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Magnetic source imaging of slow wave activity in psychiatric samples*

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1 Introduction

Large-amplitude low-frequency activity, as in slow wave sleep or coma, indicates widespread synchronization of many neurons and may characterize brain states with little ongoing information processing. If prominent during the waking state, global slow wave activity are involved in neuropathological conditions, whereas focal slow waves are found in the vicinity of lesions, tumors, or epileptic foci. They have been associated with neuropathological or dysfunctional brain tissue (1). Enhanced activity in the lower frequency bands of the EEG has also been described in psychiatric disorders, e.g., in schizophrenia (2). The present study aimed at exploring whether local foci of slow wave activity can be determined in the MEG and whether the spatial distribution of generators of this brain activity would allow the assessment of dysfunctional brain regions also in psychiatric disorders. The source distribution of focal slow waves in the delta (1.5-4.0 Hz) and the theta (4.0-8.0 Hz) band were determined for patients with psychiatric diagnoses and healthy subjects during resting and mental activity. If slow wave activity were to represent dysfunctional brain processes, it should be prominent in those areas, which are assumed to be involved in the diagnosis-specific dysfunction. The association of the focal slow wave activity and neuropsychological test performance was assessed to further elucidate the functional significance of focal slow wave activity.

2 Methods

MEG recordings were obtained with a 148-sensor while-head neuromagnetometer (MAGNES 2500 WH, BTI, USA) from patients meeting DSM-IV diagnoses of schizophrenia, major depressive disorder, and alcohol dependence, and from healthy subjects during three 5-min periods of resting, mental arithmetic, and mental imagery. The electrooculogram and the electrocardiogram were monitored for artifact control. Subjects also accomplished a neuropsychological test battery comprising tests for attention, working memory, verbal fluency, design fluency, and the Wisconsin Card Sorting Test.

The MEG was recorded with a 678.17 Hz sampling rate, using a band-pass filter of 0.1-200 Hz. The number of sample points was reduced by factor 16 and the data were bandpass filtered in the delta (1.5-4.0 Hz) and theta (4.0-8.0 Hz) band. The source distribution of focal slow waves in the delta and the theta band were determined a) by scanning for fits of a single moving equivalent dipole, whereas b) multiple sources slow activity were modeled by the minimum norm estimate. For the dipole density analysis, single ECD in a homogeneous sphere were fitted for each time point in the selected artifact-free epochs. Only dipole fit solutions with a root mean square (RMS = $(\sqrt{(1/n\Sigma(x_i)^2)})$ > 100fT < 300fT and with a goodness of fit (GOF) > 0.90 were accepted to ensure only truly dipolar fields that were generated by focal sources and to restrain artifacts or small amplitude biological noise. The number of dipoles per second was compared between groups, conditions, and 10 brain regions (left- and right prefrontal, frontal, temporal, parietal and occipital). Distributed or multiple sources were evaluated for prominent magnetic activity field patterns during artifact-free 30-sec periods by Minimum-Norm-Least-Squares, L2-norm (3). MN solutions were calculated on a shell that represented average cortical location (4). For statistical analyses, MN values on that shell were averaged across seven regions, left- and right-frontal, temporal, and posterior, and a central region. The number of dipoles/sec and the MN estimates for each region were correlated with neuropsychological test performance indices in each group, and with indices for positive and negative symptomatology in the schizophrenic patient group.

The present report is restricted to the dipole density analysis during the resting a) condition in 28 schizophrenics (6f, 31±10 yrs), 9 depressives (6f, 47±8 yrs) and 20 controls (5f, 34±11 yrs). Further results of the project are reported elsewhere (e.g., Fehr et al., this volume).

