Inhibition errors in borderline personality disorder with psychotic-like symptoms

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Abstract

Background: The aim of this study was to examine whether patients with borderline personality disorder (BPD) have deficits in cognitive inhibition as measured with an anti-saccade task similar to patients with schizophrenia (SZ). Furthermore, we investigated whether these inhibition errors were more prominent among BPD patients with psychotic-like symptoms than among BPD patients without these symptoms.

Methods: An anti-saccade task was administered to 12 BPD patients (among them, 2 had with psychotic-like symptoms), 25 patients with recent onset schizophrenia (SZ), and 20 healthy controls (HC). The percentage inhibition errors in the anti-saccade task were the primary outcome variable. In addition, the percentage of anticipatory errors was measured.

Results: BPD patients showed more inhibition errors than SZ and BPD patients without psychotic-like symptoms showed more inhibition errors than BPD patients without these symptoms (χ² = 11.92, p < 0.001). SZ patients showed more anticipatory errors than HC (χ² = 19.12, p < 0.001), whereas BPD patients scored in between (χ² = 11.92, p < 0.001).

Conclusions: The data demonstrate that inhibition deficits, as assessed with the anti-saccade task, may be characteristic among BPD patients with psychotic-like symptoms.

Keywords: Borderline personality disorder; Impulsivity; Inhibition; Psychosis; Schizophrenia

1. Introduction

Borderline personality disorder (BPD) is a complex psychiatric disorder characterized by a pervasive pattern of instability in interpersonal relationships, self-image, affect and impulse control (American Psychiatric Association, 1994). Self-destructive behavior is a key feature of BPD, leading to suicide rates of 8–10% (Work Group on Borderline Personality Disorder, 2000). BPD usually starts in early adulthood and is estimated to occur in about 1% of the population, most predominantly in women (Youngman et al., 2001). Although BPD is the most common personality disorder in psychiatric settings, our understanding of its neurobiological basis is still limited (Skodol et al., 2003).

Recent neuroimaging research suggests that a dysfunction of a frontostriatal network plays an important part in the pathophysiology of BPD. This network encompasses the prefrontal cortex, the striatum, the anterior cingulate cortex, and the orbital frontal cortex.
Another important characteristic of BPD is the propensity to develop psychotic-like symptoms. In fact, the term “borderline” was actually put forward, because clinicians believed that such patients lie on the border of psychotic functioning (Krueger, 1985). However, the criteria “transient, stress-related severe dissociative symptoms or paranoid ideation” was incorporated in the classification for BPD not until the publication of DSM-IV in 1994. The presence of psychotic-like symptoms in BPD is of utmost importance as well. The prevalence of major psychotic disorders is low, but transient psychotic-like symptoms (‘quasi’-hallucinations, ideas of reference or paranoid ideation) in response to stress occur in about 46% of BPD patients (Grazioli et al., 1995). The tendency to develop such psychotic-like symptoms is persistent over time (Berlin et al., 1995) and is considered to be associated with chronic impairment (Green, 1995).

As schizophrenia and BPD share the vulnerability to develop psychotic symptoms, our second research question focuses on the relationship between psychotic symptoms and inhibition deficits. We expect that cognitive deficits would be more prominent in the subgroup with psychotic-like symptoms, because of the clinical concerns. We hypothesized a priori that BPD patients with psychotic-like symptoms would show more inhibition deficits than BPD patterns without these symptoms.

2. Methods
2.1. Participants
We recruited 32 patients with Borderline Personality Disorder (BPD) and 21 with neuroanisoschizophrenia. Out from the in- and out-patient clinic of the two participating centers (Radboud University Nijmegen Medical Centre and GUNIJe Apeldoorn). We recruited 25 healthy controls (HC) without a personal and family history of psychiatric disorders through advertisements in newspapers. Since the group of BPD patients consisted mainly of women and the schizophrenic group of men, we choose to include both men and women in the control group. Furthermore, age between 18 and 50 was an inclusion criterion in all groups.

The clinical diagnosis of the patients was confirmed by a mixed research physician with the Structured Clinical Interview for DSM-IV Axis I (SCID-I) and Axis II (SCID-II) disorders (First et al., 1995; Spitzer et al., 1992). Since schizophrenic traits are related to anti-saccade performance, we excluded patients with a comorbid schizotypal personality disorder (Gudegast et al., 2003). During the psychiatric interview, extra attention was focused on psychotic-like symptoms. The existence of psychotic-like symptoms in the past year was assessed on the basis of the cognitive section of the Revised Diagnostic Interview for Borderline (ODI-B) (Grazioli et al., 1989).

