Available online at www.sciencedirect.com
SCIENCE DIRECT
Cognitive Brain Research 25 (2005) 936 – 947
COGNITIVE BRAIN RESEARCH
www.elsevier.com/locate/cogbrainres

Research Report

Event-related theta oscillations during working memory tasks in patients with schizophrenia and healthy controls

C. Schmiedt[a,b], A. Brand[c], H. Hildebrandt[d], C. Basar-Eroglu[a,*]

[a]Institute of Psychology and Cognition Research, University of Bremen, Grazer Str. 4, 28359 Bremen, Germany
[b]Department of Neuropsychology and Behavioral Neurobiology, University of Bremen, Grazer Str. 4, 28359 Bremen, Germany
[c]Center for Psychiatry, General Hospital Bremen-East, Züricher Str. 40, 28325 Bremen, Germany
[d]Clinic for Neurology, General Hospital Bremen-East, Züricher Str. 40, 28325 Bremen, Germany

Accepted 27 September 2005
Available online 10 November 2005

Abstract

Altered frontal lobe activity and executive control associated with working memory (WM) dysfunction are recognized as core deficits in schizophrenia. These impairments have been discussed as being associated with deficits in self-regulated action monitoring and anticipatory action plan generation. To study electrophysiological correlates of executive control – specifically action monitoring and action rule switching – under varying WM load, we used a paradigm derived from classic N-back (WM) tasks and requiring monitoring of simple actions. We focused on event-related changes in post-stimulus theta oscillatory activity during varying cognitive and WM demand in healthy controls and schizophrenia patients. The results show significant WM load and rule-switching-related increases of post-stimulus theta amplitude at fronto-central locations in controls. In patients with schizophrenia, there was no such modulation, but – apart from an increased early theta at left temporal locations – generally reduced late theta responses in all tasks and at all locations. Furthermore, the patients with schizophrenia showed significant differences in their error patterns, which imply differences in automation and anticipation of actions between controls and patients. These findings suggest that theta oscillations are involved in mediating frontal lobe activity and functions related to enhanced executive control. We conclude that the patients with schizophrenia showed deficits in acquiring a mental task set which appear to be associated with impairments in action monitoring and task-specific regulation of executive control.

Theme: Neural basis of behavior
Topic: Learning and memory: physiology

Keywords: Event-related oscillation; Theta oscillation; Working memory; Schizophrenia; Executive function

1. Introduction

Schizophrenia is associated with a variety of pervasive cognitive deficits, particularly dorsolateral and medial prefrontal lobe-related cognitive functions, so-called executive functions [5,18,37,61,72]. Executive functions are referred to as a group of abilities closely related with working memory (WM) and comprising the abilities to self-regulate initiation of tasks or activities, to organize task materials, to sequence, to prioritize, to shift between activities, and to inhibit an action. Impairments in WM function have been recently discussed as representing a core deficit or a basic disorder underlying cognitive performance of schizophrenia patients [38]. It is supposed that WM is a system, which greatly contributes to higher cognitive functions (including executive functions) such as reasoning, planning, and problem solving and that it is modulated by (pre-) frontal brain activations [6,19,20,25,44,54,58].

Theoretical and empirical investigations of the prefrontal and medial frontal cortex have provided evidence that this region mediates both mnemonic processes (such as storage and rehearsal) and non-mnemonic processes

* Corresponding author. Fax: +49 421 218 4600.
E-mail address: cbasar@uni-bremen.de (C. Basar-Eroglu).

