# Bereitschaftpotential in schizophrenia

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**Background** Several reports have documented the presence of motor abnormalities in schizophrenic patients.

**Method** Thirty schizophrenics and 28 healthy controls were included in the study. Scalp-recorded bereitschaftpotentials (BPs) generated prior to voluntary movements were recorded in all subjects.

**Results** The early (NSI) and late components of BP and peak negativity were reduced in all schizophrenic patients. In particular, the NSI was reduced in patients with positive symptoms, and the late component in patients with negative symptoms.

**Conclusions** These findings provide further support for the involvement of frontal cortex, subcortical structures and their connections in schizophrenia, and highlight some differences between positive and negative symptom clusters.

Motor abnormalities due to schizophrenia occur more frequently than is generally known and are not limited to catatonic schizophrenia. Some of them are voluntary motor abnormalities such as clumsiness, disorganisation, delayed response, postural persistence and slowness of movement completion (Manschreck, 1986). We assessed the scalp-recorded bereitschaftpotentials (BPs; readiness potentials, Deecke & Kornhuber, 1978; Dick *et al*, 1989) generated prior to voluntary movements, which comprise preparation, initiation and execution of voluntary movement.

Previous studies of movement-related potentials in schizophrenia showed that BP amplitudes were abnormal and reduced (Chiarenza *et al*, 1985; Singh *et al*, 1992). The present study intended to evaluate these potentials and their clinical correlates in schizophrenic patients.

## METHOD

Our study group consisted of 30 right-handed patients (nine women and 21 men; mean age 34.2 (s.d. 8.7) years; mean duration of illness 10.0 (s.d. 4.2) years) with a diagnosis of DSM–III–R 'chronic schizophrenia with acute exacerbation' (American Psychiatric Association, 1987). Eight of them had been drug-free for at least one month prior to recording because of non-compliance, while 22 subjects were receiving neuroleptic treatment (mean chlorpromazine equivalent dose 376 mg; range 50–1025 mg/day). Patients with a history of severe head trauma, drug misuse/dependence, alcoholism, tardive dyskinesia or drug-induced Parkinsonism were excluded on the basis of the routine neurological examination. Twenty-eight right-handed healthy subjects (12 women and 16 men; mean age 37.4 (13.9) years) with no family history of schizophrenia or movement disorder constituted the control group.

The Scales for the Assessment of Positive and Negative Symptoms (SANS and SAPS; Andreasen, 1984*a*,*b*) were applied to these psychotic subjects. Interrater reliability was 0.90 for the total score on the SAPS (range 0.24–0.95 for the items), and 0.94 for the total score on the SANS (range 0.62–0.96 for the items). These reliability coefficients were determined with intraclass correlation. Nine patients were classified as having positive schizophrenia, seven as having negative schizophrenia, and 14 as having mixed schizophrenia according to Andreasen's modified criteria, which give precedence to negative symptoms (Andreasen *et al*, 1990).

Subjects were seated comfortably keeping their eyes closed in a silent room. Self-paced brisk voluntary extension movements of the right wrist were performed at irregular intervals of more than five seconds. Electromyographic (EMG) activity was recorded with bipolar Ag–AgCl surface electrodes placed approximately 2 cm apart over extensor digitorum communis (EDC) muscle. Bandpass filters were 5 Hz to 3 kHz. The EMG signals from EDC muscle were used as the trigger events. BPs were recorded at $C_z$(vertex), $C_3$ and $C_4$ electrode sites of the 10–20 system ($C_3$ and $C_4$ being at a distance of 5–7 cm from $C_z$, in opposite directions) with Ag–AgCl electrodes, referred to linked earlobes with a forehead ground. The filter bandpass was 0.1–50 Hz. The impedance of the electrodes was less than 5 kW. The EMG signals from EDC muscle triggered the collection of bioelectrical activity from scalp electrodes. All signals were recorded for 2 s, from 1600 ms before to 400 ms after the time-locking trigger point. Fifty trials were averaged for each subject. BPs were recorded using the Nihon-Kohden (MEM-4104) Neuropack Four EMG/EPs instrument.

The following measurements of the BP amplitude were made according to the criteria of Dick *et al* (1989). BP amplitude was measured at: (a) peak BP negativity (N1); (b) the early component of BP (NS1), 650 ms before the EMG onset; (c) the late lateralised component of the BP (NS2) was calculated by subtracting the NS1 from the peak BP negativity (N1).

The BPs from all scalp electrode positions for the two groups were compared using covariance analysis (age as covariate) for repeated measure (ANCOVA) with a grouping factor of patients versus normals and a within-subject factor of electrode positions. Greenhouse & Geisser's (1959) adjusted degree of freedom (d.f.), which provides a conservative test of the repeated measures factor, was applied to the data when appropriate. In addition, complementary analyses

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were performed separately between subgroups (medicated/non-medicated/normal, and schizophrenic subtypes/normal controls as grouping factor). BP amplitudes were compared between groups using Student's *t*-test for pairwise comparisons. Correlational analysis was carried out to evaluate the relationship between symptoms and BP components using Pearson's product-moment correlations.

