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# No evidence for altered prenatal exposure to testosterone in young females diagnosed with Borderline Personality Disorder

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## ABSTRACT:

**Introduction.** Borderline Personality Disorder (BPD) is characterised, among other features, by increased impulsivity and aggression, both directed toward the self and others. These clinical signs most likely arise from complex gene-environment interactions. In our study, we sought to elucidate the role of prenatal testosterone exposure in female patients with BPD.

**Materials and Methods.** In a sample of 42 patients and 50 controls matched for age and biological sex, we measured the ratio of the second to the fourth digit of both hands (2D:4D ratio), which is established as a reliable correlate of prenatal testosterone levels in the foetus. In addition, we used several self-rating scales to determine personality dimensions, impulsivity, aggressiveness and risk-taking behaviour.

**Results.** No differences between the groups emerged with regard to 2D:4D ratio of both hands. In addition, there were almost no correlations between psychological measures and the 2D:4D ratio in the entire sample.

**Conclusions.** Contrary to predictions, female patients with BPD did not differ from controls in 2D:4D ratio bimanually, suggesting no abnormal intrauterine (prenatal) exposure to testosterone in this clinical group. As expected, differences between patients and controls in personality traits, impulsivity, aggressiveness and risk-taking were highly significant and in concordance with the existing body of knowledge. Since BPD features are highly heterogeneous, it could be interesting to study subgroups of BPD patients, rather than the broader phenotype according to DSM-5 criteria.

**KEYWORDS:** Borderline personality disorder; prenatal testosterone; digit ratio; impulsivity; aggressiveness; risk-taking.

## SAŽETAK:

NEMA DOKAZA ZA PROMIJENJENU PRENATALNU IZLOŽENOST TESTOSTERONU KOD MLADIH ŽENA S DIJAGNOZOM GRANIČNOG POREMEĆAJA OSOBNOSTI

**Uvod.** Granični poremećaj ličnosti (BPL) karakterizira, među ostalim, povećana impulzivnost i agresivnost, kako prema sebi tako i prema drugima. Ovi klinički znakovi najvjerojatnije proizlaze iz složenih interakcija gena i okoline. U našoj smo studiji nastojali razjasniti ulogu prenatalne izloženosti testosteronu u pacijentica s BPL-om.

**Materijali i metode.** Na uzorku od 42 bolesnika i 50 kontrola usklađenih po dobi i biološkom spolu, izmjerili smo omjer drugog i četvrtog prsta obje ruke (omjer 2p:4p), što je utvrđeno kao pouzdana korelacija prenatalnih razina testosterona u fetusu. Osim toga, koristili smo nekoliko ljestvica samoocjenjivanja kako bismo odredili dimenzije osobnosti, impulzivnost, agresivnost i rizično ponašanje.

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Rezultati. Nisu se pojavile razlike između skupina s obzirom na omjer 2p:4p obje ruke. Osim toga, gotovo da nije bilo korelacije između psiholoških mjera i omjera 2D:4D u cijelom uzorku. Zaključci. Suprotno predviđanjima, pacijentice s BPL-om nisu se razlikovale od kontrolne skupine u omjeru 2p:4p bimanualno, što sugerira da nema abnormalne intrauterine (prenatalne) izloženosti testosteronu u ovoj kliničkoj skupini. Kao što se očekivalo, razlike između pacijenata i kontrola u osobinama osobnosti, impulzivnosti, agresivnosti i preuzimanju rizika bile su vrlo značajne u skladu s postojećim znanjem. Budući da su značajke BPL-a vrlo heterogene, moglo bi biti zanimljivo proučavati podskupine pacijenata s BPL-om, a ne širi fenotip prema DSM-5 kriterijima.

**KLJUČNE RIJEČI:** granični poremećaj ličnosti; prenatalni testosteron; omjer duljine prstiju; impulzivnost; agresivnost; preuzimanje rizika.

## INTRODUCTION

The term “Borderline Personality Disorder” (BPD) describes a psychiatric condition that is characterised by difficulties in emotion regulation, impulsivity, risk-taking behaviour, chronic feelings of emptiness, fear of abandonment, inappropriate anger, and occasional paranoid or dissociative symptoms (1). Many of the above-mentioned symptoms emerge before a background of childhood trauma, often in the form of emotional neglect or abuse by early caregivers, causing the development of mistrustful inner working models and severe interpersonal difficulties (overview in (2)).

Neurobiologically, there is evidence to suggest that a dysregulation of the oxytocinergic system plays a key role in BPD (overview in (3)), but research has also shown alterations of the steroid hormones, including testosterone and oestrogen in BPD (4). Indeed, a few studies have demonstrated that individuals with BPD present with elevated testosterone levels in hair (5) and saliva (6), which may be a neurobiological correlate of trait aggressiveness in these patients (6). It is presently unknown, however, if individuals who develop BPD later in life have been exposed to heightened testosterone levels prenatally.

