

statistically significant treatment differences in favor of memantine were agitation/aggression, irritability/lability, and appetite/eating.

Conclusion: Memantine treatment in patients receiving stable treatment with donepezil is associated with less functional and behavioral deterioration in AD than with donepezil treatment alone.

P.4.029 **A comparison of wildtype and APP transgenic mice on titrating delayed non-match to position (DNMTP) and differential reinforcement of low rates (DRL) performance**

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The use of transgenic mice to study disease processes has produced a need for behavioral endpoints that lend themselves to drug discovery. For example, many of the procedures used to characterize APP mice, an animal model of Alzheimer's Disease, do not allow for longitudinal studies. This limits the usefulness of these procedures to assess the effects of aging or drug treatments. Delayed non-match to position (DNMTP) paradigms or similar procedures have been used to study memory in rats and primates, and differential reinforcement of low rates (DRL) schedules have been used to quantify the deficits associated with damage to various regions of the hippocampus in rats. Therefore, the purpose of these experiments was to determine if either of these behavioral tasks could be used to assess behavioral deficits in APP transgenic mice.

Experiment 1: Wildtype (n=18) and APP (n=16) mice were trained to perform a titrating DNMTP paradigm. Training began when mice were approximately 2-months old. Testing continued until 10 months of age. At the beginning of each session, a response on the sample lever resulted in a 2 s delay. Across each session, delays were increased or decreased by 2 s based on the performance on the previous 5 trials: 5/5 trials correct resulted in an increase of 2 s, 4/5 trials produced no change in the delay, 3/5 or less correct resulted in a 2 s decrease. This procedure produced a 75–80% accuracy level across all subjects. Repeated measures ANOVA was used to determine the effects of genotype on DNMTP behavior. No effects of genotype were observed on maximum delay, average delay, or percentage correct.

Experiment 2: Wildtype (n=7) and APP (n=7) mice were trained on a DRL-15 s schedule of reinforcement. For the DRL-15 baseline, only responses that occurred after an inter-response time of at least 15 s were reinforced. Mice were approximately 4 months of age at the beginning of training. Once behavior was stable, the DRL component was increased to 20 s. After 23 sessions, the DRL component was reset to 15 s. Testing continued until mice were approximately 12 months old. Repeated measures ANOVA indicated that APP mice had more short responses than wildtype controls. This effect was dependent on the DRL component. The difference between wildtype and APP mice was most pronounced during the second DRL-15 s sessions.

Discussion: APP mice showed deficits on a DRL procedure but not on a DNMTP paradigm. Changes in DRL performance may be indicative of behavioral inhibition deficits that are observed during early stages of Alzheimer's Disease, but non-specific effects of the mutation cannot be ruled out. However, it could be argued that any general deficits associated with the mutation should have been observable in both behavioral procedures. Further experimentation is required to assess the association between age and/or plaque development and behavioral deficits. These experiments suggest

that DRL performance may be a useful endpoint in screening novel Alzheimer's treatments and that operant methodologies may be useful in studying transgenic mice.

P.4.030 **Risperidone is not associated with higher risk of stroke in dementia patients compared to other psychotropics: Results from Medicaid data 1999–2001**

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Objective: To compare stroke-related cerebrovascular adverse event (CVAE) rates in dementia patients (age ≥60) treated with risperidone (RIS), olanzapine (OLA), haloperidol (HAL), benzodiazepines (BZD), and acetylcholinesterase inhibitors (ACI).

Methods: Retrospective cohort study; Medicaid data, 1999–2001. Inclusion criteria: 1) Alzheimer's Disease or (pre)senile organic psychotic diagnosis or 2) ACI prescription. Patients on initial use of RIS were compared to OLA, and HAL patients; additional comparators were BZD and ACI patients. Analysis included 6 months pre- and 3 months post-index date. Logistic regression evaluated post-index stroke risk; CVAEs defined as inpatient acute cerebrovascular events. Models included medication exposure, age, prior stroke, prior hospital days, anti-clotting agent usage, hypertension, atrial fibrillation, atherosclerosis, and diabetes.

Results: 939 RIS, 484 OLA, 395 HAL, 2419 BZD and 8773 ACI patients were analyzed. No differences found between OLA (OR=1.23, p=0.76), HAL (OR=2.69, p=0.16), or BZD (OR=1.37, p=0.55) versus RIS (reference). ACI versus atypicals (reference) was directionally different (OR=0.24, p=0.001).

Conclusions: Results suggest risperidone is not associated with higher risk of CVAEs compared to other antipsychotics or benzodiazepines in elderly dementia patients. Different stroke rates between atypical antipsychotic- and ACI-treated patients likely reflect disparities in indications and dementia severity, which is known to be associated with stroke risk.

