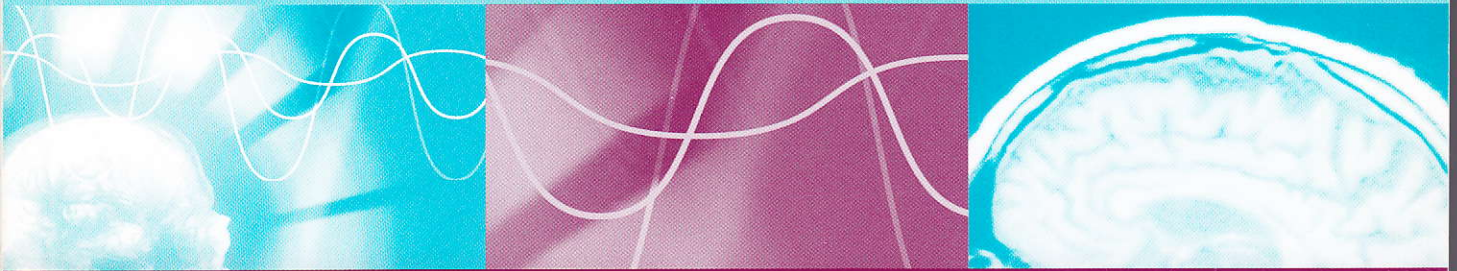
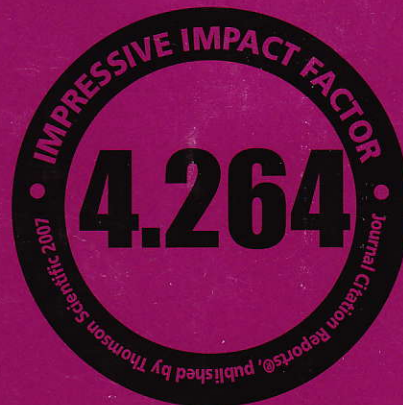


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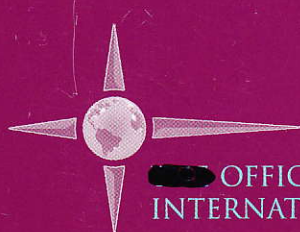


SCHIZOPHRENIA RESEARCH



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in patients with schizophrenia. Schizophrenia Bulletin, accepted with minor changes

150 – THE REDUCTION OF AUDITORY N100 TO NON-TARGET STIMULI: A NEW NEUROPHYSIOLOGICAL ENDOPHENOTYPE OF SCHIZOPHRENIA?

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Introduction: The search for “endophenotype” expects discrimination anomalies in patients and their first-degree relatives as well as the testing of these phenomena in respect to peculiarities of the disease (1). This approach was applied to all of the auditory ERPs components as they are often neglected due to exaggerated attention paid to P300.

Methods: Auditory ERPs in the standard auditory oddball paradigm (60 dB, 80% non-targets (1000 Hz), 20% targets (2000 Hz)) were recorded in 44 patients during the first episode, 14 patients with schizophrenia upon admission to the clinic and before the discharge (along with PANSS evaluation), and in 40 unaffected parents (from 22 families with sporadic cases and 22 families where the other spouse was either diagnosed with mental disease or have a first degree relative with schizophrenia). The control groups comprised, on the whole, 42 mentally healthy subjects.

Results: Anomalies that were found only in “sporadic” parents included reduction of P300 and N100 to non-targets. The same phenomena (along with N200 prolongation and N100 to targets reduction) were found during the first episode. The dynamics of PANSS summarized positive score correlated with P300 amplitude dynamics, while dynamics of N100 to non-targets amplitude correlated with dynamics of global PANSS score

Conclusions: The findings emphasize the role of N100 to non-targets amplitude reduction as the possible endophenotype of schizophrenia. N100 reduction here can be considered as an index of functional or/and morphological ability of corresponding neural substrate to process highly repeated stimuli.