An elegant and non-invasive way to study prenatal testosterone (and oestrogen) exposure is to determine the ratio between the length of the second to the fourth digit of the hand (referred to as 2D:4D ratio). Research has shown that the 2D:4D ratio differs between men and women, with men having lower ratios than women (7), and that the 2D:4D ratio correlates inversely with the prenatal exposure to testosterone, i.e. the higher the testosterone level the smaller the ratio (8), whereby the evidence seems to be stronger for the right hand compared to the left hand digit ratio (9).

Aside from correlations between the 2D:4D ratio with the number of sperm in men and the concentrations of testosterone, luteinizing hormone and oestrogen in both sexes (8), as well as with waist-to-hip-ratio in females, a few studies have reported associations of the 2D:4D ratio with the personality traits “neuroti-

cism” and “agreeableness” (10), impulsivity (11), and behavioural signs of masculinity (12), including “tomboyism” (13), and risk-taking behaviour (14). In addition, Evardone et al. (4) reported an association of the 2D:4D ratio with affective instability in a non-clinical sample. Overall, the correlations between digit ratio and personality traits seems to be more robust in women compared to men (12). To the best of our knowledge, no study exists that has examined the 2D:4D ratio in a clinical sample of female patients with BPD, and its possible associations with impulsivity, risk-taking, personality traits and aggressiveness. We hypothesised that women with BPD would have smaller 2D:4D ratios (indicative of a greater prenatal testosterone exposure) compared to female controls, and expected correlations of the digit ratio with impulsivity, aggressiveness, risk-taking, and certain personality dimensions such as neuroticism and agreeableness.

## MATERIALS AND METHODS

### *Participants*

Forty-two female patients diagnosed with Borderline Personality Disorder (BPD) according to DSM-5 criteria (mean age 26.8 ± 6.1 years) participated in the study. They were recruited from an in-patient unit of the LWL University Hospital Bochum, Ruhr University Bochum, Germany with a treatment focus on Dialectical Behaviour Therapy in the year 2019. For comparison, 50 women (mean age 25.4 ± 3.7 years) who were free of any psychiatric condition, as ruled out by a standardised diagnostic interview, the Mini-Diagnostisches Interview für Psychische Störungen (Mini-DIPS (15)), were recruited via advertisement. Individuals with a history of bony fractures of the digits were excluded.

The study was approved by the Ethics Committee of the Medical Faculty of the Ruhr University Bochum, Germany, in full accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. All participants gave fully informed consent in writing.

### *Determination of the 2D:4D ratio*

The length of the second and the fourth digit of both hands was indirectly determined on the basis of scans produced by a standard scanner, type Canon CanoScan LiDE 220. The finger base and the fingertip were used as landmarks, whereby the most proximal skin fold of the finger base was chosen. Importantly, the shade of finger nails was excluded from the determination of the fingertip and could easily be distinguished visually from the soft tissue of the digital pulp. The finger lengths were determined for the right and left hand separately. The ratio of the second (2D) to the fourth (4D) digit was calculated using AutoMetric 2.2, yielding highly precise and reliable measures (16).

### *Waist to hip ratio*

In addition, we determined the waist to hip ratio (WtH ratio) by measuring the waist circumference whereby the narrowest point between the ribs and the iliac crest was chosen. The hip circumference was measured over the buttocks.

### *Questionnaires*

#### *Neuroticism-Extraversion-Openness Five Factor Inventory (NEO-FFI)*

The NEO-FFI (17) is a widely used questionnaire tapping into the 'Big Five' personality traits comprising 'neuroticism', 'extraversion', 'openness to experience', 'agreeableness', and 'conscientiousness'.

#### *Barratt Impulsiveness Scale (BIS-15)*

The Barratt Impulsivity Scale (BIS-15) is a shortened version of the original BIS-11. It captures impulsivity on three dimensions, termed 'non-planning', 'motor impulsivity', and 'attentional impulsivity'. Here, a German version was used (18).

#### *Buss-Perry Aggression Questionnaire (BPAQ)*

The Buss-Perry Aggression Questionnaire measures aggressive behaviour on four different dimensions: 'physical aggressiveness', 'verbal aggressiveness', 'anger' and 'hostility' (German version by Werner & Collani (19)).