Examples of psychotic-like symptoms are transient paranoid or somatic delusions, hallucinations, or depersonalization. Among the 32 patients with BPD, 20 appeared to have had a pattern of several, transient psychotic-like episodes related to stress in the past year (BPD + PSYCH), although none of them had any psychotic symptoms just before or during the
measurement. 17 BPD patients reported not to have any of such symptoms (BPD+PSYCH). Recent onset Schizophrenia was defined as patients with schizophrenia disorder or schizoaffective disorder, less than 1 year after first onset of positive symptoms (see Table 1 for demographic characteristics). The three groups did not differ with respect to age (F=2.79, df=2, M=32, p=0.07), but they differed significantly in sex distribution, with more females in the BPD group and more males in the schizophrenia group (χ²=27.4, df=2, p<0.001).

Neuropsychological and psychological tests were administered to all participants in the study. The study was approved by the ethics committee of the hospital. All participants gave written informed consent and were paid €50.00 for their time.

2.2. Procedures

The subjects were seated in a darkened room, 50 cm from a bar consisting three equally spaced horizontal light-emitting diodes (LED). A chin-strap head rest was used to prevent head movements. Target lights were located at 15°, right and left from the central fixation point. Horizontal eye movements were recorded by electro-oculography (EOG) with electrodes attached on the outer canthi. A ground electrode was placed at the forehead. Low-pass filters were set at 500 Hz. Wind-up Acquisition software and interface and a universal psychophysical amplifier were used to record the EOG signal and stimulus presentation.

4 series of 40 trials each were presented to the subjects. The task order was: pre-saccade/anti-saccade/anti-saccade/pro-saccade. Each trial consisted of the illumination of the central LED for 1000–1500 ms, followed by the simultaneous extinguishing of the central LED and the illumination of one of the peripheral LEDs for 600 ms without overlap. The peripheral target appeared left or right in a random order. The instruction of the pro-saccade task was to make an eye movement to the illuminated peripheral LED. The instruction of the anti-saccade task was to make an eye movement in the direction opposite to the LED. Subjects were instructed to respond as fast and accurate as possible.

2.3. EEG analysis

EOG segments were analyzed with interactive custom-made software. The eye movements were visually assessed, blinded to group status, and divided into different response categories: "correct response" (correlated eye movement < 80 ms after baseline in the correct direction — depending on pro-saccade or anti-saccade task instruction), "adolescent error" (reflective saccade to the same side as the stimulus), and "anticipatory saccade" (anticipatory response in either direction between 300 ms before baseline and < 80 ms after baseline). Trials with eye blinks, mixing eye movements and movement artifacts were removed from the analyses.

2.4. Statistical analysis

Dependent measures were the percentages of inhibition errors, anticipation (too early errors), percentage of correct responses and latency times.

All dependent variables were analyzed in two steps. First, the effect of the factor group (BPD, SCZ, HC) was compared with an ANOVA, followed by post-hoc tests (Fisher’s LSD). Secondly, differences between the BPD group with and without psychotic-like symptoms (BPD + PSYCH and BPD -PSYCH respectively) were tested with ANOVA. Since sex was differently distributed in the groups, it was included as a between-subject factor in all analyses. Post-hoc comparisons were used to investigate the relationship between inhibition and anticipation errors. The level of significance was set at p<0.05 (two-tailed). SPSS 14.0 software was used.

3. Results

3.1. Demographics

The demographic data are presented in Table 1. The statistical evaluation showed that the three groups did not differ significantly with respect to age, however, the sex distribution was not equal in all groups (χ²=27.4, df=2, p<0.001). There were more females than males in the BPD group and more
Table 1 shows the descriptive statistics of the prosaccade and antisaccade task (percentages correct responses and errors, and latencies for the correct responses and inhibition errors).

3.2. Introductory analysis

We removed unusable trials due to missed eye movements, eye blinks or artifacts. The percentage of unusable trials was higher in Sz than in the other groups (3.9% vs 1.8%), but in the ANOVA, the group differences were not significant ($F=2.71, df=2,72, p=0.07$).

In the prosaccade task, the ANOVA with the percentage of correct responses as dependent variable revealed no main group effect ($F=0.18, df=2,72, p=0.85$). No further analysis indicated that both BD and Sz patients made less correct responses than HC (both $p>0.05$). The difference between Sz and BD patients was not significant ($p=0.97$). In the antisaccade task, the ANOVA with the number of correct responses as dependent variable revealed a main group effect as well ($F=13.6, df=2,72, p<0.01$). HC had more correct responses than both Sz patients ($p=0.001$) and BD patients ($p=0.002$). The two patient groups did not differ to this respect ($p=0.86$).

