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**CHANGES IN CEREBRAL BLOOD FLOW FOLLOWING ADMINISTRATION OF MEMANTINE HYDROCHLORIDE IN ALZHEIMER'S DEMENTIA (DAT) PATIENTS - COMPARATIVE STUDY OF SPECT SCAN FINDINGS USING SPM8**

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**Background:** Memantine hydrochloride is a drug that has antagonistic action on NMDA receptors that are kind of glutamate receptor, and has been used in the U.S. and Europe for the treatment of depression and Parkinson’s syndrome. Late phase II clinical studies in advanced DAT patients were started in 2001 in Japan and other countries based on reports of its effectiveness in improving symptoms of dementia. Finally in January 2011, memantine hydrochloride was approved as the second drug for treatment of DAT in 12 years since the approval of Aricept. We conducted a study of the effects of memantine on cerebral blood flow by monitoring changes before and after administration using SPECT scans while participating in this study, the interesting findings from which are reported here. **Methods:** The subjects of this study consisted of 30 patients (12 men, 18 women; average age: 77.7 years, mean MMSE score: 15.4) who underwent 99mTc-ECD SPECT scans before and after administration of memantine hydrochloride among 31 DAT patients hospitalized in this department who were entered in a late phase II clinical study of memantine hydrochloride for DAT and a phase II clinical study for mild and moderate DAT conducted from October 2002 to November 2007. A breakdown of the patients consisted of 12 patients who received a high dose of 20 mg/day, 8 cases who received a low dose of 10 mg/day and 10 cases who received a placebo. Each patient was administered memantine or the placebo for six months during which time changes in cerebral blood flow before and after administration were tested by performing SPECT scans and analyzed using SPM8. **Results:** 1. Although significant increases (P < 0.001) in blood flow were observed following administration in the frontolobes bilaterally, parietal lobe and cerebellar hemisphere in the memantine-treated groups (20 patients), there were no increases in blood flow observed in the placebo group. 2. Although significant increases in blood flow were observed only in the frontolobe bilaterally in the 10 mg low dose group (8 patients), significant increases in blood flow (P < 0.001) were additionally observed in the parietallobes bilaterally and from the angular gyri bilaterally to the temporal lobe in the 20 mg high dose group (12 patients). **Conclusions:** Memantine hydrochloride was suggested to be involved in increasing cerebral blood flow dose-dependently in dementia patients.

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**DONEPEZIL IMPAIRS MEMORY IN HEALTHY OLDER SUBJECTS: BEHAVIOURAL, EEG AND SIMULTANEOUS EEG/FMRI BIOMARKERS**

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**Background:** Rising life expectancies coupled with an increasing awareness of age-related cognitive decline have led to the unwarranted use of psychopharmaceuticals, including acetylcholinesterase inhibitors (AChEIs), by significant numbers of healthy older individuals. This trend has developed despite very limited data regarding the effectiveness of such drugs on non-clinical groups and recent work indicates that AChEIs can have negative cognitive effects in healthy populations. For the first time, we use a combination of EEG and simultaneous EEG/fMRI to examine the effects of a commonly prescribed AChEI (donepezil) on cognition in healthy older participants. **Methods:** The short- and long-term impact of donepezil was assessed using two double-blind, placebo-controlled trials. In both cases, we utilised cognitive (paired associates learning (CPAL)) and electrophysiological measures (resting EEG power) that have demonstrated high-sensitivity to age-related cognitive decline. Experiment 1 tested the effects of 5mg per day dosage on cognitive and EEG markers at 6-hour, 2-week and 4-week follow-ups. In experiment 2, the same markers were further scrutinised using simultaneous EEG/fMRI after a single 5mg dose. **Results:** Experiment 1 found significant negative effects of donepezil on CPAL and resting Alpha EEG. Experiment 2 replicated these results and found additional drug-related increases in the Delta band. EEG/fMRI analyses revealed that these oscillatory differences were associated with activity differences in the left hippocampus (Delta), right frontal-parietal network (Alpha), and default-mode network (Beta). **Conclusions:** We demonstrate the utility of simple cognitive and EEG measures in evaluating drug responses after acute and chronic donepezil administration. The presentation of previously established markers of age-related cognitive decline indicates that AChEIs can impair cognitive function in healthy older individuals. To our knowledge this is the first study to identify the precise neuroanatomical origins of EEG drug markers using simultaneous EEG/fMRI. The results of this study may be useful for evaluating novel drugs for cognitive enhancement.

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**ANALYSIS OF AUTOPHAGY AND APOPTOSIS GENE REGULATION IN NEURONAL CELLS INFECTED**

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**Background:** Dysfunctions in cellular mechanisms such as apoptosis and autophagy have been implicated in the neurodegeneration associated with Alzheimer’s disease (AD). Autophagy in AD pathogenesis has been linked to the endosomal-lysosomal system, which has been shown to play a role in amyloid processing. Studies have suggested that apoptosis may contribute to the neuronal cell loss observed in AD; however, there is no evidence of the apoptotic process leading to terminal completion. Aβ42 has been shown to induce apoptosis in neurons and may be an initiating factor in AD. Our previous studies demonstrated that neurons infected with C. pneumoniae are resistant to apoptosis, and that Aβ1-42 was increased by the infection. Additionally, studies have demonstrated the interactions of several pathogens on the autophagic pathway. The focus of the current study was to determine if there is a relationship