Distinct pattern of P3a event-related potential in borderline personality disorder

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P3a and P3b event-related brain potentials to auditory stimuli were recorded for 17 unmedicated patients with borderline personality disorder, 17 matched healthy controls and 100 healthy control participants spanning five decades. Using high-resolution fragmentary decomposition for single-trial event-related potential analysis, distinctive disturbances in P3a in borderline personality disorder patients were found: abnormally enhanced amplitude, failure to habituate and a loss of temporal locking with P3b. Normative age dependencies from 100 controls suggest that natural age-related decline in P3a amplitude is reduced in borderline personality disorder patients and is likely to indicate failure of frontal maturation. On the basis of the theories of Hughlings Jackson, this conceptualization of borderline personality disorder is consistent with an aetiological model of borderline personality disorder. *NeuroReport* 16:289–293 © 2005 Lippincott Williams & Wilkins.

Key words: Borderline personality disorder; Jacksonian model; P3; P3a; P3b; Single-trial event-related potential analysis

INTRODUCTION

Borderline personality disorder (BPD) is a complex and serious mental disorder characterized by a disturbance in the sphere of self, which is related to impulsivity and affect dysregulation [1]. Self can be conceived according to the definitions of Jackson [2,3] and James [4] as reflective, or 'higher-order', consciousness. Those with BPD have, in the typical case, suffered an adverse childhood marked by abuse and/or neglect [5]. The hypothesis has been put forward that maturation of higher-order consciousness in those with BPD has been impeded as a consequence of this background and by a failure of the 'sociogenetic' element necessary to this maturation [6]. Based on the theories of Jackson, the hypothesis proposes an aetiology of BPD as the failed maturation of prefrontal networks leading to a disruption in coordination, or integration, of sites of brain activity.

The present study was performed in an attempt to test the hypothesis using an auditory P3(00) event-related brain potential, one of the most investigated endogenous brain potentials [7]. Blackwood *et al.* [8] found amplitude attenuation and latency prolongation of auditory P3 in BPD patients. A later study [9] reported that these trends were present but too tiny to yield statistical differences. Recently the diagnostic power of P3 has been significantly improved using the identification of two distinct components of auditory P3: an earlier component, called P3a, and a later component, called P3b. Convergent evidence links P3a with prefrontal-dependent cortical mechanisms of automatic attention, whereas P3b has been distinguished by more goal-directed types of attentional and memorial operations supported by more posterior neural sources [10,11]. Functional relationships between systems producing P3a and P3b appear to reflect coordinated activities in the prefrontal and posterior cortical areas during the switching and updating of task sets in working memory [12].

Using P3a and P3b as markers of the Jacksonian theory, predictions were made that BPD would (1) show diminished coordination between neural generators of P3a and P3b, (2) show component abnormalities characteristic for failure of prefrontal activities, and (3) that these abnormalities will resemble maturational failure.

The predictions are approached by means of an investigation of auditory P3a and P3b elicited in a target detection task. We employed high-resolution fragmentary decomposition, a model-based technique of single-trial event-related potential (ERP) analysis that identifies single-trial ERP components and resolves their temporal overlap [13]. We compared data from BPD patients and matched mature controls with estimate P3a and P3b abnormalities caused by BPD. To access the developmental aspects of the theory, we evaluated from the group of 100 controls normative age dependencies of P3a and P3b peak amplitudes.

MATERIALS AND METHODS

Participants: Seventeen patients with BPD (4 men and 13 women; mean age=31.6 years, SD=7.9, range=20–44 years) participated in the study. The BPD patients came from an ongoing program for the treatment and evaluation of BPD patients. The diagnosis was made by two independent raters (a psychiatrist and a psychologist) according to DSM-III-R criteria in a diagnostic interview that included the Diagnostic Interview for Borderline Patients. Patients were

free of medication for at least 30 days at the time of the study.