## RESULTS

Bereitschaftpotentials recorded from three scalp locations for a single normal subject and a patient with schizophrenic disorder are shown in Fig. 1, and a summary of the bereitschaftpotential components in groups is presented in Table 1.

### Early component (NS1)

The amplitude of NS1 was less in patients ($F(1,55)=9.82$, $P=0.003$), and in both medicated ($t(48)=2.75$, $P=0.008$) and non-medicated patients ($t(34)=2.30$, $P=0.028$). There was no significant effect on the within-subject factor and interaction term. The decreased NS1 in patients with positive symptoms ($t(35)=2.54$, $P=0.016$) and in patients with mixed symptoms ($t(40)=2.57$, $P=0.014$) were significant.

### Late BP (NS2)

The amplitude of the late BP was reduced in the group of all patients ($F(1,55)=4.66$, $P=0.035$), and in non-medicated patients ($t(34)=2.13$, $P=0.030$). The group-by-electrode interaction effect was non-significant, but the within-subject effect was significant ($F=39.40$, adjusted d.f.=1.96 and 109.86, $P<0.001$), reflecting that the late BP is lateralised to the hemisphere contralateral to the movement. In the patients with negative symptoms, the NS2 component was smaller than normal ($t(33)=2.50$, $P=0.017$).

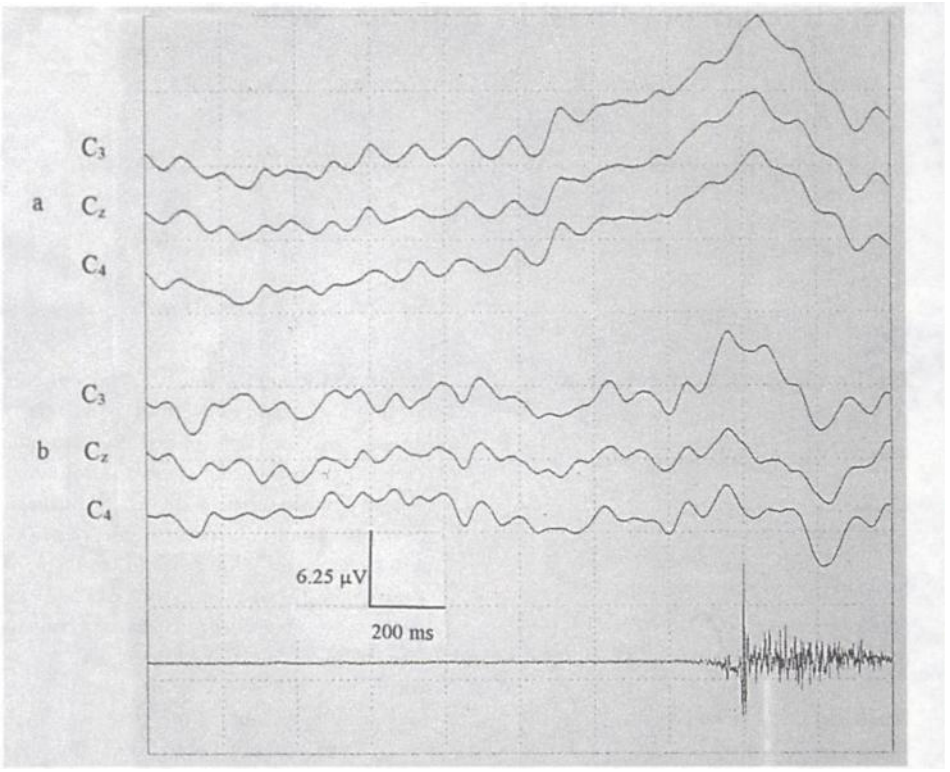


**Fig. 1** Scalp-recorded bereitschaftpotentials (a) in a control and (b) in a patient with schizophrenia at the $C_3$, $C_z$ and $C_4$ electrode sites, with the electromyographic activity.

### Peak BP (N1)

The amplitude of N1 was smaller than in normals for all patients ($F(1,55)=19.03$, $P<0.001$), both medicated ($t(48)=3.47$, $P=0.002$) and non-medicated ($t(34)=4.36$, $P<0.001$) and also schizophrenic subtypes ($F(3,53)=6.60$, $P=0.001$). The electrode effect was also significant ($F=52.57$, adjusted d.f.=1.90 and 106.30, $P<0.001$) just like the NS2 component. The group-by-electrode interaction was non-significant.

In pairwise comparison, there was no difference between medicated and non-medicated patients in the BP components.