#### *Risk Scenario Questionnaire*

The Risk Scenario Questionnaire (RSQ) comprises 20 short vignettes describing various problematic situations as, for example, the following: "Imagine you are in the middle of cooking dinner for your friends when the kitchen light bulb blows. (...) looking around, you realise that if you dragged the kitchen table over, put a chair on it and then a stool on top of the chair, you could just reach the light. (...) In such a situation, how likely is it that you would change the globe in this way?" The participant is then asked to answer on a Likert-type scale between 0 ('definitely not') and 10 ('for sure') (20). The 20 vignettes are associated with a physical risk (either due to illness or accident), a social risk or a

financial risk and thus yield four sub-scores: RSQ-A (physical/accident risk propensity), RSQ-I (physical/illness risk propensity), RSQ-S (social risk propensity) and RSQ-F (financial risk propensity).

### *Statistical analyses*

All analyses were carried out using the commercial statistics software IBM SPSS Statistics, Version 26 (IBM Corp., Armonk, NY, USA). Statistical significance levels were set at  $p < 0.05$ , and adjusted for multiple comparisons where appropriate. Group comparisons were calculated using multivariate analyses of variance (MANOVA). For correlational analyses between 2D:4D ratio and the other measures we report Spearman's rho (non-parametric) coefficients.

## RESULTS

### *Between group differences*

A Multivariate Analysis of Variance (MANOVA) revealed no difference between the BPD group and a non-affected group matched for age and biological sex. Specifically, between subject tests were non-significant for the 2D:4D ratio of the right hand ( $F = .013$ ,  $df = 1$ ,  $p = .909$ ), nor for the digit ratio of the left index to ring finger ( $F = .168$ ,  $df = 1$ ,  $p = .683$ ). Likewise, no difference between the groups emerged for WtH ratio ( $F = 2.073$ ,  $df = 1$ ,  $p = .154$ ). In contrast, and in line with expectations, the BPD group differed significantly from controls in virtually all psychometric measures capturing symptom severity, personality dimensions, impulsivity, aggressiveness and risk-taking behaviour, whereby p-values for some risk-taking scores would not survive correction for multiple comparisons. An overview is given in Table 1 with uncorrected p-values.

*Table 1. Comparison of biological and questionnaire scores (incl. SD) between the BPD patient group and unaffected controls*

	<b>BPD</b>	<b>Controls</b>	<b>p-value</b>
<b>Age (years)</b>	26.8 (6.1)	25.4 (3.7)	n.s.
<b>2D:4D right hand</b>	.98 (.027)	.98 (.030)	n.s.
<b>2D:4D left hand</b>	.97 (.028)	.97 (.030)	n.s.
<b>WtH ratio</b>	.82 (.088)	.79 (.082)	n.s.
<b>Borderline symptom severity</b>	47.4 (20.0)	4.4 (4.4)	p < .001
<b>Neuroticism</b>	37.3 (6.2)	16.8 (5.7)	p < .001
<b>Extraversion</b>	22.6 (7.7)	30.7 (6.0)	p < .001
<b>Openness</b>	29.5 (6.6)	32.7 (5.7)	p = .016
<b>Agreeableness</b>	26.7 (6.0)	37.2 (4.9)	p < .001
<b>Conscientiousness</b>	24.9 (8.0)	34.0 (4.8)	p < .001
<b>Non-planning impulsivity</b>	13.3 (3.1)	9.0 (2.5)	p < .001
<b>Motor impulsivity</b>	13.5 (3.7)	9.6 (1.9)	p < .001
<b>Attentional impulsivity</b>	13.0 (3.2)	8.2 (2.0)	p < .001
<b>Impulsivity (sum score)</b>	39.8 (6.7)	27.0 (4.8)	p < .001
<b>Physical aggressiveness</b>	18.8 (7.0)	11.0 (2.1)	p < .001
<b>Verbal aggressiveness</b>	12.4 (3.2)	9.5 (1.7)	p < .001
<b>Anger</b>	20.0 (4.2)	11.3 (2.9)	p < .001
<b>Hostility</b>	23.8 (4.3)	11.0 (2.7)	p < .001
<b>Aggressiveness (sum score)</b>	75.0 (13.7)	42.9 (7.1)	p < .001
<b>Risk (accidents)</b>	45.9 (26.2)	35.8 (17.2)	p < .032
<b>Risk (illness)</b>	57.0 (20.4)	30.8 (13.2)	p < .001
<b>Risk (social)</b>	50.6 (21.8)	65.7 (13.2)	p < .001
<b>Risk (financial)</b>	36.7 (19.7)	29.8 (12.9)	p < .048
<b>Risk (sum score)</b>	92.2 (30.6)	81.0 (17.0)	p < .033

2D:4D: second to fourth digit length ratio; BSL-23: WtH ratio: Waist-to-hip ratio.

*Correlational analyses*

We report non-parametric correlation coefficients, because questionnaires are interval scaled. However, the parametric correlations were almost identical.

