Title

P3-293: Exercise to enhance hippocampal function and memory in older adults: Proof of concept findings from a 12-week exercise intervention trial

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Authors

Pa, Judy
Skinner, Sasha
Wais, Peter
et al.

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problems in three groups; including adults, the elderly patients with and without AD. Moreover we have suggested the best pharmacological agents for each categories. **Conclusions:** The best management for the patients with AD is achievable just when the clinicians consider the whole of patients' health condition including cognitive deficit, behavioral disturbances and medical complications. To obtain this goal, professionals should be aware of medications side effects precisely, consider the advanced age, comorbidities (which play a major role in the hospitalization in these frail patients) to select the safest pharmacologic approaches.

P3-293 EXERCISE TO ENHANCE HIPPOCAMPAL FUNCTION AND MEMORY IN OLDER ADULTS: PROOF OF CONCEPT FINDINGS FROM A 12-WEEK EXERCISE INTERVENTION TRIAL

Judy Pa[1], Sasha Skinner[2], Peter Wais[2], Christian Thompson[3], Adam Gazzaley[2], [1]*University of Southern California, Los Angeles, CA, USA;* [2]*University of California, San Francisco, San Francisco, CA, USA;* [3]*University of San Francisco, San Francisco, CA, USA.*
Contact e-mail: jpa@ini.usc.edu

Background: Exercise has emerged as a promising lifestyle intervention to help remediate cognitive loss or delay onset of dementia. To fully capitalize on the investments made in exercise and to discover the full treatment potential of exercise, understanding brain mechanisms that support cognitive benefits in older adults must be understood. The objective of this pilot study was to test the feasibility of an exercise intervention to improve hippocampal-dependent memory processing for pattern separation and completion. We assessed recruitment, retention, adherence, data collection using fMRI and pre-post brain imaging analysis in a community-based sample of older adults. **Methods:** We conducted a phase II proof of concept, treatment arm only study to assess feasibility of collecting novel neuroimaging and cognitive outcome measures in an exercise trial. The 12-week exercise program included a 60-minute, twice a week, moderate-intensity, group program led by a fitness instructor at a local senior center. Primary outcomes were a memory recognition index and associated levels of fMRI hippocampal activity. Secondary outcomes for physical function were also measured. **Results:** We screened 53 individuals and recruited 10 inactive, community-dwelling, non-demented older adults with typical cognition or mild cognitive impairment (mean age: 67+5 years, 60% women). Retention was 90%, as one participant withdrew in week 3. Adherence was 85%, as measured by class attendance. 30% fit criteria for early MCI, 38% were APOE-e4 carriers, and 50% were BDNF Val66Met carriers. Pre-post comparisons suggest an effect size of 0.57 for the memory recognition index and 2.3 for fMRI hippocampal activity. Effect sizes for physical function measures were 2.4 for chair stand, 0.94 for timed up-and-go, and 0.48 for functional reach. **Conclusions:** Conducting an exercise intervention study that measures memory function and hippocampal activity using fMRI is feasible in older adults, including in individuals with MCI. A randomized controlled trial of exercise is warranted and may supply evidence of the treatment target/engagement and therapeutic changes in brain mechanisms associated with increased exercise in older adults at risk for Alzheimer's disease.

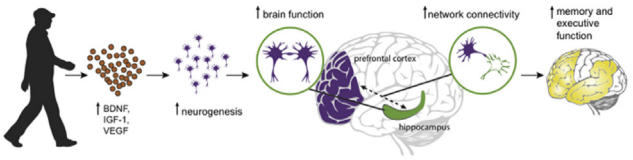

Figure 1. Hypothesized pathway of target engagement in exercise

P3-294 GENDER DIFFERENCE IN THE PROGRESSION OF ALZHEIMER'S DISEASE IN JAPANESE PATIENTS TREATED WITH DONEPEZIL: RESULTS OF THE J-GOLD STUDY

Heii Arai[1], **Kenta Sumitomo**[2], Yukinori Sakata[2], Kasumi Daidouji[2], Tetsumi Toyoda[3], [1]*Juntendo University Graduate School of Medicine, Tokyo, Japan;* [2]*Eisai Co., Ltd., Tokyo, Japan;* [3]*clinical Study Support, Inc., Nagoya, Japan. Contact e-mail: k-sumitomo@hhc.eisai.co.jp*

Background: Research on gender in the progression of Alzheimer's disease (AD) treated with donepezil is scarce. We investigated change in cognitive function by gender using Japanese real world data on donepezil. **Methods:** Data on the first 24-month period of the J-GOLD study, a nationwide 48-month prospective post-marketing observational study in patients treated with donepezil, were used. In the study, patients diagnosed with AD using DSM-IV criteria and a Functional Assessment Staging (FAST) score of 4 or 5, were recruited. Cognitive function was evaluated using the Hasegawa Dementia Scale revised (HDS-R) and Mini-Mental State Examination (MMSE) at baseline, 12 weeks, and 6, 12, and 24 months. In our analysis, patients who had not been previously treated with donepezil were drawn, and their mean changes in the HDS-R and MMSE at each evaluation point were compared by gender. **Results:** Of 3,964 patients, 1,313 (33.1%) were males and 2,651 (66.9%) were females ([mean $\pm$SD] age: 79.3$\pm$6.4 and 80.8$\pm$6.5, respectively). The HDS-R at baseline was 16.2$\pm$5.3 in males and 16.5$\pm$5.3 in females, and the mean change from baseline was lower in females at all evaluation points (12 weeks: 0.9 vs 0.8, 6 months: 0.9 vs 0.6, 12 months: 0.4 vs 0.0, 18 months: 0.3 vs -0.3, 24 months: 0.4 vs -1.0), with statistical significance in gender difference at 12, 18, and 24 months (t-test: $p < 0.05$). The mean MMSE at baseline was 19.1$\pm$4.9 in males and 18.8$\pm$5.0 in females and turned negative from 18 months in both genders (12 weeks: 0.8 vs 0.7, 6 months: 0.7 vs 0.3, 12 months: 0.1 vs 0.1, 18 months: -0.3 vs -0.3, 24 months: -0.6 vs -0.9). No significant differences were observed between genders at any evaluation point. **Conclusions:** The results of HDS-R suggest a possible gender affect in the progression of AD in patients treated with donepezil. Further investigation is necessary for long-term effect after 24 months.

P3-295 REDUCTION OF SERUM CHOLINESTERASE BY CHOLINESTERASE INHIBITOR (DONEPEZIL, GALANTAMINE, OR RIVASTIGMINE)

Kouji Hayashi[1], Tadanori Hamano[1], Aiko Ishida[1], Youshi Fujita[1,2], Yuka Hama[1], Osamu Yamamura[1], Yasunari Nakamoto[1], [1]*University of Fukui, Fukui, Japan;* [2]*Fujita Neurology Hospital, Fukui, Japan. Contact e-mail: khayashi@u-fukui.ac.jp*