The control group included 17 (4 men and 13 women; mean age=34.3 years, SD=8.6, range=20–47 years) age-matched and sex-matched healthy study participants. The study participants for the normative study (normative group) of age-related changes of P3a and P3b were 50 normal women and 50 normal men between the ages of 18 and 70 years. There were 10 women and 10 men at each age from 18 to 30, 31 to 40, 41 to 50, 51 to 60 and 61 to 70 years.

Exclusion criteria were left-handedness, recent history of substance abuse, epilepsy or other neurological disorders, and mental retardation or head injury (assessed using Section M from the Composite International Diagnostic Interview [14] and the Westmead Hospital Clinical Information Base Questionnaire). Study participants were asked to refrain from smoking or drinking caffeine for 3 h prior to the recording session. Written consent was obtained from all study participants prior to testing in accordance with National Health and Medical Research Council guidelines.

Procedure: ERP data were collected using a two-tone auditory target detection task in a method similar to that used in many previous research reports [15–17]. In brief, auditory tones were presented pseudorandomly via stereo headphones to both ears at 60 dB above each individual's auditory threshold. Fifteen percent were target (task-relevant) tones presented at 1500 Hz. The remaining 85% were background (task-irrelevant) tones delivered at 1000 Hz. Participants were asked to ignore the background tones and to press two reaction time buttons 'as fast and as accurately as possible' using the index finger of each hand when they identified a target tone.

Electroencephalographs (EEGs) were recorded from Fz, Cz and Pz electrode sites according to the 10–20 international system with linked ears as reference using a DC acquisition system. An electro-oculogram was recorded so that trials contaminated by ocular movements or blinking could be detected and excluded from analysis. Voltages were continuously digitized at 250 Hz and digitally filtered (high-pass and low-pass boxcar filters) to remove irrelevant low-frequency (<0.5 Hz) and high-frequency (>50 Hz) components. Procedures of off-line automated single-trial analysis were applied to standard 1.4 s EEG segments from 0.4 s before stimulus to 1 s after stimulus for the first 40 target stimuli.

Single-trial analysis: A model-based method of single-trial ERP analysis called fragmentary decomposition was employed to identify P3a and P3b from single-trial ERPs [17]. We applied advanced technique, high-resolution fragmentary decomposition to resolve the temporal overlap of single-trial ERPs and create a model ERP defined by a set of three parameters: κ (amplitude coefficient), ρ (shape coefficient) and O (onset time) [13]. Physically, 1.2ρ is the rise time, i.e. the time interval between the onset time (O) of the component and its peak latency (L). Conventional ERP parameters, peak amplitude (A) and peak latency (L), are defined as follows: $A=0.356\kappa$ and $L=O-1.2\rho$. Figure 1 illustrates A, L and O parameters of P3a, which are not affected by the temporal overlap with P3b. By contrast, an overlap correction improves the estimate of P3b peak amplitude.

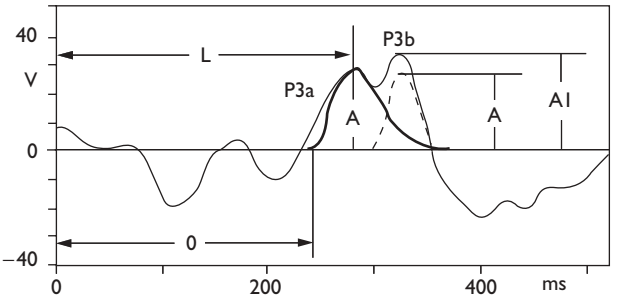

Fig. 1. The solid line exemplifies single-trial event-related potential record with identified P3a and P3b. Ordinate scale is for voltage (V, μV). Bold solid and dotted curves show models of P3a (A=28.1 μV, O=244 ms, L=280 ms) and P3b (26.9, 300, 324), respectively. Resolution of the temporal overlap between P3a and P3b provides an overlap-corrected estimate of P3b peak amplitude, A. AI is the peak amplitude of the P3b peak in the single-trial record.