In essence, there were no correlations between 2D:4D ratios (left and right hand) with any one of the other measures (except that they correlated with one another). A weak correlation emerged

between the right hand 2D:4D ratio and risk-taking behaviour, but this was only a trend level ( $p = .06$ ). As regards the left hand digit ratio, there was a significant correlation with the WtH ratio. In contrast, impulsivity and aggressiveness correlated highly with personality dimensions, and less so with risk-taking behaviour, in the expected directions (i.e. some correlations were negative). All relevant correlations are shown in Table 2.

*Table 2. Spearman non-parametric correlations of digit ratio (separate for left and right hand), borderline symptom severity, impulsivity, aggressiveness, and risk-taking behaviour (data of patients and controls pooled)*

	2D:4D R	2D:4D L	WtH	BSL-23	Neurot	Extr	Open	Agree	Consc	Impulsivity	Aggress.	Risks
2D:4D R												
2D:4D L	.555**											
WtH	.128	.218*										
BSL-23	.111	.141	.066									
Neurot	.069	.040	.095	.882**								
Extr	-.080	-.075	.088	-.589**	-.685**							
Open	.013	-.004	-.262*	-.223*	-.143	.185						
Agree	-.118	-.120	-.259*	-.677**	-.712**	.492**	.320**					
Consc	-.064	-.122	-.064	-.601**	-.680**	.461**	.173	.596**				
Impulsivity	.157	.045	.175	.785**	.771**	-.417**	-.283**	-.616**	-.647**			
Aggression	.069	.078	.193 <sup>†</sup>	.821**	.825**	-.559**	-.321**	-.834**	-.647**	.717**		
Risks	.193 <sup>†</sup>	.116	.155	.137	.109	.106	-.162	-.203*	-.209*	.329**	.207*	

BSL-23: Borderline Symptom List; Neurot: Neuroticism; Extr: Extraversion; Open: Openness; Agree: Agreeableness; Consc: Conscientiousness; Risks: Sum of risk-taking behaviours according to the Risk Scenario Questionnaire; L: left hand; R: right hand.

\*\*Significant ( $p < .001$ )

\*Significant ( $p < .05$ )

<sup>†</sup>Trend level ( $p = .06$ )

## DISCUSSION

Borderline Personality Disorder (BPD) is a severe psychiatric condition that is, among other features, associated with heightened impulsivity and aggressiveness (including auto-aggression). Here, we sought to explore whether female patients diagnosed with BPD had physical signs of increased prenatal testosterone exposure. The ratio of the length of the index to ring finger (2D:4D) has been shown to be a reliable marker for prenatal testosterone exposure, emerging around the 14<sup>th</sup> gestational week, with high stability into adulthood (10). In addition, indirect measures of this ratio have produced reliable results, such that no X-ray examination is required (21).

Contrary to predictions, female patients with BPD did not differ from age and sex-matched controls in 2D:4D ratio bimanually. Moreover, in the entire sample, no correlations emerged between the 2D:4D ratio and any psychometric dimension, including personality traits, impulsivity, aggressiveness, except two weak correlations of the right 2D:4D ratio with risk-taking behaviour (approaching significance), and left 2D:4D ratio with waist to hip ratio. These findings are in partial accordance with previous work reporting similar correlations (8, 10), however, we were unable to replicate or corroborate findings indicating an association of 2D:4D ratio with affective instability. In fact, in our study, there was no correlation of digit ratio with borderline symptom severity or neuroticism, even though the clinical group differed markedly from controls in virtually all psychometric dimensions, with somewhat weaker differences in risk-taking behaviour.

The present study has several limitations. One is that the sample size was moderate, even though similar compared to previous studies of similar design. Second, we exclusively examined female patients and control subjects, such that findings are not generalizable for both sexes. Third, we did not include a clinical control group. In summary, to the best of our knowledge, this is the first study to report digit ratio findings in young females with clinically manifest BPD. Even though this study did not reveal any differences in digit ratio between patients and controls, matched for age and biological sex, one should consider the heterogeneity of the borderline phenotype. In fact, when applying DSM-5 criteria, five out of nine criteria theoretically produce 126 different possible manifestations of the disorder. That said, it could well be that patients with BPD differ in terms of prenatal testosterone exposure from one another. Yet, identifying possible subgroups would require recruiting much larger samples. In addition, the lack of data for male subjects with BPD requires additional research. Future clinical studies may also want to include genetic variability, as research has shown significant interactions between certain polymorphisms, impulsivity and empathy with 2D:4D ratio (11, 22).

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## CONFLICT OF INTEREST STATEMENT

The authors declare that they do not have a conflict of interest.

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