconsistent findings with respect to the Big Five of Personality. In particular, the study by Lippa (2006) is noteworthy because of its large sample size (>1000 participants) reporting a weak negative correlation between the 2D:4D ratio and extraversion as well as agreeableness and a weak positive correlation between 2D:4D ratio and openness to experience.

In schizophrenia research, findings involving 2D:4D ratio and asymmetry have not always been consistent. Collinson et al. (2010) examined the 2D:4D ratio in Asian patients with schizophrenia and found less masculinized (increased) 2D:4D pattern in male patients compared to male controls but not in females, which was partly consistent with the previous finding of Arato et al. (2004), who observed more 'female' hands in both male and female schizophrenia patients (although they did not calculate the 2D:4D ratio but subtracted the length of 2D − 4D). On the contrary, another study by Venkatasubramanian et al. (2011) showed a significantly lower 2D:4D ratio in female patients with schizophrenia compared to female healthy controls, which was consistent in parts with the result reported by Procopio et al. (2006), who found a difference between the second digit when comparing females with schizophrenia and female healthy controls, but also did not calculate ratios. Venkatasubramanian et al. (2011) further analyzed the 2D:4D asymmetry index (see method section 2.3.) and found that mean 2D:4D asymmetry index was lower in male patients with schizophrenia than male healthy controls. Daly et al. (2008) investigated 2D:4D ratio in individuals at risk for schizophrenia and found no significant difference between risk and control groups. Walder et al. (2006) examined the 2D:4D ratio in adolescents with schizotypal personality disorder (SPD) and demonstrated that the typical sex difference in the 2D:4D ratio could only be observed in healthy controls (with males showing lower 2D:4D ratios), but not in patients with SPD. Gooding et al. (2010) examined two groups of participants at risk for schizophrenia (positive and negative schizotypy) and a control group and found an overall lower left digit ratio in males than females, but no group differences in the digit ratio for both hands. In sum, the 2D:4D represents an interesting approach to study schizophrenia. Nevertheless, several inconsistencies exist, which can be explained by the varying sample sizes, different ethnicities investigated (e.g. Manning et al. (2007) showed that ethnic differences might exist with respect to the 2D:4D ratio), and – perhaps most important – different approaches have been used to measure the finger length: here, studies range from the investigation of only fingers over the subtraction of the 2D − 4D to the use of the digit ratio and the inclusion of only one or both hands. All results relevant for the link between schizophrenia and 2D:4D are summarized in detail in Table 1.

To the best of our knowledge, no study has examined the link between individual differences in the 2D:4D digit ratio and schizotypal personality traits in schizophrenia and healthy controls until now – thereby going beyond classic case control designs. Our aims of the present study were: (1) to replicate the study of 2D:4D ratio and schizophrenia in a Chinese sample (compare the study of Collinson et al. (2010)); (2) to investigate the association between 2D:4D ratio and schizotypal personality traits in schizophrenia patients and healthy controls. Given the initial findings by Collinson et al. (2010) investigating in large parts a Chinese sample, we set up the hypothesis that male schizophrenia patients are associated with a higher 2D:4D ratio compared to male control persons. With respect to a potential link between schizotypal personality traits and the 2D:4D ratio in both schizophrenia patients and healthy controls, we hypothesized that more 'female' hands would be associated with higher scores on a questionnaire measuring schizotypal personality traits particularly in males.

2. Method

2.1. Participants

A total of 102 Chinese participants (51 schizophrenia patients and 51 healthy controls) were enrolled in the study. The schizophrenia patients were inpatients recruited from Shanghai Mental Health Center, Shanghai, China, with the following inclusion criteria: age between 18 and 45; a diagnosis of schizophrenia based on the Structured Clinical Interview for DSM (SCID) Patient Edition for DSM-IV (First et al., 1997). Control participants were college students and staff at Shanghai Jiao Tong University School of Medicine, Shanghai, China. One schizophrenia patient reported to be left handed and two control persons reported to be left handed. The rest of the sample stated to be right handed. Inclusion criteria for the control group were: age between 18 and 45; no Axis I or Axis II diagnosis by using the Structured Clinical Interview for DSM-IV (First et al., 1997, 1999), and no history of Axis I disorders in their first-degree relatives. Participants with a history of broken fingers were excluded. The study was approved by the local institutional ethics board (Institutional Review Board of Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine), and written informed consent was obtained from all participants prior to inclusion.

2.2. Personality measures

Each participant completed a short questionnaire, including the information of age, sex and education, and a 22-item scale of the Schizotypal Personality Questionnaire-Brief Form (SPD-B) (Raine and Benishay, 1995). The SPQ-B measures the personality traits of "Cognitive–Perceptual Schizotypy" (8 items), "Interpersonal Schizotypy" (8 items) and "Disorganization" (6 items) with yes/no format. Each "yes" response counts as one point, with total scores (adding up the numbers of the subscales) ranging from 0 to 22. The SPQ-B total score showed strong internal consistency (Cronbach's $\alpha = .871$) in the current sample (consisting of both schizophrenia patients and controls). The coefficient α value for each subscale of