P.4.031 **Effects of cerebrum compositum and ubichinon compositum in patients with postradiation brain damage**

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Introduction: It was established that patients with consequences of irradiation suffered a lot from immunodeficiency, psycho-emotional and memory impairment (Zhavoronkova et al., 1995). Previous clinical studies showed that Cerebrum Compositum and Ubichinon compositum treatment had antihomotoxic effect, proved to be an effective CNS status regulator, adaptogen and a modulator of memory (Weizer M., Cenner S., 1995). The purpose

of the present study was to evaluate the efficacy of complex Cerebrum compositum and Ubichinon compositum (Heel, Germany) treatment in patients with remote consequences of irradiation.

Methods: The open randomized case-controlled clinical, neuropsychological and EEG examination of complex Cerebrum Compositum and Ubichinon compositum treatment effect was performed in 55 patients aged 31–64 years (male, mean age 44±10.2) entered this study after giving consent. Patients received 10 injection of Cerebrum Compositum and Ubichinon compositum at dose 4.4 ml/day (each drug – 2.2 ml) for 20 days. EEG, neuropsychological and clinical examination was performed before and after drug treatment. Neuropsychological study included evaluation of memory, mental and emotion functioning. Psycho-neurological status was examined during clinical examination. EEG study was based on visual inspection, power and coherence mapping and dipole source localization analysis. Ten persons took part in placebo experiment. The other patients entered longitudinal studies without any treatment. Data of 20 healthy persons were used as a control.

Results: EEG examination showed that before BN treatment all patients had low level of power and EEG coherence (intra- and interhemispheric) in all deviations ($p < 0.01$, ANOVA). After treatment course values of interhemispheric EEG coherence demonstrated the increase of EEG coherence in central and frontal leads the most evident in theta- and alpha-bands ($p < 0.05$) and had a tendency to normal values approximation. These EEG coherence data most corresponded to the results of psychological tests and demonstrated improvement of memory processes (85.4%) and psycho-emotional functions (94.5%). The clinical study showed decrease of headache (72.3%), increasing of capacity for work (85.4%). In general, an improvement in neurological, psychological and physical status and EEG signs after complex drug treatment by Cerebrum compositum and Ubichinon compositum was revealed in 48 patients (87.3%). Results of placebo and longitudinal examinations showed no sufficient changes in status of patients.

Conclusion: The obtained results showed that Cerebrum compositum and Ubichinon compositum treatment might be recommended for treatment of patients in remote terms after irradiation. Our investigations and literature data permitted us to propose that this complex drug treatment influenced brain functions, probably diencephalic and limbic structures and cortical-subcortical interaction as well as provide improvement of patients' quality of life.

References

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P4.032 The effects of scopolamine in elderly volunteers using the Cogtest battery

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Background: Cogtest (Cogtest plc, London) is a computerized neurocognitive test battery of 16 subtests currently being used in over 300 organizations across 16 countries. It is designed for use with a variety of clinical populations and in clinical trials. The platform allows for accurate recording of reaction time data, enhanced standardization relative to examiner administered tests and is easily adapted for implementation in functional neuroimaging environments. Its internet data capture and web reporting facilities makes it unique amongst current cognitive test providers. Additionally, its multiple parallel forms make it amenable to repeated testing sessions across time making it an excellent tool for clinical trials.

Methods: In order to verify the sensitivity of the Cogtest system to pharmaceutical interventions, we administered a single 0.3 mg subcutaneous dose of scopolamine to N=8 elderly study participants. Scopolamine has been routinely used to induce cognitive dysfunction in a bid to mimic the loss of acetylcholine transmission seen in patients with Alzheimer's disease. All participants were tested on a battery of three Cogtest assessments, a test of continuous performance, one of strategic rule learning and a word-learning task. Participants were assessed 1-hour prior to drug administration and then 0:45, 1:45, 3:45 and 7:5 hours after drug.

Results: Consistent with the known effects of scopolamine, a decline in performance was seen on each task 1.45 hours after drug administration. Also consistent with known effects, cognitive decline was most marked on the word memory task, with performance falling from a mean total trials score of 10.1 (SE 1.16) to 5.9 (SE 0.8). Also consistent with our knowledge of scopolamine's effects, performance at 7.5 hours was restored to baseline levels 9.9 (SE 1.2). This effect was found to be statistically significant when analyzed by ANOVA ($F=3.75$, $P=0.01$).

Conclusion: The results of this study reaffirm our understanding of the dementia-mimetic properties of scopolamine. The study also confirms the capacity of the Cogtest battery to detect scopolamine induced memory impairments in small groups of normal volunteers and its application in Alzheimer's Disease.

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P4.033 The amnesic effects induced by β -amyloid fragment 1–42 involve cannabinoid neurotransmission in the brain

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There is evidence that i.c.v. infusion of the β -amyloid (A β) fragment (BAP 1–42) may cause brain dysfunction as evidenced