Psychiatry Research: Neuroimaging 211 (2013) 251–256

Contents lists available at SciVerse ScienceDirect

Psychiatry Research: Neuroimaging

journal homepage: www.elsevier.com/locate/psychresns

Impulsivity is related to striatal dopamine transporter availability in healthy males

Anna Costa [a], Christian la Fougère [b], Oliver Pogarell [a], Hans-Jürgen Möller [a], Michael Riedel [a,c], Ulrich Ettinger [d,*]

[a] Department of Psychiatry, Ludwig-Maximilians-Universität, Munich, Germany
[b] Department of Nuclear Medicine, Ludwig-Maximilians-Universität, Munich, Germany
[c] Clinic for Psychiatry, Psychotherapy, Gerontopsychiatry und Neurology, Vinzenz-von-Paul Hospital, Rottweil, Germany
[d] Department of Psychology, University of Bonn, Kaiser-Karl-Ring 9, 53111 Bonn, Germany

ARTICLE INFO

Article history:
Received 13 December 2011
Received in revised form
16 July 2012
Accepted 26 July 2012

Keywords:
Dopamine transporter
SPECT
Neuroticism
BIS
ADHD
ASRS

ABSTRACT

Impulsivity characterises various psychiatric disorders, particularly attention-deficit/hyperactivity disorder (ADHD). Evidence shows that ADHD symptoms are associated with dopamine dysfunction and alleviated with methylphenidate, a drug that reduces dopamine transporter availability. ADHD-like symptoms and impulsive traits are continuously distributed across the general population. Here, we aimed to investigate the dopaminergic basis of impulsivity and other ADHD-related traits in healthy individuals by studying the association of these traits with striatal dopamine transporter availability. Single-photon emission computed tomography with [^{123}I] FP-CIT was performed on 38 healthy males. Impulsivity was measured using the Barratt Impulsiveness Scale (BIS) and hyperactivity-impulsivity and inattention using the Adult ADHD Self-Report Scale (ASRS). We found that greater dopamine transporter availability was associated with higher BIS impulsivity but not with ADHD-related traits. The association with BIS was significant after accounting for individual differences in age and neuroticism. These results suggest that individual differences in the dopamine system may be a neural correlate of trait impulsivity in healthy individuals.

1. Introduction

Impulsive behaviour is a feature of a number of psychiatric disorders including attention-deficit hyperactivity disorder (ADHD), substance abuse, obsessive–compulsive disorder and borderline personality disorder (Chamberlain et al., 2005; Ersche et al., 2010; Moeller et al., 2001). One of the most common self-report measures of impulsivity is the Barratt Impulsiveness Scale (BIS) (Patton et al., 1995), which has been implemented both in healthy and in patient groups (Koch et al., 2007; Peluso et al., 2007; Preuss et al., 2008).

The neurochemical basis of impulsivity has been suggested to be linked to the monoaminergic system (Buckholtz et al., 2010; Cools et al., 2007; Dalley et al., 2007; Robbins and Arnsten, 2009; Winstanley et al., 2004). Evidence from imaging studies with single-photon emission computed tomography (SPECT) has shown that serotonin transporters are associated with self-report measurements of impulsivity (Koch et al., 2007; Lindström et al., 2004). Likewise, a role of dopamine in impulsivity is suggested in SPECT studies of ADHD. ADHD patients suffer symptoms of hyperactivity and impulsivity and have in some studies been shown to have increased availability of dopamine transporter (Dougherty et al., 1999; Dresel et al., 2000; Krause et al., 2000; Larisch et al., 2006; however, see van Dyck et al., 2002; Volkow et al., 2007, 2009). Methylphenidate, a drug which blocks the dopamine transporter (Volkow et al., 1999), has been shown to be effective in alleviating the clinical symptoms of ADHD (Greenhill et al., 1999) whilst reducing striatal dopamine transporter availability (Krause et al., 2000). In addition, elevated dopamine transporter availability has been shown to be associated with better therapy response to methylphenidate (la Fougere et al., 2006).

