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Deficits in prefrontal and sensory interactions in top-down control in schizophrenia

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Introduction

Deficits in selective attention are one of the most important cognitive problems in schizophrenia. However, the underlying neurophysiological mechanisms are still not completely understood. Fronto-parietal networks have been implicated in visual selective attention (Womelsdorf and Fries, 2007) and disruption of these networks might underlie the pathophysiology of selective attention deficits in schizophrenia. We investigated the double dissociation between automatic processing and selective attention in schizophrenia by analyzing event related potentials (ERPs) related to these processes in frontal and sensory areas of the brain. Moreover, we looked at the connectivity between the frontal and sensory areas as a putative mechanism for the deficits indexed by the investigated ERPs.

Methods

Event related potentials were analysed for 16 schizophrenic/schizoaffective patients (partial remission with predominant negative symptoms) and 20 age-matched healthy controls undertaking an Emotional Stroop task. We analysed the following processes indexed by different ERPs:

1) ***Sensory processing of general and task relevant stimulus feature:*** The consecutive occipito-temporal negative potentials, N1 (at P7'/P8', 100-200ms post stimulus) and N2 (at P7'/P8', 200-250ms post stimulus), were analysed. They reflect a progressive change in the specificity of the differential processing of the irrelevant and relevant features of the stimuli, with N1 reflecting the automatic processing of the general stimulus characteristics and N2 reflecting the processing on the basis of specific task relevant stimulus characteristics (Harter and Guido, 1980).

2) ***Top-down executive processes*:** Two consecutive frontal positive potential, an early frontal positivity (at F5'/F6', 100-200ms post stimulus) and P2 (at F5'/F6', 200-250ms post stimulus), which are temporally coincident with N1 and N2 were analysed. P2 has been associated with the executive processes in the frontal lobes involved in the evaluation of the task relevance and salience of the stimuli while the functional significance of the early frontal postivity is ambiguous (Potts et al., 1996).

Connectivity analysis: Time-resolved linear coherence was calculated between the frontal and posterior electrode pairs included in the ERP analysis, separately for the right hemisphere/RH (F5-P7) and the left hemisphere/LH (F6-P8), by applying a Short Time Fourier Transform (STFT) using the EEGLAB software.

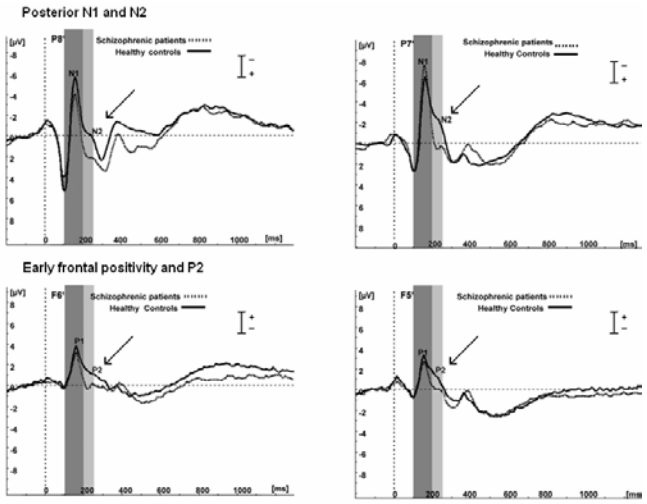
Results

We found a significant reduction in patients of the posterior N2 (RH: p=0.004, LH: p=0.0004) and a trend for reduction of the prefrontal P2 (RH: p=0.09, LH: p=0.09), both of which are implicated in controlled attention, while the posterior N1 (RH: p=0.10, LH: p=0.25) and the early frontal positivity (RH: p=0.72, LH: p=0.84) associated with automatic sensory processing were relatively spared.

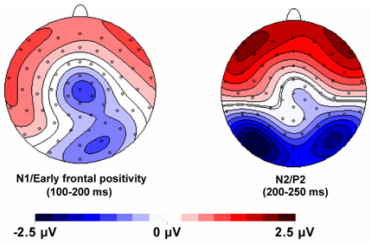
Moreover, the event-related cortico-cortical coherence between the frontal and posterior sites was reduced in patients compared to controls during the same time windows (100-200ms, 200-250ms) as the examined ERPs, for the delta and theta frequencies (Delta: p=0.01, Theta: p=0.03).

Discussion

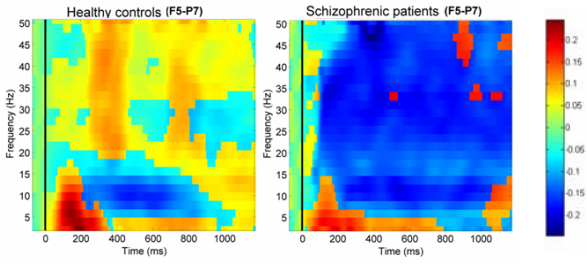
Patients revealed a specific disruption of the target specific perceptual and evaluative executive processes while the more automatic sensory processes were relatively spared indicating that schizophrenic patients are unable to efficiently use task specific information to guide the specific sensory processing of task relevant features. Even though the ERPs during the early time interval were spared in patients, the coherence was reduced in patients for both the early (possibly reflecting bottom up flow of information from sensory to frontal areas) and late (possibly reflecting top down modulation of sensory areas by the frontal areas) time intervals. This suggested that the selective attention deficits in schizophrenia might be driven by compromised interactions between the frontal and posterior areas during time intervals crucial for selective attention instead of merely reduced absolute activity of the frontal and sensory areas.



Grand averages over the sensory and frontal cortices: Patients show a differnetial reduction of the later, target related ERP components.



Current source density maps for the difference waves (healthy controls minus schizophrenic patients): Patients show a greater reduction in the posterior and frontal components in the later time interval.



Time resolved left hemisphere fronto-posterior coherence: Patients show a reduced coherence in both the early (100-200ms) and late (200-250ms) time intervals in the delta and theta frequencies as well as in higher frequencies around 300-400ms.

References

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