



Digit ratio (2D:4D), impulsiveness and aggression in male heroin addicts: A prospective controlled study



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ABSTRACT

The ratio of the length of the index finger to ring finger (2D:4D) is considered to be an indicator of prenatal testosterone exposure. The androgen theory suggests that the masculinizing effects of fetal androgens may play a role in certain psychiatric disorders. We have examined the relationship between impulsiveness, aggression and adult attention deficit along with the 2D:4D digit ratios in male heroin abusers. The study included 62 male patients with heroin dependence and a control group comprising of 50 healthy individuals having similar socio-demographic features. Scores of the Barratt impulsiveness scale, Buss Perry Aggression Scale and attention deficit hyperactivity disorder (ADHD) self-report scale were obtained from the participants. The lengths of second and fourth digits of the right hands were measured. The patients group had significantly higher scores of impulsiveness, aggression and ADHD compared to the healthy control group; and their digit ratios were significantly lower. No correlations were found between digit ratios of heroin addicts and their impulsiveness, aggression and ADHD scores. Our study is the first to examine the relationship between digit ratio and impulsiveness, aggression and ADHD levels in patients with heroin dependence. Prenatal high testosterone exposure might have a role in the etiology of heroin addiction.

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1. Introduction

Heroin dependence is accepted to be as a biopsychosocial disorder and its etiology includes alterations in genetic, environmental and psychosocial factors, neurotransmitter levels and neuro-anatomic structures (Sigara, 2010).

Sex hormones play an important role in the development of human brain and body, and enable the formation of gender based behaviors (Goy & McEwen, 1980). The influence of steroid hormones on brain development in terms of neuronal and behavioral differentiation is well defined (De Vries et al., 2009). Studies have shown a specific relationship between testosterone levels and behavioral alterations (Archer, 1994; Olweus, Mattsson, Schalling, & Low, 1980; Tajima-Pozo, Bayón, Díaz-Marsá, & Carrasco, 2015).

It has been suggested that independent of the influence of plasma testosterone levels, androgen exposure in the fetal period may affect brain development and behavior. Psychological, anatomical and behavioral masculinity were shown to increase in girls with congenital adrenal hyperplasia who have higher level of testosterone exposure in

prenatal period (Hines & Kaufman, 1994). It is also argued that high androgen exposure in fetal period decelerates phases of brain development and that its influences on dopaminergic system increases sensitivity to fetal stress (Martel & Roberts, 2014). Fetal programming is defined as early incidents such as fetal androgen fluctuations on the formation of effective developmental paths in later life. It is suggested that fetal programming might have a role in the etiology of several neuropsychiatric disorders such as schizophrenia, affective disorders and autism (Bale et al., 2010). Additionally, fetal programming, especially the masculinization theory, might also have an influence on addiction development (Kornhuber et al., 2011; Kornhuber et al., 2013; Verster & de Haan, 2011).

The Hox family of genes regulates the differentiation and development of digits and genital structures (Kondo, Zakany, Innis, & Duboule, 1997). Manning et al. (J. T. Manning, Scutt, Wilson, & Lewis-Jones, 1998) suggested that the ratio of index finger to ring finger (2D:4D) might be an indicator of prenatal testosterone exposure. Several subsequent studies have utilized 2D:4D as an indicator of prenatal androgen exposure (Brown, Hines, Fane, & Breedlove, 2002; McIntyre, 2006). In these studies, a low digit ratio is stated to be related to psychiatric disorders such as attention deficit hyperactivity disorder (ADHD) (Demirci, Öztö, & Melikgazi, 2015; Stevenson et al., 2007), disruptive behavior (Roberts & Martel, 2013), autistic spectrum disorders (Hönekopp,

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2012; Noipayak, 2009), physical aggression (Bailey & Hurd, 2005) and increase in masculinization (Cohen-Bendahan, van de Beek, & Berenbaum, 2005), alcohol addiction (Kornhuber et al., 2011) and video game addiction (Kornhuber et al., 2013) that are more commonly seen in males. Moreover, low digit ratios were associated with better performance in sports (Hönekopp & Schuster, 2010; Tester & Campbell, 2007), better spatial skills (Puts, McDaniell, Jordan, & Breedlove, 2008), that may also be associated with males.

Various studies suggest a strong link between heroin addiction and other addiction types (Cacciola, Alterman, McKay, & Rutherford, 2001; Nielsen et al., 2012), ADHD (Capusan, Bendtsen, Marteinsdottir, & Larsson, 2016) and other behavioral disorders (Lloyd, 1998; Shand, Degenhardt, Slade, & Nelson, 2011) in which impulsiveness and aggression coexist and therefore may have a common etiology.

In the published literature, no studies have examined the influence of prenatal testosterone exposure in the etiology of heroin addiction. Here, we have aimed to determine the relationship between digit ratio (2D:4D) and impulsiveness, aggression and ADHD levels of heroin addicts compared to healthy individuals. This is based on the hypothesis that prenatal testosterone exposure is higher in heroin addicts and is related to impulsiveness, aggression and ADHD.

2. Material and methods

2.1. Participants

This prospective controlled study included 111 consecutive male patients aged between 18 and 45 years, who applied to a psychiatry clinic and were diagnosed with heroin dependency according to the DSM-IV. The patients included in the study had undergone at least 5 years of education. Additionally, 50 healthy individuals who did not have any psychiatric or chronic diseases and had similar age and education profile as the patient group were included in the study as the control group.

