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THE IMPACT OF COGNITIVE TRAINING ON BRAIN ACTIVITY AND CONNECTIVITY IN AMYLOID POSITIVE AND NEGATIVE 11C-PIB PET MCI AND HEALTHY ELDERLY INDIVIDUALS USING FMRI



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Background: The aim of this study was to investigate, for the first time, the brain correlates and connectivity of mild cognitive impairment (MCI) patients with 11C-PIB PET+ and PIB PET- in comparison to healthy controls (HC) before and after cognitive training (CT). **Methods:** A total of 25 participants (mean age: 71.42/education: 13.07 years) were included: PIB+ (n=8), PIB- (n=8) and HC (n=9). They underwent 6 sessions of CT using visual imagery to encode and recall newspaper reports and scanned with fMRI before and after CT during resting state and task performance using a newspaper encoding paradigm. A 3 T MR and FSL were used to analyze the data. For resting state we used one seed in the right and one in the left hippocampus. **Results:** Before CT, all participants showed consistent activation in the left precentral and fusiform gyrus, bilateral occipital cortex and cerebellum (Fig 1-A). However, only HC and PIB- individuals showed left hippocampus, inferior frontal gyrus and intraparietal cortex activation. After CT, only HC demonstrated bilateral hippocampus activation (Fig 1-B). PIB+ participants showed a new cluster of activation in the left hippocampus. Consistent deactivation was found after CT only for HC and PIB- participants in bilateral medial prefrontal and anterior cingulate cortex, areas of the default mode network (DMN). There was increased connectivity after CT in HC when compared to PIB+ and PIB- individuals between right hippocampus and left parietal and pre and post-central gyri (Fig 1-C). **Conclusions:** These findings showed different beneficial effects of CT in PIB+, PIB- and HC participants. Consistent brain activation was found in bilateral hippocampus in HC and left hippocampus in PIB- and PIB+ individuals after CT, in addition to areas of frontoparietal and visual networks. The deactivation of DMN areas in HC and PIB- participants might suggest more beneficial effects of CT in the latter two groups. Along with the increased connec-

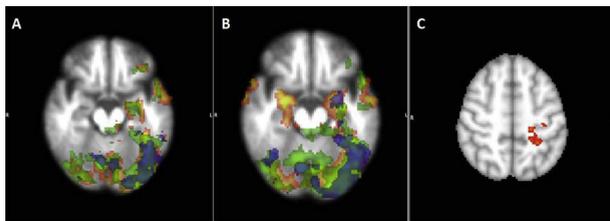


Figure 1. Brain activation maps (HC in orange, PIB- in green; PIB+ in blue; slice in Z = -16mm) before CT (A), after CT (B) and increased resting state connectivity (slice in Z=52mm) after CT (C) for HC in comparison to PIB+ and PIB- MCI participants between the right hippocampus and left superior parietal, pre and post-central gyri.

tivity results, these findings indicate a spread effect of CT in HC, with bilateral recruitment, and a more restricted one in left hemisphere for PIB+ and PIB-.

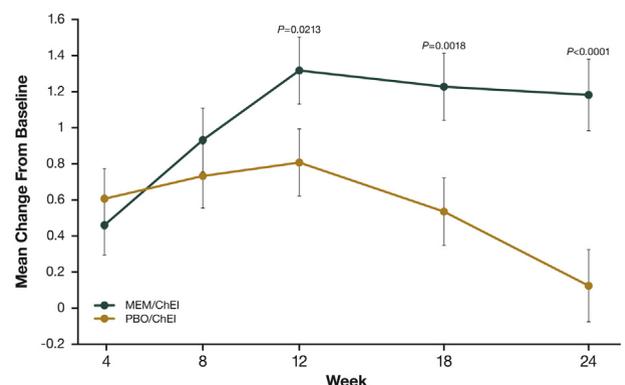
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EFFICACY OF MEMANTINE ADDED TO CHOLINESTERASE INHIBITORS ON SIB BEHAVIORAL DOMAINS: POOLED POST HOC ANALYSIS OF TWO RANDOMIZED CONTROLLED TRIALS IN PATIENTS WITH MODERATE TO SEVERE AD



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Background: The Severe Impairment Battery (SIB) is used to assess cognitive changes in patients with Alzheimer's disease (AD), allowing for the reliable, valid, and sensitive measurement of treatment effects when floor effects may be present on other cognitive tests. Memantine results in significant improvements on the SIB compared with placebo in moderate to severe AD patients treated concurrently with cholinesterase inhibitors (ChEI). This post hoc analysis evaluated the effects of memantine+ChEI vs placebo+ChEI on total SIB and three higher-order cognitive domains (memory, language, and praxis). **Methods:** Data were pooled from two phase 3, randomized, double-blind, placebo-controlled 24-week trials (Tariot et al. *JAMA*, 2004; Grossberg et al. *CNS Drugs*, 2013) evaluating memantine in patients with moderate to severe AD receiving stable ongoing treatment with ChEIs. The SIB, which comprises 40 items with scores ranging from 0 to 100, was administered at baseline and weeks 4, 8, 12, 18, and 24. In addition to the domains of attention, orientation, language, memory, visuospatial ability, and construction, there are three brief evaluations of praxis, social interaction, and orienting to name. To create higher-order subscales, the domains were aggregated based on a face-valid approach that follows clinical neuropsychological tradition, combining those domains that were related to memory (memory, attention, orientation, orienting to name), language (language, social interaction), and praxis (praxis, visuospatial ability, construction). **Results:** Compared with placebo+ChEI treatment, memantine+ChEI significantly improved total SIB scores at



ChEI, cholinesterase inhibitor; ITT, intention-to-treat; MEM, memantine; PBO, placebo; OC, observed cases; SIB, Severe Impairment Battery

Figure 1. SIB Higher-Order Domains: Memory (OC; ITT population). ChEI, cholinesterase inhibitor; ITT, intention-to-treat; MEM, memantine; PBO, placebo; OC, observed cases; SIB, Severe Impairment Battery.