54. TOUCH FEEL ILLUSION IN SCHIZOPHRENIC PATIENTS

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The rubber hand illusion (RHI) is a tactile sensation referred to an alien limb. The RHI has been explained by a spurious reconciliation of visual and tactile inputs reflecting functional connectivity in the brain and may be used to explore alterations of functional connectivity in schizophrenia. Twenty-six controls and 27 schizophrenic inpatients participated in this study. For the RHI subjects were seated with the left arm resting upon a small table. A standing screen was positioned beside the arm to hide it from view and a life-sized rubber model of a left hand was placed on the table directly in front of the subject. The subject was instructed to look at the artificial hand while two small paintbrushes were used to stroke the rubber hand and the subject’s hidden hand synchronously. After the occurrence of the illusion, subjects completed a two-part questionnaire providing a description of their experience, affirming or denying the occurrence of nine specific perceptual effects. Schizophrenics felt the illusion stronger and faster than did normal controls. Some RHI effects correlated with positive symptoms of schizophrenia, but not with negative symptoms. Based on this study we argue that altered functional integration of environmental inputs could constitute the basis for erroneous interpretations of reality, such as delusions and hallucinations.

55. ERP EVIDENCE OF FRONTAL/POSTERIOR DISCONNECTION IN SCHIZOPHRENIA

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Disruption of attention is a hallmark symptom of schizophrenia. Event-related potential (ERP) studies of attention in schizophrenia consistently report auditory, but not visual, P300 amplitude reductions. Monkey single-unit recording and human hemodynamic neuroimaging results suggest that selective attention requires interaction between posterior cortical areas of perceptual representation and attention networks in prefrontal cortex. The disconnection hypothesis of schizophrenia proposes a disruption in these frontal/posterior connections in the disease. Recent ERP studies of auditory and visual selective attention suggest that the Selection Negativity (SN) and Frontal Selection Positivity (FSP) may index frontal/posterior interaction in target detection. The SN (or N2) is an ERP index of selective attention over modality specific areas of posterior cortex. The SN is accompanied by a modality independent FSP over prefrontal cortex. Several studies have reported auditory N2 reduction or absence in schizophrenia, and the single study reporting the visual N2 in schizophrenia also found a reduction, despite an unaffected P300. To our knowledge there are no reports on the impact of schizophrenia on the FSP. Here we report dense-sensor array (64 channel) ERP data from auditory and visual attention tasks in schizophrenic patients and controls. In the auditory data the P300 is reduced and an SN/FSP is not apparent in the patients. In the visual data the SN/FSP is also greatly reduced or absent in the patients despite a preserved P300. These findings support a differential impact of schizophrenia on the neural systems indexed by the SN/FSP and are consistent with the disconnection hypothesis of schizophrenia.

56. VIRAL INFECTIONS AND CYTOKINE LEVELS IN “NONORGANIC” PSYCOSES

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The effect of viral infections on immunomodulators (cytokines) in psychoses is uncertain. This is important in the context of abnormalities of cytokine levels in schizophrenia. Consenting, consecutive patients (n = 120) with DSM-IV schizophrenia or brief psychotic disorder were tested for viral antibodies to Cytomegalovirus, Herpes simplex (HSV), Mumps, Measles, Rubella, Varicella Zoster, Japanese Encephalitis (ELISA). Patients testing positive for HSV (HSV-positive, n = 21), positive to any other single virus (HSV-negative, n = 22) or negative to all viruses (viral-negative, n = 41) did not differ with respect to sex, age, diagnosis and psychopathology scores except PANSS positive syndrome score; HSV-positive and viral-negative groups had higher mean scores than the HSV-negative group (F = 3.2; df = 2.80; p = 0.047). Gamma interferon (IFN) and Interleukin-2 (IL-2) levels were assayed without knowledge of clinical and viral status. IFN levels were higher in HSV-negative group (n = 19) than in both HSV-positive (n = 19) and viral-negative (n = 22) groups (Kruskal Wallis; serum, p = 0.005; CSF, p = 0.012). IL-2 levels in the three groups (n = 14, 18 & 21 respectively), however, did not differ (serum, p = 0.69; CSF, p = 0.74). Symptom and immunomodulator status is different depending on the nature of viral infection. HSV failing to evoke an IFN elevation like other viruses, suggests that it may be a reactivation in the presence of psychoses. Being a relatively focal neuro-infection in temporal lobe it may not evoke less IFN response. Interestingly all HSV-positive patients were positive only in CSF.

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57. DONEPEZIL AUGMENTATION OF ANTIPSYCHOTICS IN SCHIZOPHRENIA: COGNITIVE AND fMRI EFFECTS