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151 – COMBINING PHASE ANALYSES AND PHASE MODELING TO UNDERSTAND DISTURBANCES IN EARLY INFORMATION PROCESSING IN SCHIZOPHRENIA PATIENTS

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Introduction: In schizophrenia, disturbances in early information processing involving the thalamo-cortical circuit are well known. Disturbances in the precise timing of coupled brain areas are discussed as the neurophysiological basis of schizophrenia.

Methods: We analyzed EEG data from schizophrenia patients and controls (from an auditory double click paradigm) using time-frequency methods and concentrated on phase analysis for five frequency bands (γ , β , α , θ and δ). Phase analyses are better suited to distinguish between the two groups than standard ERP analysis or amplitude analysis, which we showed in our recent publication (Brockhaus-Dumke et al. 2008). To get a better insight into the early information processing, we constructed a phase oscillator model which describes the timing of coupled brain areas (thalamus, thalamic reticular nucleus, cortex, hippocampus). These phase descriptions are associated with the postsynaptic potentials of synchronized neural assemblies, which are reflected by the EEG. Thus we can validate our model with the EEG phase analyses.

Results: Simulations of the phase oscillator model showed the same phase alignments and occurred during similar time intervals as in real EEG data. Additionally, we could simulate EEG data typical of controls and those typical of schizophrenia patients by just changing those parameters in the model, which describe the amount of synchronization in the different brain areas, and their impact on others areas.

Conclusions: The combination of phase analyses and simulations from the phase oscillator model gives new insights into the understanding of real EEG data and the underlying time-adjusted neuronal processes and their disturbances in schizophrenia patients.

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152 – α 2-NORADRENERGIC EFFECTS ON HABITUATION AND PREPULSE INHIBITION OF THE HUMAN STARTLE REFLEX

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Introduction: Evidence is accumulating that cognitive deficits form core features in schizophrenia. Several studies have shown improvements of prefrontal cognitive function by α 2 agonists in schizophrenia. In the present study the influence of clonidine (an α 2 adrenoceptor agonist) was investigated on sensorimotor gating and habituation.

Methods: Twenty healthy male volunteers were tested for their habituation and prepulse inhibition of the startle reflex (PPI) on two occasions separated by a minimum of one week: once after oral administration of placebo and once after 150 μ g clonidine.

Results: Although clonidine did not affect the response of the subjects on the first pulse alone trials, it did reduce the response on later trials. Clonidine did not affect PPI.

Conclusions: Since clonidine did not affect the initial response of the subjects on the pulse alone trials, but did reduce the subjects' response in later trials, this indicates an accelerated habituation as a result of the administration of clonidine, instead of a more general reduction of startle amplitude as a result of sedation. Furthermore, the results indicate that habituation and PPI are fundamental different processes, which can be manipulated separately from each other.

Acknowledgements: This study was financially supported by The Danish Research and Innovations Agency.

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153 – MODIFIED DICHOTIC LISTENING APPLIED IN TURKISH SCHIZOPHRENIA PATIENTS

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Introduction: The cognitive functions constitute a great spectrum of information processing. The pathological processes have two-way importance in this prospect; firstly that findings can serve as trait or state marks for clinical applications, secondly abnormal functional activity itself can elucidate mechanisms behind information processing. The objective behind to study schizophrenia by means of battery of elec-

trophysiological tests, was to constitute optimal recording parameters and make use of cross-domain data to elucidate possible mechanisms. **Methods:** 12 patients (mean age 35.2) with schizophrenia (DSM-IV criteria) and 12 healthy control subjects (mean age 30.8) were recruited and underwent 64-channel EEG recording (Neuroscan). The stimuli consisted of a modified Dichotic Syllables (CV) test and other auditory ERP stimuli.

