

Negative Difference (Nd), an ERP Marker of Stimulus Relevance: Different Lateral Asymmetries for Paranoid and Nonparanoid Schizophrenics

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Summary

We studied Nd in psychotic patients with varying degrees of paranoid symptoms. Nd is an ERP measurement of the difference in the way a nonattended tone is registered and the way the same tone is registered when used later as a discrimination target. In a three-tone oddball paradigm with passive-tone presentation and active discrimination, we recorded from 19 sites in 22 young healthy subjects and 28 schizophrenics. Nd (200–260 ms) was bilaterally symmetrical in healthy subjects. Paranoid patients showed a left frontal/right temporoparietal amplitude reduction which was reversed in nonparanoid subjects (reduced at right frontal/left posterior sites). These asymmetries were clearer when the groups were separated according to active paranoid symptoms rather than by diagnosis. There would therefore seem to be functional asymmetries mediating stimulus relevance in schizophrenics which differ from controls and differ between patients with and without active paranoid symptoms.

“Negative Difference” (Nd) als EKP-Marker der Stimulusrelevanz: Unterschiede in lateralen Asymmetrien von paranoiden und nichtparanoiden Schizophrenen

Nd wurde bei psychotischen Patienten mit und ohne paranoider Symptomatik untersucht. Nd ist ein ereigniskorreliertes Potential, das den Unterschied der Informationsverarbeitung zwischen nicht beachteten Tönen und dem gleichen Reiz als Unterscheidungszielton widerspiegelt. In einem „3-Ton-oddball“-Paradigma mit passiver und aktiver Tondarbietung wurden mit 19 Elektroden bei 22 gesunden und 28 schizophrenen jungen Probanden abgeleitet. Nd kam mit 200–260 ms bilateral bei Gesunden vor. Nd war kleiner bei links-frontal/rechts temporoparietalen Ableitungen bei Paranoiden und rechts-frontal/links posterior bei Nichtparanoiden. Diese Asymmetrien waren betonter bei Patienten mit aktiven Symptomen. Diese Ergebnisse zeigen, daß eine topographische Asymmetrie in der Verarbeitung der Bedeutung eines Reizes psychotische Patienten mit und ohne paranoider Symptomatik unterscheidet.

Introduction

We recently showed that mismatch negativity (MMN), an ERP measure of the difference in pitch and frequency registered between two nonattended tones, is decreased in paranoid schizophrenics and further reduced in nonparanoid schizophrenics (Oades et al., 1993; Oades, 1993). It was thus of interest to see if other subtraction waves in the three-tone oddball paradigm discriminate psychotic from healthy subjects and subgroups of psychotic patients from each other.

A pertinent wave is Nd, which is derived by subtracting the ERP to a rare deviant from that elicited when it later becomes the target. This controls for the effects of pitch and rarity and should reveal the role of stimulus relevance under conditions of attention.

We have found that MMN, PN, and Nd differ from each other on some features of latency and amplitude in young adults and in their development from eight to 22 years of age (in prep.). They may thus be considered, in part, as representing different attention-related processes. Having characterized these differences we decided to study young psychotic patients at an acute and early stage of illness. Further, as Frith (1992) advocated subgroup separation by symptom cluster rather than diagnosis, we compared subgroup division by diagnosis with division according to the presence of active symptoms of reality distortion.

Methods

Subjects were 12 patients with a DSM-III-R diagnosis of paranoid schizophrenia and 16 with nonparanoid schizophrenia (both with mean age of 18.4 years) and 22 age/sex-matched healthy controls. Paranoid symptoms were rated post-test using Andreasen's scale for the assessment of positive symptoms (SAPS). A median split at a score of 8 resulted in 13 patients with active paranoid symptoms and 15 with little reality distortion.