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Neurocognitive impairments in multiple domains are common in schizophrenia and are powerful predictors of functional impairments and poorer quality of life. We report the results of an ongoing double-blind, placebo controlled randomized crossover study of donepezil augmentation of both typical and atypical antipsychotics in stable outpatients with schizophrenia. To date, during the IRB approved study protocol six subjects have had serial measurements of psychosis, mood and multiple cognitive measures at baseline (BL), and then in a random order after 3 months of placebo, and after 3 months of donepezil (DP). Four of these subjects also received serial echoplanar BOLD fMRI studies during a verbal fluency task (the Controlled Oral Word Association Test (COWAT) on a 1.5 Tesla scanner at the same timepoints.
A within subjects ANOVA for TIME and DRUG (DP and PL) revealed that there was significant improvement on DP for neuropsychological tasks of verbal fluency (p = 0.07) and attention (p = 0.03). The serial IMRI data in four subjects were spatially normalized in Talairach space (Statistical Parametric Mapping) and then analyzed as a group. At all three time points during the verbal fluency task compared to rest there was significant activation in the occipital cortex and posterior cingulate (p < 0.001, extent threshold p < 0.05 for all imaging results). These posterior brain areas were the only areas of significant activation during the PL condition. However, during the DP condition there was also activation in the right dorsolateral prefrontal cortex as well as the anterior cingulate. Thus, uniquely while on DP augmentation, the schizophrenia subjects had a more normal pattern of activation of prefrontal cortex and cingulate.

58. 5-HT2A RECEPTOR BLOCKADE BY QUETIAPINE IS RELATED TO ITS SIDE EFFECT PROFILE

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Antagonist activity at serotonergic (5-HT2A) receptors may contribute to the novel therapeutic actions of atypical antipsychotic drugs. Six schizophrenic subjects and six healthy volunteer controls had a single photon emission tomography (SPET) study using 123I-5-I-R91150, a selective 5-HT2A ligand, after at least 6 weeks quetiapine monotherapy at a mean (SD) dose of 350 mg (123) daily. Patients had a full clinical assessment before starting quetiapine and at time of scan. A SME 810 multidetector SPET scanner acquired a whole brain multi-slice sequence at 120 minutes after injection of 180 MBq 123I-5-R91150. Region-of-interest templates were fitted to cortical and cerebellar regions. The ratio of activity in cortical areas relative to the cerebellum provides a measure of regional specific binding to 5HT2A receptors. Reduced frontal cortex: cerebellum ratio implies greater specific drug binding to 5HT2A receptors within the frontal cortex. Mean frontal cortex:cerebellum ratio in the quetiapine treated patients of 0.98 (SD 0.09) was significantly lower than in healthy controls of 1.33 (p < 0.001). All patients showed improvement in either schizophrenic symptoms or movement side effects during the study. Mean frontal cortex:cerebellum ratio afterquetiapine treatment was significantly negatively correlated with reduction in AIMS score (p = 0.025 Bonferroni corrected) or Simpson-Angus rating (p = 0.04 Bonferroni corrected), but not with the reduction in SAPS score (p = 0.4), SANS (P = 0.6) or MADRS score (p = 0.25). Significant in vivo cortical 5-HT2A receptor blockade by quetiapine may be relevant to its low propensity to induce extrapyramidal symptoms compared to typical antipsychotic drugs.

59. EXPANDING USE OF ATYPICAL ANTIPSYCHOTICS

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We are witnessing a period of rapid change in the pharmacotherapy of schizophrenia, as evidenced by the replacement of conventional antipsychotics by novel antipsychotics as the drugs of choice for first episode and maintenance therapy. More recently, use of novel antipsychotics has also expanded to beyond schizophrenia with potential efficacy in agitation/aggression, suicidality, and movement disorders which are features of other nonpsychotic psychiatric and neuropsychiatric disorders. To address this burgeoning clinical interest in a manner complementary to prescription use, we sampled the perceptions and clinical experience across general and specialist psychiatrists in 2 U.S. states. Among 284 respondents, 97% had used risperidone, 93% olanzapine, 71% quetiapine and 66% clozapine in their clinical practice. The overwhelming majority of respondents (96%) favored the use of novel antipsychotics as first-line treatments for schizophrenia. Additionally, respondents considered these drugs to be of therapeutic value in dementia (94% of respondents), autism (78%), developmental delay/mental retardation (78%), and personality disorders (75%). The most frequently cited drawbacks to the expanding clinical use and profile of novel antipsychotics were cost, weight gain and the current lack of a long-acting intramuscular preparation. These findings confirm and extend the impression gained from prescription data of an increase and broad shift in the use of novel antipsychotics.

60. CRAVING REDUCTION AND CLOZAPINE RESPONSE IN PATIENTS WITH COMORBID SUBSTANCE ABUSE AND SCHIZOPHRENIA

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Accumulating evidence suggests that clozapine is efficacious in patients with schizophrenia and comorbid substance abuse (SA), with some data suggesting this effect occurs partly by attenuating drug craving. The present study examines in a prospective cohort the comparative efficacy of clozapine (mean dose 449 mg/day) in schizophrenic patients with and without active SA who are assessed at baseline, 6 weeks and 12 weeks for psychopathology, functional outcome, craving and drug use, medication tolerability, and plasma homovanillic (HVA) acid and 5-hydroxyindoleacetic acid (5HIAA). In a comparison of 22 SA and 22 nonSA patients who completed the 12-week trial, the SA patients were of older age at onset (25.1 yrs vs. 20.2 yrs; p = 0.029) but did not differ otherwise on baseline demographic, symptomatic or functional measures. At 12 weeks, mean PANSS scores had declined comparably between SA (103.6–92.0) and nonSA (108.0–91.4) groups; similar patterns of response were evident for the QLS and GAF. Notably, 77% of SA patients were either not abusing or had diminished SA. These preliminary findings confirm clinical experience that many patients who commit to