The ANOVA with latency time of the correct responses as the dependent variable did not reveal a group effect in the prosaccade task ($F=2.14, df=2,72, p=0.12$), but a significant group effect in the antisaccade task ($F=4.1, df=2,72, p=0.05$). Sz patients had longer initiation times than HC ($p=0.08$) and BD patients ($p=0.01$).

Table 2. Eye movements in prosaccade task

<table>
<thead>
<tr>
<th>Group</th>
<th>% antisaccade response (mean, SD)</th>
<th>% correct response (mean, SD)</th>
<th>Latency time (mean, SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy controls</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>77.1 (17.1)</td>
<td>82.1 (17.1)</td>
<td>206.1 (58.5)</td>
</tr>
<tr>
<td>BD patients</td>
<td>69.9 (17.7)</td>
<td>70.5 (17.7)</td>
<td>205.5 (86.0)</td>
</tr>
<tr>
<td>BD with psychotic-like symptoms</td>
<td>68.1 (17.7)</td>
<td>68.1 (17.7)</td>
<td>206.4 (56.0)</td>
</tr>
<tr>
<td>BD without psychotic-like symptoms</td>
<td>68.1 (17.7)</td>
<td>68.1 (17.7)</td>
<td>206.4 (56.0)</td>
</tr>
</tbody>
</table>

3.3. Inhibition errors

The primary outcome measure of this study was the percentage of inhibition errors in the antisaccade task; the ANOVA revealed a significant group effect ($F=7.4, df=2,72, p=0.001$). The data are shown in Fig. 1. Sz patients had more errors than HC ($p=0.001$) and BD patients ($p=0.03$). The difference between BD patients and HC was significant as well ($p<0.05$). The effect for sex was not significant ($p=0.72$).

The prospective analysis revealed that BD patients with psychotic-like symptoms had more inhibition errors than BD patients without psychotic-like symptoms ($F=10.2, df=2,72, p=0.001$). The effect for sex within the BD group was significant as well ($F=7.42, df=2,72, p=0.05$). An additional post hoc ANOVA analysis revealed that BD patients with psychotic-like symptoms did not differ from the Sz patients ($p=0.41$), while BD patients did differ significantly from Sz ($p=0.01$). When the analyses on inhibition errors were restricted to only females or to only medicated-naive patients, the results were essentially similar, though $p$-values were higher due to loss of power.
3.4. Anticipatory errors

The percentage of anticipatory errors did not differ between the pre- and anti-suicidal task \( (F = 1.96, df = 1.8, p = .16) \), therefore the data of both tasks was pooled in further analyses.

In the ANOVA with percentage of anticipatory errors as dependent variable, a significant group effect was found \( (F = 4.40, df = 2.73, p < .05) \), the post-hoc test showed that BP patients had higher percentages of anticipatory errors than healthy controls \( (p < .01) \), while the differences between Sk and BPD \( (p = .13) \) and HC \( (p = .30) \) were not significant. There was no significant difference between BP patients with and without psychotic-like symptoms \( (p = .76) \). In addition, there was no significant correlation between the percentage of anticipatory and inhibition errors \( (r = .03, p = .25) \).

4. Discussion

In the present study, no difference in both BP patients scored in between schizophrenia and healthy controls on the anti-suicidal task (Kaplan’s B. Moreover, BP patients with psychotic-like symptoms had significantly more inhibition errors than BP patients with non-psychotic symptoms (Kaplan’s B). The BP patients with psychotic-like symptoms had a similar rate of inhibition errors as patients with Sk, whereas BP patients without psychotic-like symptoms showed health controls. The inhibition deficit was distinct from a general preoccupation to respond impulsively, which was found in the whole group of BP patients.

There may be similar underlying depressive symptoms in BP and schizophrenia. Recently, an essential role for dopamine in BP pathology has been proposed in the dopaminergic pathways projecting to the PFC. It may be involved in disturbed cognitive perceptual processing and thought processes in BP (Hirayasu, 1995). Psychotic-like symptoms have been regarded as one of the clinical dimensions in the neurobiological research of BD (Kishida et al., 2002). Moreover, antipsychotic drugs have secured a position in the pharmacological treatment of BD (Rabinovitz and Yaryiva, 2005).