Component identification employed the following latency windows: P3a, 240–299 ms; P3b, 300–360 ms. Insignificant and artefact contaminated peaks were removed by a procedure of amplitude and shape discrimination that selected analysis peaks with maximum $|A|$ between 2 and 45 μV and ρ between 8 and 50 ms.

Statistical analyses: Depending on the Gaussianity of single-trial ERP parameters (Kolmogorov–Smirnov test), a parametric t-test or nonparametric Mann–Whitney U-test was employed for intergroup comparisons.

The decrease or increase in peak amplitude with target stimulus repetition was tested using linear regression $Y=\alpha+\beta m$, where Y is the peak amplitude, m is the number of target stimuli and α and β are parameters. If the slope (β) indicates statistically significant dependency, it is regarded as the index of dynamic development (IDD).

Simultaneous cross-correlation analysis was applied to onset times of P3a versus P3b elicited in one and the same trial in order to infer time locking (functional connectivity) of underlying neural sources [18]. The measure of synchronicity or time locking is provided by the index of temporal locking (ITL). ITL was computed as a linear correlation coefficient between pairs of quantities (Oa_i, Ob_i), where Oa and Ob denote onset times of P3a and P3b, respectively, and i is the index of the sweep.

Regression analysis with age as an independent variable was applied to P3a and P3b peak amplitudes from the normative group in order to estimate normative age dependencies of these components in the form of a regression line $Y=\alpha+\beta x$, where Y is the peak amplitude, x is the age and α and β are parameters.

RESULTS

Borderline personality disorder patients in comparison with matched healthy controls: The intergroup comparisons employed a nonparametric Mann–Whitney U-test for peak amplitudes (A) and a parametric t-test for temporal parameters (L and O). Major relationships were similar for all recording sites. Table 1 shows typical results referring to Cz.

The range of P3a mean peak latency from 268 to 271 ms indicates 'classical P3a', i.e. a positive component at a mean latency of 270 ms (P270) associated with rare (target)

Table I

0	1 PG	2 CG	3 1 vs. 2
P3a, *A*	16.2 (9.14)	12.8 (6.73)	***
P3a, *L*	268 (17.3)	269 (17.6)	ns
P3a, *O*	242 (19.7)	245 (19.5)	*
P3b, *A*	14.9 (8.36)	14.8 (7.5)	ns
P3b, *L*	328 (16.8)	328 (16.5)	ns
P3b, *O*	303 (20.7)	301 (20.7)	ns

Columns 1 and 2 show the mean (SD) of parameters A (peak amplitude, μV), L (peak latency, ms) and O (onset time, ms) listed in column 0 for P3a and P3b. Column 3 shows intergroup comparisons: patient group (PG) vs. control group (CG), respectively. Significance levels: $*p<0.05$; $***p<0.001$; ns – nonsignificant.

acoustic stimuli [19]. P3b timing is in good agreement with a latency range of 300–350 ms associated with P3 from auditory paradigms. Intergroup differences in peak latencies are nonsignificant for both P3a and P3b.

The estimates of onset time reveal a statistically significant decrease of the P3a onset time in BPD patients. A better sensitivity of onset time to the timing of P3a is probably because this parameter is a more direct measure of component timing than conventional peak latency, which is a composite of onset and rise times.

The estimates of peak amplitudes reveal a statistically highly significant increase of the P3a peak amplitude in BPD patients. The increase is most pronounced at the Fz recording site, where the relationship of P3a peak amplitudes for patient and control groups is 1.36. The corresponding ratios for Cz and Pz recording sites are 1.26 and 1.12, respectively. The significance levels are at $p<0.001$ for the Fz and Cz recording sites and at $p<0.01$ for the Pz recording site. Independent of the recording site, BPD has no impact on the amplitude of P3b.

The results of simultaneous correlation analysis indicate statistically significant time locking of P3a and P3b for normal study participants: ITL=0.26 ($p<0.002$), 0.221 ($p<0.002$) and 0.196 ($p<0.01$) for Fz, Cz and Pz recording sites, respectively. Low degrees of the P3a versus P3b synchronicity in BPD patients, 0.109, 0.087 and 0.042 for Fz, Cz and Pz, respectively, were nonsignificant.