0926-6410/$ - see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.cogbrainres.2005.09.015

(such as strategy selection, error monitoring, updating, inhibition, attention shifting), which are involved in control of behavior [24,30,54,57,62,69,73]. Findings of aberrant and impaired self-regulated action monitoring and error monitoring indicate the necessity to expand our notion of a working memory deficit in schizophrenia and our understanding of executive disorders observed in such patients [29,48,55,64]. Concerning error monitoring deficits in patients with schizophrenia, it has been proposed that they may be associated with a failure to properly monitor voluntary intentions and self-initiated actions [32,71]. It has been shown that, in comparison to healthy controls, patient with schizophrenia, irrespective of the specific symptoms, made significantly more recognition errors of own actions in trials with temporal delays [29]. Furthermore, it was found using the Wisconsin Card Sorting Test, a classic test of frontal lobe function, that perseveration in patients with schizophrenia could be explained by a failure to generate a plan, and this was related to the psychomotor poverty syndrome [51]. Several event-related potential (ERP) studies found that schizophrenic patients showed smaller error-related negativity (ERN) after error responses and a similarly distributed correct-related negativity (CRN) after correct responses [13,48,55]. Reduced ERN/CRN in schizophrenia patients was suggested to reflect impairment in the ability to represent the intended and/or predicted state. Using different paradigms it has been shown that schizophrenia patients exhibit deficits in anticipation and expectation of incoming events [64] and impairments in voluntary movement processes [68]. In line with these results, earlier studies used a WM paradigm for simple actions with different task difficulty. For instance, our group has found a significant correlation between reduced frontal negativity during increasing cognitive demand in schizophrenic patients and dominating negative symptoms [15].

The findings presented above suggest that schizophrenia is related to deficits in action monitoring for predicting incoming events and generation of action plans. But, there is also a growing number of findings indicating a close relationship between ERP components related to response monitoring, theta range (4–7 Hz) activity measured by surface EEG, and limbic theta activity (for review see [43,53]). Different frequency oscillatory brain activity in distributed networks has been suggested to participate in information processing and information transfer among different mnemonic networks [36,39,52,65,66]. Especially increases in frontal theta activity have been shown to be associated with enhanced cognitive and anticipatory control during learning processes or high demand contexts [8,10–12,36,42,44–47,65–67,70,74]. These and other results support the view that components of the average ERP not only reflect transient EEG events, but may also be elicited by phase-alignment of ongoing EEG rhythms due to externally or internally triggered phase-resetting in processing networks [10,22,47,66].

Therefore, the present study focused on event-related theta oscillatory activity and its association with anticipatory action plan generation and rule switching under different WM load conditions in patients with schizophrenia and healthy controls. These abilities were investigated by using three cognitive tasks varying in WM load of simple actions. The aims of the study were:

i. Investigation of theta oscillatory activity during increased task-related WM load in schizophrenics and healthy controls.
ii. Group specific investigation of changes in theta oscillatory activity during interference of response selection and/or WM processing due to a task-inherent variation in stimuli frequency and stay or shift instructions, respectively.
iii. Investigation of differences between the groups (controls and patients with schizophrenia) in performance and/or event-related theta activity.

It was hypothesized that:

a. In easy tasks, automatic processing would dominate and that interference – induced by infrequent stimuli or alternation of response instructions – would have little impact on cognitive executive control needed for performance; accordingly, this would be associated with less theta activity in comparison with the hard WM condition;
b. By enhancing WM load, the impact of interference would increase and require higher executive control; in comparison with easy tasks, this should be associated with an increase in event-related theta activity.
c. Impairments in schizophrenic patients should be observable in altered theta activity in tasks with different working memory load and interference.

To study these processes, we used a WM paradigm for simple actions derived from the classic N-back tasks requiring continuous response monitoring. In classic N-back paradigms, subjects are presented with a continuous series of items and must indicate whether the displayed item matches the one presented N items back. It is generally assumed that the higher WM load involves complex updating processes of WM as a series of items have to be kept in mind and chunking strategies need to be activated to correctly solve the tasks [50]. To investigate interference effects under increasing WM demand, we used three graduations of the N-back task (0-back, 1-back, 2-back). The three N-back tasks had condition-inherent variations of the presentation frequency of one stimulus and varying frequency of a certain response instruction (stay vs. shift). These variations were introduced to induce interference (higher cognitive