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 schizophrenic 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 $^{123}$I-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 $^{123}$I-5-I-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 after quetiapine 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, suicide, 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 data, 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 PANS 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