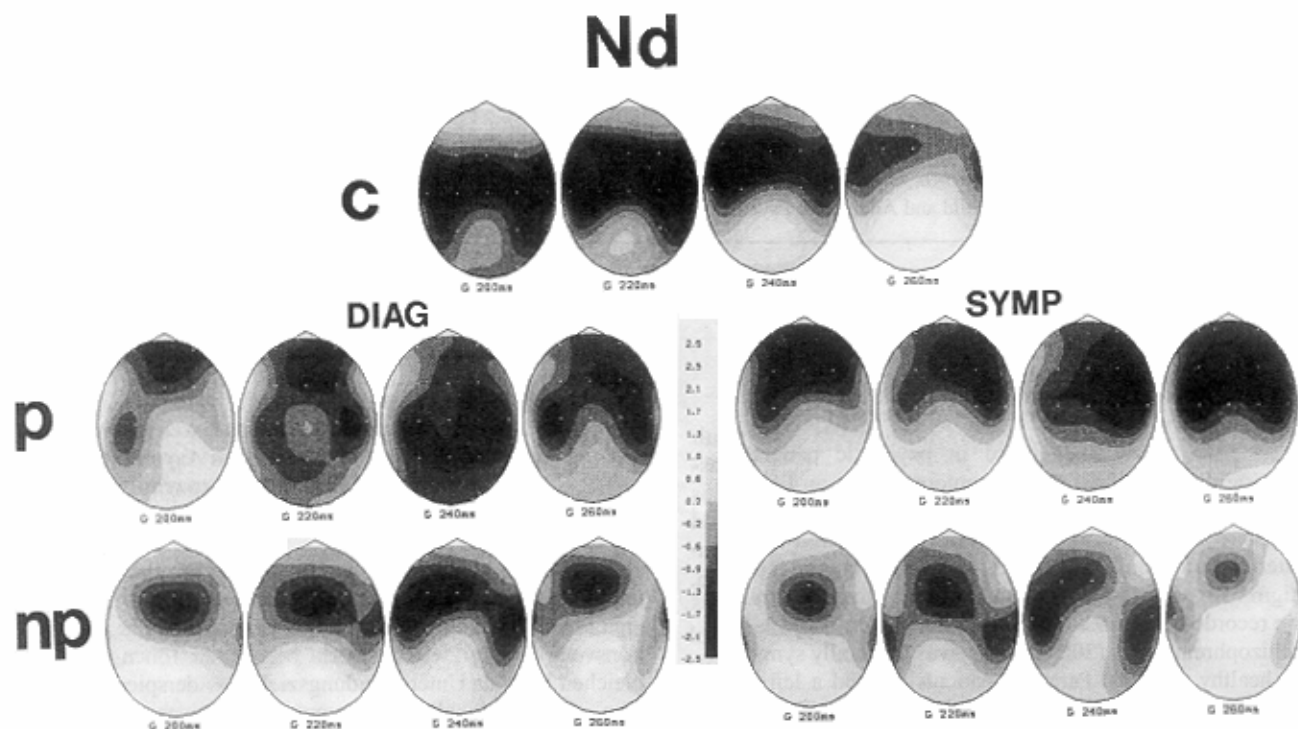


Fig. 1 Bilateral symmetric frontoparietal distribution of Nd (amplitude in μV) in healthy subjects (C, $n = 22$) at 200–260 ms. Left: Nd in schizophrenic diagnosed as paranoid (DIAG, P, $n = 12$) and nonparanoid (NP, $n = 16$); topography 200–260 ms, no significant t-test differences between P and NP groups 200–260 ms post-stimulus at 15

recording sites. Right: Nd amplitude in schizophrenics with active paranoid symptoms (SYMP, P, $n = 13$) and in nonparanoid schizophrenics (NP, $n = 15$); topography 200–260 ms, t-tests $P > NP$ at right frontal and left temporal, $NP > P$ at left frontal and right temporal sites $p < 0.05$.

Three tones were played during periods of passive nonattention and active discrimination (0.8 kHz, p 72%; 1.4 kHz, p 14% (target), 2.0 kHz, p 14%; 65 dB SL, duration 50 ms [+ 10 ms rise/fall], 100/run, interstimulus interval 1.5 [1.2–1.7 s Bernoulli sequence]). Electrocap records from 19 sites used Fpz-Oz ground, linked ear reference (< 2 Kohm), 4 ms bins, 50 ms pretrigger time, and were amplified by 12 K (band pass 0.3–70 Hz). Data were evaluated using a 25 Hz filter. EOG artifact (> 65 μV) was eliminated by amplitude hysteresis.

Results

At the top of Fig. 1 we show a broadly bilateral symmetry for the distribution of Nd in healthy subjects (peak latency 241 ms sd 46). A preliminary comparison with 22 psychotic patients separated by the presence or absence of clinically relevant paranoid features showed no significant amplitude differences in the latency range of 100–300 ms.

The rest of Fig. 1 compares the topographic distribution from 200 to 260 ms for paranoid and nonparanoid patients defined by diagnosis (DIAG, left) or according to active symptoms (SYMP, right). Paranoid patients ("p") show a normal waveform at right frontal and left temporoparietal sites and marked attenuation at left frontal and right temporoparietal sites. The nonparanoid patients ("np") manifest the opposite pattern. The difference between subgroups approaches significance only when the symptoms are active (Fig. 1 right, group

SYMP, running t-test, $t = 2.1$ – 2.3 where $t(31) 1.7$, $p < 0.05$ at F4, F8, T5, and F7, T6, 200–300 ms). These differences are confirmed by the procedure of Guthrie and Buchwald (1991) for frontal sites with a trend for the temporal sites (Nd window 140–300 ms = 40 sampling points, eight points required for 5% significance, 10 obtained at F7 and F4 and six at other sites).

Discussion

This is an exploratory study of the effects of psychopathology on ERP measures of attentional operations. Our work shows that the MMN registration of perceptual differences between unattended stimuli has a different latency, amplitude, and ontogenetic profile from PN/Nd measures that incorporate the registration of task relevance.

We find an asymmetric reduction of Nd where opposite lateralization patterns are found in psychotic patients with and without active paranoid symptoms (e.g., left and right frontal areas, respectively). This contrasts with the symmetrical attenuation of MMN in psychotic patients (Oades et al., 1993).

We conclude that 1) schizophrenics register stimulus significance in the brain differently from healthy subjects, 2) this difference varies with the nature and activity of symptoms and 3) frontotemporal asymmetries reflect the presence/absence of reality distortion. Our results broadly sup-

port reports that lateralized frontotemporal dysfunction obtained from ERPs, cerebral blood flow measurements, and magnetic resonance images is a sign of the presence or absence of paranoid symptoms (Liddle et al., 1992; McCarley et al., 1993). We are preparing an analysis of normalized data for Nd and a comparison with other subtraction waveforms to confirm that a) separate difference-waveforms represent separate processes and b) these processes are sensitive to dimensional differences in schizophrenic symptomatology.

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