The exclusion criteria for the study were as follows: 1. Co-existing axis-I psychiatric disorders, 2. Any additional substance use disorder (except smoking), 3. Presence of a psychiatric, neurologic or systematic disease that can affect the cognitive and physical functions, 4. Congenital or acquired deformity in the hands, 5. Left handedness.

Twelve patients were excluded from the study due to the presence of a comorbid psychiatric disorder, 20 patients due to usage of other substances, 14 patients due to incorrect filling of the scales during interviews, 1 patient due to hand deformity and 2 patients for left handedness. In total, 62 patients were included in the study.

3. Methods

The patients and healthy controls that met the study criteria were informed about the objectives and procedures of the research. Only those patients who provided consent were included in the study. The study procedure was approved by the institutional ethical review board. Clinical interviews were carried out when the participants were not undergoing withdrawal symptoms. The demographic features and clinical characteristics of the participants such as name, age, education, age of onset of heroin use, duration of substance usage, method of drug use, psychiatric and physical disorders such as schizophrenia or related psychotic disorders, affective disorders, anxiety disorders, substance use disorders; history of brain damage/trauma, neurological disease and concomitant severe medical illnesses (e.g., uncontrolled endocrine abnormalities, cardiovascular or pulmonary diseases were recorded on the data forms developed by the researchers. The socio-demographic and clinical features of the patients and then evaluated. The diagnosis of heroin dependence was made by a psychiatrist by using the DSM-IV diagnostic criteria. Moreover, the existence of any other substance usage was confirmed by urine analysis. Structured Clinical Diagnostic Interview (SCID-I) was carried out for Axis I diagnoses (First, Spitzer, Gibbon, & Williams, 1997; Özkürkçügil, Aydemir, Yildiz, Esen Danaci,

& Köroğlu IV, 1999). In the clinical interview, Barratt impulsiveness Scale (Güleç et al., 2008; Patton & Stanford, 1995), Buss-Perry Aggression Scale (Buss & Perry, 1992; Evren, Çınar, Güleç, Çelik, & Evren, 2011) and Adult ADHD Self-Report Scale (ASRS) (Doğan, Öncü, Varol Saraçoğlu, & Küçüköncü, 2009; Kessler et al., 2005) were used to predict impulsiveness, aggressiveness and ADHD, respectively. The lengths of the second and fourth digits of the right hand of the patients and healthy individuals were measured with an Astor brand digital caliper that can measure with a sensitivity of 0.01 mm. In the measurement protocol, the individuals are asked to open their hands widely, palm facing upward, and the measurement is performed when the thumb is slightly apart while the other four fingers are tightly apposed to each other. The distance between the central point of proximal line, which separates the root of the finger from the palm and the fingertips, is measured.

3.1. Statistical analysis

The data were analyzed with the Statistical Package for the Social Sciences (SPSS), version 15.0, for Windows. The normal distribution of the data was evaluated by Shapiro-Wilk test. Non-normally distributed variables including age, duration of education, age of onset of heroin use, duration of disorder and the 2D:4D ratio were compared Mann-Whitney *U* test. Student's *t*-test was used to compare normally distributed variables including Buss-Perry Aggression Scale scores, BIS-11 scores; ASRS scores in patients and control subjects. Chi-square test were carried out for comparing the categorical variables between the groups. Correlations among numeric variables were examined with Pearson correlation analysis. $p < 0.05$ was determined to be statistically significant.

4. Results

The mean age of the participants in the current study ($n = 112$) was found to be 24.24 ± 4.55 years. There were no significant differences between the patient and control groups in terms of age ($t = 0.37$, $p = 0.71$) and education status ($t = 0.63$, $p = 0.52$). In the patient group, the mean age of first incidence of substance use was found to be 15.91 ± 2.77 years; mean age of initiation to heroin use was found to be 19.12 ± 4.09 years and the mean duration of disorder was found to be 4.88 ± 2.13 years. Among the patients, 31.1% were injecting heroin intravenously and the other 68.9% were using by inhalation (Table 1).

The 2D:4D ratio was significantly lower in heroin addicts compared to the control group ($p = 0.02$). Additionally, the Buss-Perry aggression scores ($p = 0.000$), total BIS scores ($p = 0.000$) and total ASRS scores ($p = 0.001$) were significantly higher in heroin addicts than the control group (Table 2).

A significant positive correlation was determined between Buss-Perry aggression scores and total ASRS and BIS scores. At the same time, a significant positive correlation was determined between total BIS and ASRS scores. No significant correlation was detected between the 2D:4D ratios and scores from the other scales (Table 3).

Table 1
Characteristics of groups.

	Patient ($n = 62$)	Control \pm SD ($n = 50$)	<i>P</i>
	Mean \pm SD	Mean \pm SD	
Age (years)	24.09 ± 4.16	24.42 ± 5.03	0.716
Duration of education (years)	9.25 ± 2.41	8.96 ± 2.49	0.526
Method of drug use			
Inhalation (%)	68.9		
IV (%)	31.1		
Age of onset of heroin use (years)	19.12 ± 4.09	–	
Duration of disorder (years)	4.88 ± 2.13	–	

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