However, not much is known about the dopamine system correlates of individual differences in trait impulsivity and ADHD-related traits in the non-clinical population. Studies have suggested that symptoms of ADHD and other psychiatric disorders lie on a continuum from health to illness (Markon et al., 2011; Verdoux and van Os, 2002). A similar continuum model may be assumed in relation to impulsivity in the normal population, with clinical conditions such as ADHD, personality disorders or substance abuse at the extreme end of the spectrum (Levy et al., 1997).

Confirming such dimensional views, recent evidence revealed that trait differences in impulsivity are associated with dopamine

* Corresponding author. Tel.: +49 228 73 4208.
E-mail address: ulrich.ettinger@uni-bonn.de (U. Ettinger).

0925-4927/$ - see front matter © 2012 Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.pscychresns.2012.07.011

autoreceptor availability in the midbrain in healthy subjects (Buckholtz et al., 2010), raising the question whether trait differences in impulsivity might also be associated with other mechanisms involved in dopamine signalling in the brain, such as the dopamine transporter. Thus based on the continuum hypotheses of psychiatric disorders, it might be expected that an association may be present between trait impulsivity and dopamine transporter availability in healthy subjects that reflects changes seen in clinical conditions such as ADHD, substance abuse and obsessive–compulsive disorder (Amsterdam and Newberg, 2007; Kim et al., 2003; Malison et al., 1998).

However, only two studies to date have investigated the association between impulsivity or related traits and dopamine transporter availability in the non-clinical population and no prior association has been found (Burke et al., 2011; Lindström et al., 2004) despite suggestive evidence of such a relationship from clinical studies (Dougherty et al., 1999; Krause, 2008; Krause et al., 2000). Therefore, the present study aimed to further add to this literature by examining the association between dopamine transporter availability and impulsivity-related traits. We used [^{123}I] FP-CIT SPECT and measured impulsivity (Patton et al., 1995) and ADHD-related traits (Kessler et al., 2005) using self-report questionnaires in a carefully screened, non-clinical sample. Additionally, in order to confirm the specificity of any such findings with regards to general psychopathology (Claridge and Davis, 2001), we also controlled for negative trait emotionality, or neuroticism, in the association between impulsivity and striatal dopamine transporters.

2. Methods

2.1. Subjects

Subjects were recruited through advertisements placed around the local community and universities. Inclusion criteria were male gender, right-handed, non-smoker and between 18 and 40 years of age. Potential subjects were first pre-screened by telephone. If they fulfilled the general study criteria, they were invited to participate in a baseline screening session that included an electroencephalogram (EEG), an electrocardiogram (ECG), a blood test and a detailed interview to exclude any psychiatric, neurological and medical illness, including alcohol and drug abuse. None of the subjects had a history of psychiatric and neurological illness and none were under medication at the time of testing. Additionally, they were asked to refrain from alcohol 24 h prior to each study appointment. Subjects who passed the baseline screening session were invited to return on another day for the SPECT scan.

The study was approved by the local ethical committee. All subjects provided written informed consent and received monetary compensation for their participation.

2.2. SPECT data acquisition and analysis

SPECT scans were acquired 4 h after the intravenous injection of approximately 185 MBq [^{123}I] FP-CIT (DaTSCAN, GE Healthcare, Amersham, UK) using a Prism 3000 triple-headed gamma camera (Philips, formerly by Picker, Cleveland, Ohio) equipped with high resolution fan beam collimators (120 projections at 60 s/view; total scan time of 43 min). The projection data were checked for participant motion. The projection images were reconstructed by filtered back-projection (Butterworth 3-D post-filter; 0.60 cycles/cm, 5th order) and corrected for attenuation according to Chang's method (Chang, 1978).

The data were semiquantitatively evaluated using a modified version of the Brain Analysis Software (BRASS, version 3.5; Hermes Medical Solutions, Stockholm, Sweden) and standardized 3-dimensional volumes of interest. This software has been validated previously and the procedure has been described in detail elsewhere for SPECT with [^{123}I] FP-CIT (Koch et al., 2005) and PET with ^{18}F-DMFP (la Fougere et al., 2010). Specific binding in the striatum corrected for unspecific uptake in the occipital cortex was calculated according to the following formula: (striatum—occipital cortex)/occipital cortex. We additionally extracted binding measurements for putamen and caudate separately.

