distributed and Mann-Whitney U statistics were used. There was no difference in volume of the total intracranial contents. The SPD subjects showed a 21% reduction in left Heschl’s gyrus volume, but no difference in right Heschl or planum temporale volume or Heschl or planum asymmetry. These findings suggest that the reduced left STG finding may be, in part, due to the volume reduction of Heschl’s gyrus. This is intriguing as Heschl’s gyrus participates in early processing of auditory stimuli (tones) and is consistent with the finding of abnormal P300 amplitude in a similar group of SPD subjects.

45. GENDER DIFFERENCES IN AGING EFFECT ON THE 5-HT1A RECEPTOR WITH [11C-CARBONYL]WAY100635 PET


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The effects of age on serotonergic function have been implicated in aging changes in human mood and behaviors. Large reductions in 5-HT2A receptor density with normal aging have been documented. However, the influence of age on 5-HT1A receptors is less well-characterized in vitro, and selective PET ligands have not been previously available.

Dynamic PET imaging (60 min) was performed in 16 healthy subjects (7 M, 9 F; ages 21–80 yrs) following injection of 8–15 mCi [11C-carbonyl] WAY100635 using an ECAT HR+ tomograph in 3D. Time-activity data were generated from MR-guided regions of interest, and binding potential (BP) values determined from a reference tissue model using cerebellar data as reference. Regional BP values were corrected for partial volume effects.

There were significant inverse correlations (*p ≤ 0.05) between age and BP in several cortical regions in men but not in women. These included lateral orbitofrontal cortex [Brodman area (BA) 47]: r = 0.87*, r = 0.88; subgenual cingulate (BA 10): r = 0.89*, r = 0.23; pregenual cingulate (BA 32): r = 0.80*, r = 0.06; hippocampus: r = 0.88*, r = 0.16; occipital r = 0.92*, r = 0.32, in men and women, respectively. Similar trends were observed in the region of the dorsal raphe nucleus in men (r = 0.68), with no significant age effect in women (r = 0.16).

Preclinical data support gender differences in the effect of age on the 5-HT1A receptor, with aging reductions in binding observed in men only. This may contribute to differential vulnerability of men and women to aging changes in mood, cognition and serotonergetically-mediated behaviors, such as sleep.

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46. APOE E4 MAY MODULATE WHITE MATTER MICROSTRUCTURE IN THE ELDERLY

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Patients with Alzheimer’s disease (AD) reveal patterns of reduced frontal and posterior glucose metabolism that correlate with atrophy in the corresponding regions of the corpus callosum, suggestive of cortical disconnection. Individuals at genetic risk for AD, who have the apolipoprotein E epsilon 4 allele (apoE E4+), show similar patterns of reduced cortical metabolism, indicating possible white matter involvement. Fractional anisotropy (FA), a measure derived from diffusion tensor imaging (DTI), quantifies the directionality and relative coherence of white matter fiber tracts. In healthy individuals, reduced FA in the anterior corpus callosum has been associated with advancing age. This pilot study examined whether age-related changes in FA might be modulated by the apoE E4 allele. Two age-matched groups of cognitively intact elderly subjects (age range: 61.1–75.6; 13 apoE E4+; 2 homozygous; 14 apoE E4–) underwent a DTI scan. Regression analyses were performed separately by group with age as a predictor of FA in three cortical white matter regions. Results showed group differences in the relationship between age and white matter microstructural organization (i.e., FA). In the apoE E4+ subjects, increasing age was significantly associated with decreased FA (i.e., worse fiber organization) in the anterior corpus callosum, the posterior corpus callosum, and the parietal white matter. In contrast, age was a predictor of FA only in the anterior corpus callosum of the apoE E4– subjects. These preliminary findings suggest the apoE E4 allele may modulate white matter microstructural changes in individuals at risk for AD. DTI may be useful in the early detection of AD neuropathology.

47. STRIATAL D2 RECEPTOR BLOCKADE PREDICTED EPS WITH NOVEL ANTIPSYCHOTICS: A [123I] IBZM SPECT

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Extrapyramidal symptoms (EPS) are common with conventional antipsychotics and have been related to extensive blockade of striatal dopamine-2 (D2) receptors. Clozapine and other novel antipsychotic substances with lower in vitro affinity for these receptors showed lower EPS risk.

We present a SPECT study in 71 patients with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder. We investigated, whether striatal D2 receptor occupancy predicted the occurrence of EPS. [123I] Iodobenzamide (IBZM) and SPECT were used for visualisation of D2 receptors. Striatal tracer binding was compared to an age-corrected value obtained in untreated healthy controls to calculate receptor occupancy. EPS were rated according to the Simpson-Angus-Scale (SAS). EPS were judged to be relevant, if (1) the SAS score was 5; or (2) anticholinergic comedication was required. Patients received antipsychotic monotherapy for at least 14 days with amisulpride (n = 2), clozapine (n = 6), haloperidol (n = 10), olanzapine (n = 6), quetiapine (n = 4), risperidone (n = 14), sertindole (n = 13), or zotepine (n = 16).

The striatal D2 receptor occupancy ranged from <20% to almost saturation. The lowest occupancy was seen with quetiapine and clozapine, and the highest with haloperidol. The 23 patients (32%) experiencing EPS displayed higher mean striatal D2 receptor occupancy (77%) than those without relevant EPS (61%; student’s t-test: t = 3.14; p = .003). We found a weak but positive correlation between the percentage of striatal D2 receptor occupancy and the SAS score (Pearson R = .26; p = .02), despite 18 patients (25%) received anticholinergics. In summary, the striatal D2 receptor occupancy measured with [123I] IBZM SPECT predicted the occurrence of EPS.