Figure 2a illustrates that dynamic amplitude changes appear as a statistically significant decline of P3a peak amplitude in normal study participants whereas the decline is absent in BPD patients. Parameters of regression for controls are as follows. Fz: α=13.8 μV, β(IDD)=–0.1 μV ($p<0.01$); Cz: 14.7, –0.1 (<0.002); Pz: 14.5, –0.09 (<0.01). Dynamical changes of P3a in BPD patients are minor and statistically nonsignificant. The data from both groups did not reveal dynamic changes in P3b amplitudes.

Normative age dependencies: Regression analysis of P3a and P3b peak amplitudes with age as an independent variable revealed statistically highly significant ($p<0.001$ for all recording sites) rates of decrease for both components. The rates of decrease are as follows (μV/year): P3a, –0.11, –0.13 and –0.13 for Fz, Cz and Pz, respectively; P3b, –0.1, –0.08 and –0.08 for Fz, Cz and Pz, respectively. Being repeated for subgroups of 50 men and 50 women, the calculations did not reveal statistically significant gender differences.

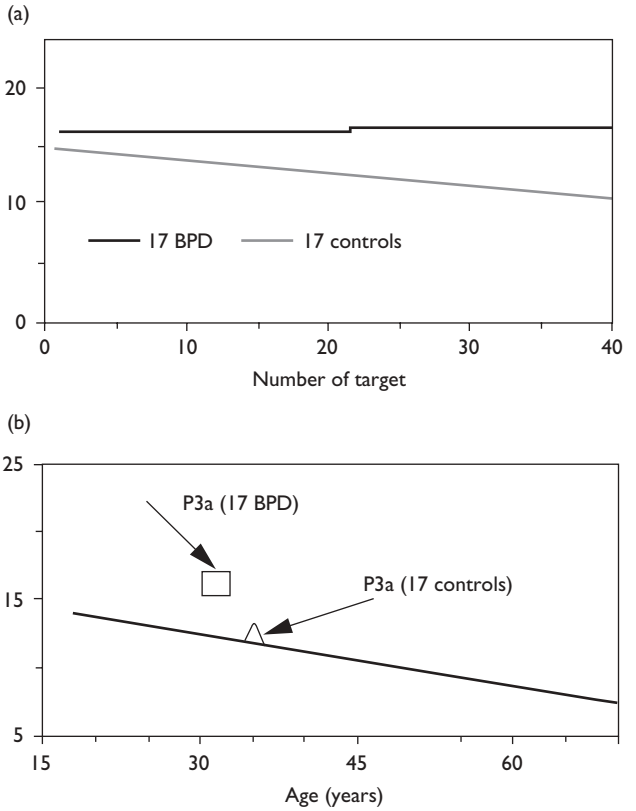

Fig. 2. (Cz recording site). (**a**) Dependencies of the P3a peak amplitude on the number of target stimuli. (**b**) The bold solid line shows P3a normative age dependency between the ages of 18 and 70 years (normative group). The square and triangle show P3a peak amplitudes for borderline personality disorder patients and the control group, respectively. Ordinate scales in (a) and (b) are for peak amplitude (μV).

The bold solid line in Fig. 2b illustrates the regression line (α=16.4 μV, β=–0.13 μV/year, $p<0.001$) for ages between 18 and 70 years for peak amplitudes of P3a (normative group). The mean peak amplitudes of P3a for BPD patients and normal study participants from the control group are shown at mean ages of participants from these groups by the square and triangle, respectively.

DISCUSSION

This study was conducted to test a hypothetical model of BPD on the basis of theories of Jackson using P3a and P3b as markers. Given that P3b and P3 are widely accepted as synonyms, our study is consistent with previous reports in that the timing of P3 is slightly delayed by BPD [8,9]. The results indicate a minor BPD influence on P3b. To our knowledge, this is the first study to report that P3a event-related potential distinguishes BPD. Compared with age-matched controls, major P3a abnormalities in BPD patients are abnormally enhanced amplitude, failure to habituate and a loss of temporal synchronicity with P3b. Such a profile of disturbances tends to support three main predictions derived from the model.