3 Results

The number of focal slow waves fitting a single dipole model was generally higher for schizophrenic patients than for controls in the delta band ($F(1,46) = 8.9$, $p<.01$) and the theta band ($F(1,46) = 6.6$, $p< .05$). This was confirmed for the comparison of three groups of 9 Ss each, including depressive patients (delta band: $F(2,24) = 6.7$, $p< .05$; theta band, $F(2,24) = 7.2$, $p< .01$), while the two patient groups did not differ significantly from each other. The distribution of focal slow wave activity differed between groups. Schizophrenic patients displayed more slow wave dipoles in left frontal and bilaterally in temporal and posterior regions than depressives (delta: $F(9,144) = 4.3$; $p<.05$; theta: $F(9,144) = 4.8$, $p<.01$) and controls (delta: $F(9,414) = 3.0$, $p<.05$; theta: $F(9,414) = 2.8$, $p<.05$). Depressives had fewer dipoles in the left and right prefrontal regions than schizophrenics and controls ($F(9,144) = 4.8$, $p< .01$).

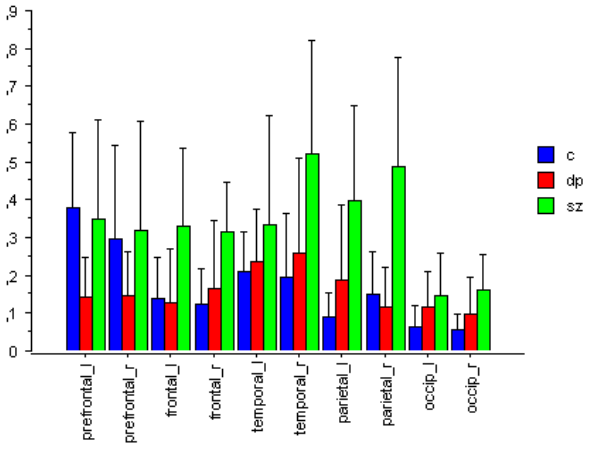

Figure 1: *Number of dipoles/sec (ordinate) in controls (c), depressives (dp) and schizophrenics (sz) in ten regions (from left to right: prefrontal left, prefrontal right, frontal left, frontal right, temporal left, temporal right, parietal left, parietal right, occipital left, occipital right).*

Negative correlation coefficients were found for schizophrenics for the number of dipoles/sec in the delta band in the left (-.46), and the right (-.51) prefrontal and the right temporal (-.47) region with performance in working memory tests, and for left frontal (-.44) and right prefrontal (-.44) activity with word fluency. Temporal delta activity was related to more perseveration errors in the WCST (.52). In contrast, correlation coefficients were positive for depressives and controls (<.54 >.83) indicating better performance with a higher number of delta/theta dipoles/sec. This suggests a different functional significance of slow wave activity in schizophrenics compared to depressives and controls. In the schizophrenic group, positive symptom scores were related to slow wave activity in prefrontal, frontal, temporal and parietal regions, while negative symptoms showed only weak relationship with left fronto-temporal slow wave activity.

4 Discussion

Enhanced slower activity in schizophrenics, as often reported from EEG analysis, was confirmed by magnetic source imaging analysis in the present study. The considerable proportion of slow waves that fit a single dipole model in patients supports the presence of focal slow wave generators In addition, the dipole density analysis suggest that the regional distribution of slow wave activity differs between schizophrenics, depressives and controls. Schizophrenic patients displayed augmented slow wave activity in the left-frontal and temporal areas, that is, in areas that have been linked to schizophrenic pathology in different methods of inquiry. Depressives, on the other hand, displayed reduced lower frequency activity in prefrontal areas than schizophrenics and controls. This result provides new information to the report of reduced left-frontal and enhanced fronto-temporal EEG-alpha activity in affective disorders (2).

If regional slow wave activity were related to abnormal functioning of the generating neuronal tissue, the present results of group-specific distribution of slow wave activity suggest a potential diagnostic value of methods that allow the monitoring of the regional distribution of slow waves. Brain regions that exhibit enhanced numbers of focal and distributed slow waves can be determined on an individual basis and could then be related to clinical data. However, the pattern of correlation coefficients between focal slow wave activity and neuropsychological test performance unveils the link of slow waves and dysfunctional brain tissue too simplistic: In schizophrenics, enhanced slow wave activity is associated with poorer performance in tasks which are assumed to uncover typical schizophrenic dysfunction. In controls and depressives, more slow wave activity (though possibly not excessive as in schizophrenics) is associated with better performance. These results require to further clarifying the functional meaning of slow wave activity for different individuals or groups.

References:

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