2.3. Psychometric assessment

Impulsivity was measured using the 30-item German version of the Barratt Impulsiveness Scale (BIS), version 11 (Preuss et al., 2008). The questionnaire comprises items such as attention, self-control, motor impulsiveness, cognitive complexity, perseverance and cognitive instability. Items are rated from 1 (never) to 4 (always). As the German version did not replicate the factor structure with six subscales of the English version of the BIS (Patton et al., 1995), the sum of the score on the BIS-11 was used in the analyses following recommendations by Preuss et al. (2008). The internal consistency (Cronbach's alpha) for the BIS questionnaire in our sample was $\alpha=0.77$.

ADHD-related traits were measured using the German version of the Adult ADHD Self-Report Scale (ASRS) (Reuter et al., 2006). The ASRS is an 18-item questionnaire and the items were rated from 0 (never) to 4 (very often). It measures the frequency of ADHD symptoms based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), including inattention and hyperactivity-impulsivity symptoms. The internal consistency for the ASRS questionnaire in our sample was $\alpha=0.79$.

Neuroticism was measured using the German version of the NEO Five Factor Inventory (NEO-FFI) (Borkenau and Ostendorf, 1991). Neuroticism comprised 12 items in the questionnaire, which included questions such as: "I often feel tense and jittery; I often feel interior to others; Sometimes I feel completely worthless". The items were rated from 0 (strongly disagree) to 4 (strongly agree). Scores for neuroticism were obtained by summing up the scores on the 12 items. The internal consistency for the items measuring neuroticism in our sample was $\alpha=0.74$.

2.4. Statistical analysis

Statistical analyses were carried out in PASW Statistics (release version 19.0, SPSS Inc., 2010, Chicago, Illinois). Multiple regression analysis was carried out with striatal dopamine transporter availability as dependent variable. Given the known association of age with dopamine transporter availability (Volkow et al., 1996), age was forced in as a predictor in a first step. Additionally, in order to confirm that any observed associations are independent of negative trait emotionality (Claridge and Davis, 2001), neuroticism was forced in as an additional predictor alongside age in the first step. In a second step, BIS and ASRS sum scores were included as independent variables (predictors) using the stepwise method (probability to enter set at $p<0.05$). The analyses were then repeated with dopamine transporter availability from the caudate and the putamen as separate dependent variables in order to explore anatomically specific effects within the striatum. In order to correct for multiple tests we used a Bonferroni adjustment of the p-Value for the three regression analyses carried out (threshold $p=0.0167$). Finally, Pearson correlations between all continuous variables were also carried out and are reported for inspection purposes.

3. Results

A sample of 38 subjects completed the study. Descriptive statistics of all variables are given in Table 1. Pearson correlations between BIS, ASRS, neuroticism, dopamine transporter availability, and age are shown in Table 2. As can be seen, dopamine transporter availability was negatively correlated with age and positively correlated with BIS total score, but not with ASRS or neuroticism. Correlations were also carried out between dopamine transporter availability and ASRS subscales (inattention and hyperactivity–impulsivity). No significant correlation was found between any of the ASRS subscales and dopamine transporter availability.

Multiple regression analysis revealed that the BIS emerged as only significant predictor of dopamine binding in the striatum ($R^2=29\%$) over and above the effects of age and neuroticism. Dopamine transporter binding was inversely related to age ($\beta=-0.40$, $p=0.009$) and positively related to BIS scores ($\beta=0.33$, $p=0.03$). The final ANOVA model was statistically significant (F [3, 37]$=4.54$, $p=0.009$).

Dopamine transporter measures of putamen and caudate were highly significantly correlated ($p<0.001$, Table 2). Not surprisingly, therefore, the results of the regression analysis were essentially identical when the analyses were carried out separately for caudate and putamen.

The BIS emerged as the only significant predictor of dopamine binding in the caudate ($R^2=26\%$) over and above the effects of age and neuroticism. Dopamine transporter binding was inversely related to age ($\beta=-0.39$, $p=0.01$) and positively related to BIS scores ($\beta=0.32$, $p=0.045$). The final ANOVA model was statistically significant (F [3, 37]$=4.01$, $p=0.015$).