A discoordination hypothesis: It is well established that P3a and P3b arise from different neural generators [10,12]. Simultaneous cross-correlation analysis revealed

statistically significant temporal locking between P3a and P3b in the controls. This finding indicates temporal synchronicity of underlying neural sources, i.e. their functional coordination. On the other hand, participants with BPD showed no significant correlation between P3a and P3b. These findings suggest that the coordination between sources of P3a and P3b is impaired in BPD patients.

Frontal origins of borderline personality disorder: Recent multidisciplinary evidence shows that P3a is a reliable marker of electrical activities in prefrontal cortical areas and connected cortico-limbic structures [10]. The P3a abnormalities caused by BPD may be relevant to the frontal hypometabolism in BPD patients, which is pronounced prefrontally [20].

Frontal origins of P3a are supported by its cognitive function associated with the automatic attention and orienting response [10,11]. In this context, it is generally accepted that the amplitude decrement of P3a with stimulus repetition is habituation [10]. Our study shows habituation of P3a in normal study participants with a statistically significant decline rate of about –0.1 μV per stimulus. On the other hand, BPD patients showed an absence of statistically significant habituation of P3a. An earlier study using autonomic markers of the orienting response demonstrated a failure of sympathetic skin response to habituate in hysterical individuals [21]. 'Hysteria' can be seen as an ancestor of the current diagnosis of BPD.

Given that the damage of the posterior hippocampal region causes profound abnormalities in the characteristics of P3a and habituation [22], the failure of P3a to habituate in BPD patients may indicate pathologies in limbic-prefrontal connections that disturb the formation of adequate central representation of past stimuli against which new stimuli are matched.

Maturation deficits in borderline personality disorder: In general, the amplitude of average P3 (P3b) is smaller in older study participants than in younger ones [7,23]. No studies have provided assessment of P3a (P270) normative age dependencies and their comparison with P3b. However, because both P3a and P3b contribute to the average P3, a more rapid decrease in P3a with age is expected from the evidence that P3 amplitude has a greater age-related decline when elicited during automatic than during effortful attention [11]. Consistent with this, our study shows that P3a declines faster than P3b, specifically at Cz and Pz recording sites (an approximately 1.6 times larger rate of decline).

The absence of significant differences between P3b amplitudes in patient and control groups gives no indication that BPD affects the normal pattern of age-related reduction of P3b amplitude. By contrast, estimates of the P3a peak amplitudes for different ages from regression lines indicate that P3a amplitudes in the group of BPD patients are significantly larger than expected values. Given the mean age of BPD patients (31.6 years), the regression line in Fig. 2b suggests 12.3 μV as a normative value of P3a peak amplitude. The actual mean value for BPD patients is 16.2 μV (the square in Fig. 2b). Reference to the estimated rate of P3a normative age decline (–0.13 μV per year for the Cz recording site) shows that such an increase arises if the age-dependent changes in P3a amplitude were negligible during a period of time of about 30 years. It is tempting to speculate that neural mechanisms that govern the decrease of P3a amplitude are impaired by BPD.

CONCLUSION

Both conventional (peak amplitude) and complementary (onset time, IDD and ITL) single-trial component measures show that BPD affects major functional characteristics of P3a, whereas the changes in P3b characteristics are minor. A most prominent abnormality of P3a is a significant increase in the peak amplitude. The estimated normative age dependencies for P3a suggest that the increase in P3a amplitude in BPD reflects disturbances of developmental processes in the systems producing P3a. The character and distinct role of P3a abnormalities suggest that the pathophysiology of BPD includes (1) attention and novelty evaluation deficits, which are likely to be because of a failure of frontal maturation, and (2) a breakdown in coordination between frontal and more posterior cortical networks. These findings are consistent with a conceptualization of BPD on the basis of Jacksonian theory.

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