Brain plasticity in mild Alzheimer's Disease. Effects of a computer-based cognitive training on functional connectivity

Francesco Barban[1], Laura Serra[2], Roberta Perri[3], Roberta Annicchiarico[3], Giovanni Augusto Carlesimo[3,4], Matteo Mancini[5], Fulvia Adriano[3], Claudia Ricci[3], Maria Giovanna Lombardi[3], Mara Cercignani[6], Lucia Fadda[3,4], Carlo Caltagirone[3,4], and Marco Bozzali[2]

[1]Clinical and Behavioral Neurology Laboratory; Neuroimaging Laboratory, IRCCS S Lucia Foundation, Rome, Rome, Italy, [2]Neuroimaging Laboratory, IRCCS S Lucia Foundation, Rome, Rome, Italy, [3]Clinical and Behavioral Neurology Laboratory, IRCCS S Lucia Foundation, Rome, Rome, Italy, [4]Department of Neuroscience, University of Rome "Tor Vergata", Rome, Rome, Italy, [5]Department of Engineering, University of Rome "Roma Tre", Rome, Rome, Italy, [6]Brighton & Sussex Medical School, Clinical Imaging Sciences Centre, University of Sussex, Brighton, Sussex, United Kingdom

TARGET AUDIENCE: Clinical and basic neuroscientists with an interest in Alzheimer's Disease, cognitive training and brain plasticity.

PURPOSE: Brain plasticity has been observed throughout lifespan[1]. Computerized cognitive training[2] is a promising tool to delay the progression of the cognitive impairment that characterizes Alzheimer's Disease (AD)[3] and to promote brain plasticity. The aim of the present study was to investigate, with resting state-fMRI, the effects of a computerized cognitive training vs. an active placebo condition on brain networks of patients in the early stages of Alzheimer's Disease (mAD).

METHODS: The sample of this preliminary analysis comprised 19 mAD patients. They underwent a memory and executive functions cognitive training period of 24-sessions long, twice a week for one hour, and a placebo activity period with the same intensity and length. The order of training and placebo period was randomised among subjects with a cross-over design: 11 mAD patients received first the training and after the placebo and 8 mAD patients received first the placebo and after the training. Outcomes of the treatment were measured at T0, at T1 (after 3 months, when mAD switched between periods) and at T2 (after 6 months, at the end of the study). At each time-point mAD patients underwent an extended neuropsychological battery tapping mainly memory and executive functions and a neuroimaging protocol acquired on a 3T Siemens Allegra scanner, including 1) 3D Modified Driven Equilibrium Fourier Transform (MDEFT) scan (TR=1338 ms, TE=2.4 ms, Matrix=256x224, n. slices=176, thickness=1 mm); 2) T2* weighted Echo Planar Imaging (EPI) sensitized to blood oxygenation level dependent (BOLD) contrast (TR=2080 ms, TE=30 ms, 32 axial slices parallel to AC-PC line, matrix=64x64, pixel size=3x3 mm2, slice thickness=2.5 mm, flip angle:70°) for resting state fMRI. BOLD EPIs were collected during rest for 7 min and 20 s, resulting in a total of 220 volumes. During resting state acquisition, participants were instructed to keep their eyes closed, not to think of anything in particular, and not to fall asleep. EPI images were pre-processed for resting-state fMRI using SPM8 and in-house Matlab scripts. A connectivity graph was obtained by defining the nodes based on the Automated Anatomical Labelling (AAL) atlas and the edges assigning to each pair of nodes strength of connectivity equal to the correlation between their BOLD time series. Network-Based Statistics (NBS)[4] was used to compare the connectivity matrices between pre and post training and pre and post placebo (regardless of the order of administration to each subject), using a two-sample paired t-test. A false discovery rate (FDR) corrected p-value was then ascribed using permutation test.

RESULTS: During the placebo period we found no significant connectivity changes, whereas during the training period we found a significant reorganization of connectivity. In fact, we found increase connectivity in a network comprising 10 nodes and 6 edges (Fig 1) including: the bilateral medial temporal lobes (the left hippocampus and right parahippocampal cortices), the bilateral occipital poles and the bilateral front-parietal network (angular gyri and the inferior frontal gyri). Conversely, we found a reduction of connectivity in a network comprising 12 nodes and 7 edges (Fig 2) including: the bilateral cerebellum, the left amygdala and in the right hemisphere the insula, the inferior frontal gyrus and the supramarginal gyrus.

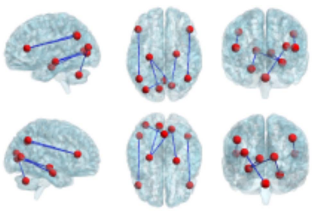

Figure 1. Increased functional connectivity during Training

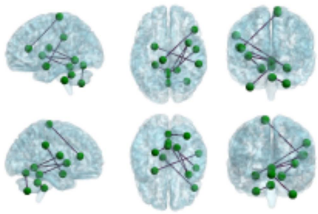

Figure 2. Decreased functional connectivity during Training

DISCUSSION: The present study shows for the first time a reorganization of functional connectivity after a period of computerized cognitive training, and not during a placebo activity, in patients in the early stages of Alzheimer's Disease. This reorganization involved brain regions crucial for memory.

REFERENCES: [1] Kelly et al., 2006. Arch Phys Med Rehabil, 87, S20-9. [2] Caltagirone & Zannino,2008. Funct Neurol,23, 195-9. [3] Coyle et al., 2014. Am J Geriatr Psychiatry. [4] Zalesky et al., 2010. Neuroimage, 1197-207.