



P300 in Twins Concordant and Discordant for Schizophrenia

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Background

It is widely accepted that schizophrenia is genetically determined to some extent. Abnormalities of the P300 component are one of the most robust biological findings in schizophrenia. They outlast clinical impairment, are not influenced by medication, and are present in relatives of schizophrenic patients, too. Therefore, the P300 is a promising candidate of a vulnerability marker.

The P300 amplitude and latency of affected and non-affected twins of discordant and concordant mono- and dizygotic pairs were compared with healthy twins. Non-affected twins of monozygotic discordant pairs share all, while non-affected twins of dizygotic pairs share half of their genes with their schizophrenic co-twins. Therefore, by comparing non-affected twins of discordant pairs with healthy controls and schizophrenic patients a vulnerability marker can be identified as follows: whenever the non-affected twins are similar to schizophrenic twins and different from healthy control twins, the respective measure is a possible vulnerability marker. Vulnerability may be caused by genetic or environmental factors. The genetic and the environmental contribution to vulnerability markers can be separated since both mono- and dizygotic twin pairs share environmental factors equally. Whenever non-affected twins of monozygotic discordant pairs are similar to schizophrenic patients and when non-affected twins of dizygotic pairs are similar to healthy control twins, the respective vulnerability marker is genetically influenced.

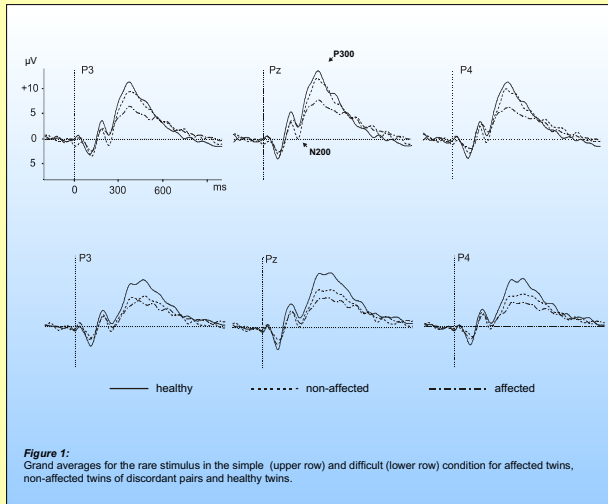


Figure 1: Grand averages for the rare stimulus in the simple (upper row) and difficult (lower row) condition for affected twins, non-affected twins of discordant pairs and healthy twins.

Methods

Subjects: 28 twin pairs discordant (20) or concordant (8) for schizophrenia spectrum disorders and 21 healthy twin pairs participated in the study (for sociodemographic and psychopathological data see Table 1). Zygosity was established by microsatellites (Erdmann et al., 1993).

Experimental Procedure: The P300 component was elicited by two auditory oddball paradigms in counterbalanced order across groups. In the simple task, 1,000 Hz tones were used as frequent (80%), and 1,500 Hz tones as rare (20%) stimuli. In the difficult task, the disparity in pitch between the frequent and the infrequent tone was smaller and adjusted to the subject's ability to discriminate tones.

Data Acquisition and Handling: Evoked potentials were recorded from 20 sintered Ag/Ag-Cl scalp electrodes positioned accordance to the international 10-20 system.

Statistical analysis: P300 peak amplitude and P300 latency on Pz were analysed with multiple regressions. Explanatory variables consisted of sex, age, verbal intelligence, condition (repeated measures factor), and group. The variable group covered three subgroups in the first model: healthy control twins, schizophrenic twins, and non-affected twins of discordant pairs. In the second model non-affected twins were separated according to zygosity. Only affected twins were included into the third model and separated into concordant affected, affected twins of monozygotic discordant pairs, and affected twins of dizygotic discordant pairs.

