Delayed early proprioceptive information processing in schizophrenia

SIDSE M. ARNFRED, RALF P. HEMMINGSEN and JOSEF PARNAS

Summary It was first suggested that disordered proprioception was a core feature of schizophrenia by Sandor Rado in 1953. Using a recently designed proprioceptive event-related potential paradigm based on a change of load, we studied 12 unmedicated male out-patients with schizophrenia and 24 controls. In the patients, the early contralateral parietal activity was delayed and later central activity had increased amplitude, but gating was unaffected. The results could be understood within the ‘deficiency of corollary discharge’ model of schizophrenia but not within the ‘filtering’ theory. Further studies, including psychiatric controls, are necessary to verify the specificity of the abnormality.

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In 1953, proprioceptive malfunction was proposed as a core feature of schizophrenia by Sandor Rado (Rado, 1953). It was this hypothesis that spurred the development of a new method to investigate proprioceptive information processing through electroencephalographic event-related potentials (Arnfred et al., 2000).

A brisk change of load on a hand-held handle elicits a proprioceptive event-related potential consisting of an early contralateral component (P60/N70) followed by the more central orienting response components (N160-P200) and, when associated with an experimental task, also late cognitive components (P360) (Arnfred, 2005). Previous event-related potential research in schizophrenia has followed two directions. The early cortical processing of stimuli has been investigated using passive paradigms such as the auditory P50 gating paradigm, whereas later processing has been examined in active cognitive tasks. Similarly, we investigated proprioceptive event-related potentials in a passive paradigm of paired stimuli and an active task paradigm requiring the participants to discriminate between weight loads. Because deficient auditory P50 gating and attenuated auditory P300 amplitude are well documented in schizophrenia (Braff & Light, 2004) we expected corresponding deficits in the proprioceptive event-related potentials, i.e. decreased gating of the early components and attenuated amplitude of the late target-related components.

METHOD

The study was approved by the local ethics committee and all participants gave written informed consent. We studied 12 male patients with schizophrenia and 24 healthy male controls. All participants were right-handed. The patients were diagnosed according to DSM-IV criteria (American Psychiatric Association, 1994), using the Schedules for Clinical Assessment in Neuropsychiatry (SCAN version 2.1; Wing et al., 1990, 1998). Their level of psychopathology was rated with the Scales for the Assessment of Positive and Negative Symptoms (SAPS and SANS; Andreason, 1984a,b).

The age-range of the patients was 18–49 years (mean 33.8; s.d. = 9.0) and of the controls was 19–54 years (mean 29.3; s.d. = 7.9); the difference was not significant. The duration of illness ranged from 0.5 to 23 years (mean 9.5; s.d. = 8.7; median 8.5) and the cumulative length of treatment periods with antipsychotic medication ranged from 1 to 28 months (mean 9.7; s.d. = 9.8; median 6.5), apart from two patients who were drug naïve. Those previously treated had been without medication for at least 1 month, the range being 1–210 months (mean 54.4; s.d. = 72.2; median 24). Mean positive symptom score was 4.3 (s.d. = 2.3), mean negative symptoms score was 6.8 (s.d. = 4.5), disorganised symptoms 2.9 (s.d. = 2.6) and total sum of scores 14.0 (s.d. = 4.0). Cognitive functions were assessed in both participant groups using the cognitive screening elements in the SCAN (the Mini-Mental State Examination, Oral Trail Making and Category Verbal Fluency), and through simple reaction-time and cognitive load reaction-time measures obtained by the California Computerized Assessment Battery (Miller, 1990). No significant differences were seen.

Proprioceptive evoked potentials

We recorded evoked potentials at the following electrode positions: FP1, FP2, Fz, Cz, Pz, C3 and C4, the last two placed 2 cm posterior to C3 and C4 above the somatosensory cortices. The proprioceptive stimuli were administered using a custom-built device, which applied 100g instantaneous changes to a vertical static load (400g) of a paddle which the participants held freely in their hands with their wrists supported (Arnfred et al., 2000). To avoid fatigue and drowsiness, other experiences and tasks were interspersed between the runs with the proprioceptive stimulus. The passive paired data were recorded in a mixed-method paradigm where a loop of three stimulus pairs lasted 12s. The reports of the other stimulus pairs (auditory clicks and right median nerve stimulation) are given elsewhere (Arnfred et al., 2003; Arnfred & Chen, 2004). The interstimulus interval between the paired load increments was 1s. After artefact rejection and baseline correction, visual peak detection was performed on the event-related potential waveforms. The latencies and amplitudes of each of the components were analysed separately through repeated-measures analyses of variance.

RESULTS

Contrary to our expectations, we did not observe significant deficits in proprioceptive gating or attenuation of P300. Significant differences between the two groups were observed only in the passive
The delayed latency of the initial activation of contralateral somatosensory cortex in the patient group was an unexpected and important finding, because the earlier stages of information processing are less influenced by top-down factors such as motivation and attention (Stephan et al., 2006). The patients were stable without medication and lived alone, so the latency difference cannot be attributed to florid psychosis or to medication. Cognitive impairment was not significant, and no general mental slowing was observed.

We suggest that the delayed activation of contralateral somatosensory cortex at P60 is the result of imprecision in the cortical response based on a diminished or unstable maintenance of proprioceptive readiness. Increased amplitude of the early contralateral activity of the electrically induced somatosensory evoked potential has been observed when attention is directed at the hand of the stimulus, and this is assumed to be a manifestation of increased cortical readiness for the side in focus. (Desmedt et al., 1984). In a situation of voluntary isometric muscle contraction, the cortical readiness could be attenuated if the corollary discharge signal preparing the sensory cortices for feedback was weak or unstable. This interpretation is in agreement with the hypothesis of a deficiency of corollary discharge in schizophrenia (Frith et al., 2000). As the P60 latency is normalised at the second stimulus, the difference is not owing to peripheral nerve transmission delay.

Although the augmented P200 amplitude at the first stimulus reflects an increased orienting response in the patients, in contrast to the commonly reported attenuation of amplitude, this effect lends support to our interpretation of diminished cortical readiness where a less-expected stimulus elicits a larger orienting response. Our results support Rado’s original hypothesis of a proprioceptive defect, whereas the lack of gating deficit is inconsistent with the ‘filtering’ theory. The proposed weakening of proprioceptive readiness could be understood as instability in feed-forward activations and, considering the influence of proprioception on the formation of self-awareness (Aitken & Trevarthen, 1997), it could be basic to anomalies of self-experience, which are frequent in schizophrenia. It is, however, pertinent to verify this proposal in another study including psychiatric controls.

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