Results: The preliminary results point to laterality, with Right Ear Advantage (REA) for 56.82 patients and 52.17 for controls. Respectively, Left Ear Advantage (LEA) was 33.32 and 33.51. The error rates were higher for patients than controls ($p < 0.05$). Furthermore, within patients group, ANOVA revealed differentiation between latency of responses to different conditions (REA, LEA and diotic) of Late Negativity (N450) responses ($F = 4.741$, $p = 0.015$) at central electrode (Cz).

Conclusions: The results confirm the sensitivity of DL paradigm as well as the possible implications to conflict processing mechanisms. Accordingly, electrophysiological tools may prove to be beneficial in the research of psychophysiology, as these methods are comparatively low-cost and valid across different cultures.

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154 – P300 AND N100 COMPONENTS IN SCHIZOPHRENIA PATIENTS AND THEIR FIRST-DEGREE RELATIVES

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Introduction: Abnormal P300 waveforms of the event-related potentials are one of the most robust biological findings in patients with schizophrenia and seem to be promising as endophenotype since alterations of the amplitude and latency can also be observed in first-degree relatives of patients.

Methods: In the present study, we investigated the P300 amplitude and latency in schizophrenia patients and their siblings. ERP data were obtained from approximately 20 patients, 20 unaffected siblings and 20 healthy controls during a standard auditory oddball paradigm. One week later, the oddball paradigm was again administered in order to investigate consistency of the ERP components.

Results: Significant differences in P300 amplitude and latency were found between controls and patients. In contrast, no significant differences were found between siblings and controls. N100 latency abnormalities were seen in patients as well as siblings. Test-retest correlations were generally high.

Conclusions: P300 amplitude and latency may be stable abnormalities in patients with a psychotic disorder. N100 latency abnormalities may be an endophenotypic marker for psychosis, but it seems less stable.

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155 – INTERNAL MODEL DYSFUNCTION IN SCHIZOPHRENIA PATIENTS WITH FIRST-RANK SYMPTOMS: ELECTROPHYSIOLOGICAL EVIDENCE

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Introduction: The processes that give rise to first-rank symptoms (FRS) are not fully understood and remain largely under-researched, but one model posits a disruption of internal model mechanisms [1]. The aim of the current study was to conduct a broad examination of electrical brain responses and antisaccade performance in patients with FRS using well-validated electrophysiological components. We also tested hypotheses arising from the proposal of an internal model dysfunction, by examining performance on the P300 feature and error correction on the antisaccade task as indices of internal model functioning (sensory evaluation and central error correction respectively).

Methods: The P300, P50, MMN and antisaccade paradigms were administered to 34 schizophrenia patients (21 with and 13 without FRS) and 30 healthy controls.

Results: On the P300 feature, patients with FRS had significantly reduced amplitude and tended to have longer latencies compared to controls. On the antisaccade task, patients with FRS had longer self-correction times relative to controls. There were no other significant group differences on the P50 or MMN features.

Conclusions: The results are consistent with a deficit in internal model functioning in patients with FRS. P300 abnormalities and increased antisaccade correction times may provide an index of impaired cognitive motor control in FRS.

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156 – ROLES OF FRAGILE X MENTAL RETARDATION PROTEIN IN CORTICAL PLASTICITY AND MODULATION

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Introduction: Fragile X syndrome, caused by the lack of fragile X mental retardation protein (FMRP), is often accompanied by neuropsychiatric disorders.

Methods: A mice model for Fragile X mental retardation was used and neurons from these mice cultured.

Results: Here, we reported that FMRP plays a critical role in dopaminergic modulation of synaptic potentiation in the prefrontal cortex (PFC). The surface expression and phosphorylation of AMPA GluR1 receptor GluR1 due to D1 receptor activation was reduced in cultured PFC neurons of *Fmr1*^{-/-} mice. The facilitation of LTP and functional GluR1 synaptic insertion by D1 receptor activation was impaired in the PFC neurons of *Fmr1*^{-/-} mice. Furthermore, the coupling of D1 receptors to Gs protein is impaired, accompanied by D1 receptor hyperphosphorylation at serine sites and the increased