	Index Twins		Healthy Control Twins	Total
	Non-affected	affected		
n	36	20	42	98
Sex (f/m)	15/21	9/11	22/20	46/52
Age	30.3 (8.0)	31.4 (8.3)	31.1 (10.3)	30.8 (9.1)
IQ ¹	107,2 (16.0)	110,3 (15.0)	111.9 (12.9)	109,8 (14.6)
Years at School	10.8 (1.8)	11.3 (1.9)	11.4 (2.0)	11.1 (1.9)

Table 1: Demographic data (with standard deviation) for healthy control twins, affected twins and non-affected twins of discordant pairs

Results

P300-latency: Informative explanatory variables were condition ($F[1/48] = 14.04; p < .001$) and verbal intelligence ($F[1/48] = 10.95; p < .01$). Groups did not differ in any model (ERPs are provided in Figure 1).

P300-amplitudes: Condition and group were informative explanatory variables which were qualified by a significant condition x group interaction ($F[2/47] = 3.27; p < .05$). Non-affected twins of discordant pairs showed P300 amplitudes like healthy control twins in the simple condition and like affected twins in the difficult condition (see Figure 2). Further analyses revealed that in the difficult task non-affected twins of monozygotic discordant pairs showed higher P300 amplitudes than non-affected twins of dizygotic pairs ($F[1/48] = 4.50; p < .05$). Comparison of affected twins resulted in a significant effect for group and condition and a significant group x condition interaction ($F[2/25]=3.80; p<.05$). Affected twins of monozygotic discordant pairs showed higher amplitudes than both other groups in the simple condition and higher amplitudes than concordant twins in the difficult condition (see Figure 3).

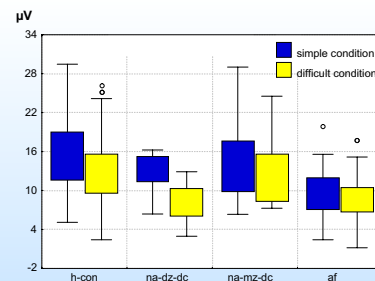


Figure 2:

P300-amplitudes with mean, 25% and 75% quartiles and extreme values for the difficult and easy condition on Pz of healthy control twins (h-con), non-affected twins of discordant monozygotic (na-mz-dc) and dizygotic (na-dz-dc) pairs and affected twins (af)

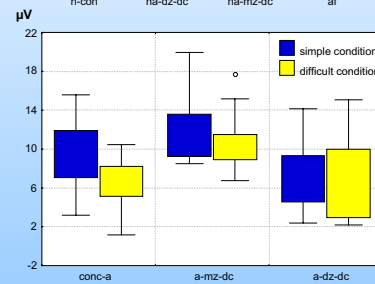


Figure 3:

P300-amplitudes with mean, 25% and 75% quartiles and extreme values of the difficult and easy condition on Pz with affected twins of discordant monozygotic (a-mz-dc) and dizygotic (a-dz-dc) pairs and concordant-affected twins (con-a)

Discussion

Several findings emerged from this study: 1) P300 peak amplitude was reduced not only in schizophrenic subjects but also in non-affected twins of discordant pairs. 2) P300 amplitude reduction in non-affected twins of discordant pairs was present in the difficult but not in the simple task. 3) Non-affected twins of monozygotic discordant pairs showed similar P300 amplitudes as healthy controls whereas non-affected twins of dizygotic pairs showed amplitudes similar to the affected twins. 4) Affected twins of monozygotic discordant pairs showed higher P300 amplitudes than both the concordant affected twins and the affected twins of dizygotic pairs. 5) In contrast to P300-Amplitude, P300-Latency neither discriminated between affected and non-affected subjects, nor between non-affected twins of discordant pairs and healthy controls.

These findings demonstrate that P300 amplitude reduction has the potential to be a vulnerability marker of schizophrenia. The usefulness of this marker is somewhat limited since P300 amplitude reduction is not found in all schizophrenic subgroups. At least one subgroup in which manifestation of schizophrenia depends mainly on environmental factors seems to show no P300 amplitude reduction. Insofar, the results are in accordance with the findings of Strik et al. (Strik et al 1993) and Franzek et al. (Franzek and Beckmann 1998) who identified a schizophrenic subgroup (cycloid psychosis according to Leonhards Classification), which is relatively independent on genetic factors and exhibits similar or even higher P300 amplitudes than healthy controls.

Annotation:

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