### Correlations

In the overall schizophrenic group, there were significant correlations between the NS1 at $C_4$ and the subscale 'positive formal thought disorder' global score on the SAPS (Pearson's $r=-0.45$, d.f.=29, $P<0.02$), and between the late BP at $C_4$ and some negative symptoms, such as 'alogia' ($r=-0.44$, $P<0.02$), 'anhedonia–asociality' ($r=-0.36$, $P=0.052$) and total score on the SANS ($r=-0.37$, $P<0.05$). These correlations were also significant in the non-medicated patients between the late BP at $C_4$ and negative symptoms ('alogia',

**Table 1** Summary of the bereitschaftpotential (BP) components in patients with schizophrenia and control subjects

| | Control | Schizophrenia | nonMedSch | MedSch | PosSch | NegSch | MixedSch |
|---|---|---|---|---|---|---|---|
| *n* | 28 | 30 | 8 | 22 | 9 | 7 | 14 |
| Early component of BP (NS1) | 2.9 (2.0) | 1.3 (1.6) | 1.1 (1.3) | 1.4 (1.7) | 1.1 (0.9) | 1.9 (1.6) | 1.2 (2.0) |
| Late component of BP (NS2) | 7.7 (3.1) | 6.0 (3.2) | 5.1 (2.5) | 6.3 (3.4) | 6.8 (3.9) | 4.4 (3.0) | 6.2 (2.6) |
| Peak BP negativity (N1) | 10.7 (2.7) | 7.2 (3.2) | 6.3 (1.6) | 7.6 (3.6) | 7.8 (3.9) | 6.3 (2.1) | 7.4 (3.3) |

Mean values averaged across all electrode positions. Values show average (s.d.) μV.
MedSch, schizophrenic patients with medication; nonMedSch, schizophrenic patients with no medication; PosSch, positive schizophrenia; NegSch, negative schizophrenia; MixedSch, mixed schizophrenia.


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'anhedonia' and 'total score' on the SANS respectively −0.90, −0.71 and −0.80), and between the peak BP at $C_4$ and 'anhedonia' ($r$=−0.82). However, there was no significant correlation in the medicated subjects.

## DISCUSSION

The main finding of this study is that all components of the BP are smaller in schizophrenic patients compared with normals. Despite methodological differences, our results in schizophrenics are consistent with the findings of other investigators (Chieranza *et al*, 1985; Singh *et al*, 1992). The reduction in the early component of the BP was seen in patients with positive symptoms, and of the late component in patients with negative symptoms. These results revealed significant neurophysiological differences between positive and negative schizophrenic patients.

Abnormal BP in schizophrenics might correlate with motor abnormalities intrinsic to schizophrenic disorder, and may be related to deficits in those processes in schizophrenia. Although some significant correlations were present between components of the BP and clinical symptoms in non-medicated patients, neuroleptics did influence these correlational data. We could not find any significant correlation coefficients in the medicated patients. This finding might reflect that antipsychotic medication tends to reduce voluntary motor abnormalities, although they produce many motor side-effects (Manschreck, 1986).

Widespread amplitude reductions were present in all the components in the schizophrenic subjects, and reduction of the NS1 was prominent in patients with positive symptoms. In Parkinson's disease, abnormal BP, particularly decreased amplitude of the early component (NS1), has been reported (Dick *et al*, 1987, 1989). Administration of levodopa causes augmentation of the amplitude of the BP in both normal subjects and parkinsonian patients, while haloperidol administration results in reduction of the peak BP amplitude in normals (Dick *et al*, 1987). According to our results, we could speculate that administration of drugs has not affected the amplitude changes because there were no significant effects of medication on the amplitude between medicated and drug-free schizophrenic groups, although BP amplitudes had decreased in all patients with either positive or negative symptoms. On the other hand, schizophrenic patients were exposed to long-term and cumulative antidopaminergic drug effects, which might lead to structural changes causing abnormal BP findings or tardive dyskinesia. The neural origins of the BP have been extensively studied previously (Deecke & Kornhuber, 1978). For several different types of voluntary movements (eye, hand, arm and foot), it has been suggested that primary sensorimotor, supplementary (SMA), premotor, and prefrontal cortices contribute to the BP generation shown by neurophysiological and neuroimaging techniques. Recently, Schröder *et al* (1995), using functional magnetic resonance imaging techniques, reported that sensorimotor cortex and SMA dysfunction have been associated with motor disturbances in schizophrenia.

These neurophysiological findings provide further support for the involvement of frontal cortex, subcortical structures and their connections in schizophrenia, and also highlight differences between positive and negative symptom clusters. Further studies will be needed to incorporate more complex motor tasks and multiple electrodes, and to investigate the impact of neuroleptic treatment.

### CLINICAL IMPLICATIONS

- Bereitschaftpotential recordings revealed significant differences between positive and negative schizophrenia.
- Abnormal bereitschaftpotential might be related to motor abnormalities in the pathophysiology of schizophrenia.
- The study provides further support for the involvement of frontal cortex, subcortical structures and their connections in schizophrenia.

### LIMITATIONS

- The possible drug effect on bereitschaftpotential remains to be clarified.
- Recordings were limited to $C_z$, $C_3$ and $C_4$ electrode positions.

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