114. ONDANSETRON IMPROVES P50 AUDITORY SENSORY GATING IN MEDICATED SCHIZOPHRENIC PATIENTS

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P50 auditory sensory gating is impaired in schizophrenic patients. A schizophrenic patient does not show a decrease in the amplitude of the P50 waveform of the auditory evoked potential to the second of two closely paired click stimuli. In contrast, a normal control has a greatly decreased amplitude of the P50 waveform to the second stimulus. Expressed as a percentage (amplitude to the 2nd stimulus/amplitude to the first stimulus × 100), the P50 ratio is significantly higher in schizophrenic patients. This genetic deficit in inhibitory neuronal processing is mediated by the alpha-7 nicotinic receptor, which is rapidly desensitizing to nicotine. Nicotine briefly ameliorates this deficit in schizophrenic patients, but the effect is usually lost after one hour. Clonazepam treatment, but not conventional antipsychotic medication, improves P50 auditory gating. We hypothesized that blockade of the 5HT3 receptor by clonazepam may result in release of acetylcholine which then acts directly at the alpha-7 nicotinic receptor to enhance gating.

To test this hypothesis, we gave 16 mg of oral ondansetron, a selective 5HT3 receptor antagonist, to 7 stable medicated schizophrenic outpatients in a double-blind placebo design. On two different days, the same subject had baseline auditory evoked responses recorded followed by either oral ondansetron or placebo. ERPs were recorded hourly for the next three hours. Ondansetron, but not placebo, resulted in a significant decrease in P50 ratio in these patients (Repeated measures ANOVA: F = 21.44, d.f. = 1, 12, p = 0.001) that lasted significantly longer than nicotine treatment. These results support a possible role of 5HT3 antagonism in enhancing P50 gating by atypical antipsychotics.

115. CONFIRMATION OF DIFFERING DISTRIBUTION OF P50 RATIOS IN SCHIZOPHRENIC PATIENTS VS CONTROLS

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P50 auditory sensory gating is impaired in schizophrenic patients. A schizophrenic patient does not show a decrease in the amplitude of the P50 waveform of the auditory evoked potential to the second of two closely paired click stimuli. In contrast, a normal control has a greatly decreased amplitude of the P50 waveform to the second stimulus. Expressed as a percentage (amplitude to the 2nd stimulus/amplitude to the first stimulus × 100), the P50 ratio is significantly higher in schizophrenic patients. We studied the distribution of the P50 ratios of 89 schizophrenic patients versus 163 normal controls with no history of psychosis in themselves or first degree relatives. Mean P50 ratio for the schizophrenic patients was 86.4% ± 5.2% s.e.m., with a median of 75.0%. Skewness (G1) was positive (G1SES = 0.81/0.26 = 3.1), whereas kurtosis (G2) was low (G2/SEK = 0.28/0.51 < 1). Coefficient of variation (C.V.) was 0.57. For normal controls, mean CTR was 19.2% ± 1.6% s.e.m. with a median of 15.3%. Skewness (G1) was quite high (G1SES = 1.58/0.19 > 7.5) Kurtosis (G2) was significantly higher than for the schizophrenics, (G2/SEK = 4.77/0.38 = 12.6) Thus, P50 ratios for schizophrenic patients more closely resemble a slightly skewed normal distribution, whereas the normal controls have a highly kurtotic and skewed distribution most having P50 ratios under 20% and a significant number with P50 ratios of zero. These data suggest that the commonly applied upper cutoff of 40% or lower for “normal” gating is actually quite conservative, as is the requirement that “impaired” gating have a P50 ratio of >50%.

116. THE EFFECTS OF AGING IN SCHIZOPHRENIA ON AN ANTISACCADE EYE MOVEMENT TASK

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The antisaccade eye movement task, which has been linked to frontal lobe function, presents a target in one visual field and requires subjects to move their eyes to the same location in the opposite field. The task involves inhibition of the reflexive prosaccade to the cue, initiation of an antisaccade to the opposite field and visuo-spatial memory of the cue location. Older normal subjects make more incorrect prosaccadic movements to the cue and have greater processing time to inhibit the incorrect movement to the cue. Forty-nine schizophrenic patients from age 17–64 years of age performed this task and a control task, visually-guided saccades to the cue itself, to determine which functions are affected by aging in schizophrenia. As in normal subjects, aging in schizophrenia increases the rates of prosaccadic movements to the cue and has no effects on visuo-spatial memory. Additionally, latency of the visually-guided saccades increases with aging in schizophrenia. However, the latency of the antisaccade and the processing time show no relation to age in schizophrenia. Thus, the initial deficits in initiation of an antisaccade and inhibition of the incorrect movement to the cue in schizophrenia may be so severe that they may not have the ability to decline further with aging.

117. VULNERABILITY MARKERS IN SCHIZOTYPAL PERSONALITY DISORDER: DEFINING A PHENOTYPE


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Schizotypal personality disordered (SPD) subjects are phenomenologically similar to schizophrenic patients and is likely that at least a subgroup of individuals who meet the SPD criteria are genotypically linked to schizophrenia. SPD subjects have been shown to have abnormalities of cognition, attention and information processing, similar to those observed in schizophrenic patients, as assessed by specific laboratory measures. Because SPD subjects are typically not medicated, actively psychotic or chronically institutionalized, the attention and information processing paradigms that may identify trait-linked deficits that will lead to a better characterization and understanding of the pathophysiology and genetics of the schizophrenia spectrum. To achieve this end, it will be important to first determine whether information processing-defined markers identify the same or different domains of vulnerability to developing schizophrenia. An additional important question is whether a subgroup of individuals with SPD can be identified (based on information processing task performance) who are genotypically