ERPs in schizophrenia subtypes: qualitative differences between subjects with deficit and nondeficit subtypes

Nash Boutros, Klevest Gjini, Susan Bowyer Clinical Electrophysiology Laboratory, Saint Luke's Marion Bloch Neuroscience Institute, Department of Psychiatry, University of Missouri-Kansas City.

The deficit syndrome (DS) is characterized by the presence of primary negative symptoms and is associated with poor outcome. A recent study from our group investigated the EEG/MEG during resting state and evoked EEG/MEG responses. Ten subjects were recruited for each group (Control, DS and Non-Deficit Schizophrenia [NDS]). Subjects were first recorded for 10 minutes eyes open (no task), then underwent an odd-ball paradigm (P300) and mid-latency evoked responses in a sensory gating paradigm. Significant differences were found between deficit and non-deficit patient groups: P50, N100 and P3a amplitudes were significantly decreased in NDS compared to DS subjects. NDS patients had abnormalities of both early (gating) and late processes (P300), and an increased response to novelty. The main deviance in the DS group was an increased response to ongoing irrelevant stimuli. These data suggest that subjects with primary negative symptoms have qualitative difference in ERP abnormalities, with respect to subjects with other forms of schizophrenia. These subjects might specifically present difficulties in the assessment of the relevance of stimuli to the ongoing task, in line with recent models of negative symptoms.

Neural correlates of negative symptoms domains: evidences of their heterogeneity from an auditory oddball task

Vignapiano A.[1], Mucci A.[1,] Giordano G.M.[1], Di Lorenzo G.[2], Ferrentino F.[2], Altamura M.[3], Bellomo A.[3], Galderisi S.[1]

[1]Department of Psychiatry, University of Campania "L. Vanvitelli", Naples, Italy
[2]Department of Systems Medicine, University of Rome "Tor Vergata", Rome, Italy
[3]Department of Clinical and Experimental Medicine, Psychiatry Unit, University of Foggia, Foggia, Italy

Negative symptoms represent a heterogeneous psychopathological dimension, associated to poor outcome in subjects with schizophrenia (SCZ). A large consensus was reached on the inclusion of 5 constructs in the negative symptom dimension: anhedonia, asociality, avolition, blunted affect and alogia. Factor analyses showed that these constructs cluster in two domains: avolition-apathy (AA; including avolition, asociality and anhedonia) and expressive deficit (ED; including alogia and blunted affect) associated to different neurobiological abnormalities and outcome indices. Few studies used event-related potentials (ERPs) to investigate the neurobiological basis of negative symptom domains with controversial findings In the context of a multicenter study of the Italian Network for Research on Psychoses, our study investigated the relationship of N100 with AA and ED domains. ERPs were recorded, during an auditory odd-ball task, in 115 chronic stabilized SCZ and 63 healthy controls (HC). The BNSS was used to assess the negative symptoms and their domains in SCZ. Multiple stepwise linear regression analyses were used to determine the variables that predicted N100 amplitude for standard and target stimuli. Depression, parkinsonism, positive and disorganization dimensions, neurocognitive composite score, AA and ED domains, were used as independent variables. Our results showed highly significant N100 amplitude reductions in SCZ. Regression models revealed that only ED was an independent predictor of N100 amplitude for standard (b=0.287, p=0.004), and target stimuli (b=0.290, p=0.005). Our results showed a specific pattern of association between N100

abnormalities and ED, suggesting that only some negative symptoms are associated with early processing deficits in SCZ.

Relations between auditory P300 and cognitive impairment in Schizophrenia

Di Lorenzo G.[1], Mucci A.[2], Vignapiano A.[2], Giordano G.M.[2], Ferrentino F.[1], Niolu C.[1], Marasco D.3, Bellomo A.[3], Galderisi S.[2]

[1]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy
[2]Department of Psychiatry, University of Campania "L. Vanvitelli", Naples, Italy
[3]Department of Clinical and Experimental Medicine, Section of Psychiatry, University of Foggia, Foggia, Italy

People with schizophrenia present abnormalities of event-related potentials (ERPs) and cognitive deficits. The P300 reflects global cognitive efficiency, measuring neural activations of attention and memory systems during information processing. Despite the consistent finding of impaired P300 and cognitive domains in subjects with schizophrenia (SCZ), the relation between these deficits was not fully investigated in Schizophrenia. As an add-on to the Italian Network for Research on Psychoses study, we investigated the relation between P300 and cognitive indices. ERPs were recorded in 112 chronic, stabilized SCZ and 63 healthy controls (HC) during a standard auditory oddball task. P300 latency and amplitude were assessed at Pz. MATRICS Consensus Cognitive Battery (MCCB) was used for cognitive assessment. Two separate stepwise multiple linear regression analyses were used to investigate MCCB domains that predicted, respectively, P300 latency and amplitude, controlling for sociodemographic and clinical variables. SCZ showed significant longer latency (p=0.001; Cohen's *d*=0.52) and lower amplitude (p<0.0001; Cohen's *d*=0.71) of auditory P300 compared to HC. In SCZ, a significant regression model (adjusted R2=0.163, p<0001) revealed that independent predictors of P300 latency were MCCB working memory (R2 change=0.106, b=-0.298, p=0.002) and age (R2 change=0.075, b=0.275, p=0.004). No variable entered in the regression model with the P300 amplitude as dependent variable. These findings showed an association in SCZ between slower neural processes during an attentive task (as measured by auditory P300 latency) and working memory impairment. We were able to confirm a substantial independence of P300 amplitude from other clinical variables.

Event-Related Potentials Index Visual Working Memory Deficits in First-Episode Schizophrenia

Brian A. Coffman[1], Tim K. Murphy[1], Justin Leiter-Mcbeth[1], Gretchen Haas[2], Carl Olson[3], Raymond Cho[2,4,5], Avniel Singh Ghuman[6], and Dean F. Salisbury[1]

[1]Clinical Neurophysiology Research Laboratory, Western Psychiatric Institute & Clinic, Department
of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA
[2]Western Psychiatric Institute & Clinic, Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA
[3]Center for Neural Basis of Cognition, Carnegie Mellon University, Pittsburgh, PA, USA
[4]Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine, Houston, TX, USA
[5]Michael E. DeBakey Houston VA Medical Center, Houston, TX, USA
[6]Laboratory of Cognitive Neurodynamics, Department of Neurosurgery, Presbyterian Hospital, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Working memory dysfunction may be central to neurocognitive deficits observed in schizophrenia. Maintenance of visual information in working memory, or visual short-term memory, has been linked to general cognitive dysfunction and is predictive of functional outcome. Lateralized change detection tasks provide a useful mechanism for investigation of neurophysiological indices of visual short-term memory, such as the contralateral delay activity (CDA), which may provide insight into the underpinnings of working memory dysfunction in schizophrenia. We investigated CDA amplitude during lateralized visual short-term memory of one versus three items using sensor-level electroencephalography and source-level magnetoencephalography in 24 individuals at their first episode of psychosis within the schizophrenia spectrum (FESz) and 21 healthy controls matched for age, gender, IQ, and parental socioeconomic status. Individuals at their first episode of psychosis were unable to modulate CDA with increased memory load, and CDA at high load was reduced compared to controls (p<0.05). Further, source-level CDA was reduced in FESz within posterior parietal cortex, bilaterally (p<0.05), and behavioral and neurophysiological indices of working memory were correlated with neurocognitive deficits and symptom severity (p's<0.05). These results support theories that working memory dysfunction is a central and early component the disorder. Targeted intervention focusing on working memory deficits may therefore be warranted to alleviate downstream effects of this disability.

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