Our results raise the question whether the anti-suicidal error is a specific marker for schizophrenia or a marker for psychosis in general. These deficits have also been found in patients with bipolar disorder (Ramos and Hirsch, 1991), Sk et al., 1996). In addition, the association between psychotic-like symptoms and inhibition errors has been found earlier in a group of studies with questionnaire-identified schizotypy (Hodgins, 1999, O’Connor et al., 1996). The percentage of inhibition errors and latency times based on the schizotypy group are in line with percentages previously found by others (Beninger et al., 2000, Fecteau and Trzebinski, 1999). Of importance is the fact that the Sk patients in our sample had a recent onset of the syndrome. Our results show that inhibition abnormalities can be established in early stages of the syndrome in patients without a history of long-term medication.

Another way of interpreting the shared high number of inhibition errors both in BPD and in the anti-suicidal task is to take the developmental perspective, because both BPD and Sk have an early age of onset. In healthy subjects, there is a clear relation between age and antisuicidal performance, in that a dramatic improvement in the performance of the anti-suicidal task has been found between age 5-6.5 (Fischer et al., 1997, Luna et al., 2001, Munar et al., 1998). The ability to inhibit prepotent responses is viewed as a direct result of structural and functional maturation of the prefrontal cortex and its connections, that gradually improves through childhood and adolescence (Mishkin et al., 1996). One might suggest a disturbed functional development of the PFC or associated neuroanatomy in both Sk and a subgroup of BD patients, a hypothesis which is in line with previous findings (de Jonge et al., 2006, De la Fuente et al., 1997, Lysy et al., 1996, Saposnik et al., 2000, 2003, Tabary et al., 2003, Tsai et al., 2004). Since normal anti-suicidal performance reflects normal PFC development, the poor performance on this task has been regarded as a biological marker for several neuropsychiatric disorders. Not surprisingly, only biological, but also psychological events may interfere with normal brain development in BD. Therefore, it is interesting to examine the relationships between severe negative life events, disorganization and psychotic-like symptoms in BPD in the future.

Next to inhibition errors, we found a higher percentage of anticipatory errors in BP patients in comparison to healthy subjects. In contrast to the inhibition deficit, satisfying for the presence or absence of psychotic symptoms did not differ with respect to the number of anticipatory errors. The tendency to make ‘false alarms’ can be view as a form of disinhibition as well. However, it is not an automatic response to a stimulus that is inhibited, but a disinhibition of a motor response to an internal cue. The absence of a correlation between anticipatory and inhibition deficits indicates that the two error types are essentially different. It is an interesting question whether anticipatory errors reflect clinical impulsivity, which is traditionally viewed as a core feature of BD. Since 31 of 32 BD patients of our sample were positive for the DSM-IV criteria for impulsivity (at least two potentially self-damaging impulsive behaviors), it was not possible to further analyze the association between the anticipatory response style and clinical impulsivity.

As expected, the pre-suicidal task revealed no differences between the three groups in latency time. However, the low percentage of correct responses – especially in the two patient groups – is agreement with previous reports (Rabinovitz et al., 2000). We think our strict definition of ‘correct response’ may have contributed to this; next to eye movements in the wrong direction, we labeled all trials with non-linear eye movements (with ‘violation’ or with a latency outside the timeframe 300-500 ms) as incorrect.

A possible limitation to our finding is the effect of drug treatment. Although recent literature suggests that anti-suicidal errors in schizophrenia remain even after drug treatment, it is possible that medication effects did occur in our study (Hrusch et al., 2006). However, in an extra post hoc analysis analysis with different drug types as co-factor, we did not find any effects of medication, suggesting that recent use of medication did not contaminate the findings of our study. Moreover, acute drug effects were excluded because there was a 12-hour medication-free period prior to the assessments. In addition, the
literacy and donation times did not indicate that relative effects were present. Thus, possible limitation is the sex distribution of the three groups. Our sample reflected the male typical sex distribution of a male predominance of 5:1 and a female predominance of 1:1. To adjust for this as much as possible, we ran all our analyses including sex as a cofactor. The outcomes of our analyses do not show that the differences in sex jeopardise our conclusions.

In conclusion, our data suggest that inhibition deficits may be characteristic among BPD patients with psychosis-like symptoms, but do not reflect the whole group of BPD patients. The cooccurrence with schizophrenia is striking and possibly implicates a shared involvement of dopaminergic pathways in the disinhibited PVF and/or ACC. Therefore our results are in line with a prefrontal-dysfunction hypothesis for BPD. Psychosis-like symptoms may be an important target dimension for future BPD research and treatment.

References


