Impact of the BDNF Val66Met polymorphism within and beyond the retrosplenial cortex in females with Mild Cognitive Impairment: A magnetoencephalography study

Inmaculada C. Rodríguez-Rojo1,2,3, Pablo Cuesta1,2, María Eugenia López1,2, Ana Barabash4,5, Jose Antonio Cabranes4,5, Marisa Delgado6, Miguel Yus7, Alberto Marcos8, Fernando Maestú1,2,3

1. Laboratory of Cognitive and Computational Neuroscience, Center for Biomedical Technology, Complutense University of Madrid and Technical University of Madrid, Spain.
2. Biomedical Research Networking Center in Bioengineering Biomaterials and Nanomedicine (CIBER-BBN), Madrid, Spain.
3 Department of Basic Psychology II, Faculty of Psychology, Complutense University of Madrid, Madrid, Spain.
4 Laboratory of Psychoneuroendocrinology and Molecular Genetics, Biomedical Research Foundation, Clínico San Carlos Hospital, Madrid, Spain.
5 Institute of Sanitary Investigation (IdISSC), Clínico San Carlos Hospital, Madrid, Spain.
6 Seniors Center of the District of Chamartín. Madrid, Spain.
7 Radiology Department, Clínico San Carlos Hospital, Madrid, Spain.
8 Neurology Department, Clínico San Carlos Hospital, Madrid, Spain.

PURPOSE
Mild Cognitive Impairment (MCI) can be influenced by genetic risk factors. The Brain Derived Neurotrophic Factor Val66Met polymorphism is one of them. This mutation may affect the brain functional connectivity (FC), especially for those carriers of the Met allele (A). The retrosplenial cortex (RSC), essential component of the Default Mode Network (DMN), could be altered by this polymorphism. Our aim was to examine the influence of the Val66Met polymorphism within the RSC's functional network, and its interconnections between the frontal medial cortex (FMC) and the anterior cingulate (ACC).

METHODS
We conducted a magnetoencephalography (MEG) study together with the genotyping of the BDNF Val66Met polymorphism (AG vs. GG). The sample consisted of 44 elderly females, both healthy and with MCI. All of them were ApoE 33. In order to determine the connectivity of the DMN, three-minutes of MEG resting state (eyes closed) were recorded.

RESULT
MCIs AG showed an anterior hyposynchronization and a posterior hypersynchronization within the RSC, while healthy elders AG exhibited the inverse pattern. Additionally, MCIs AG presented a hypersynchronization in both inferior parietal lobes (IPL) compared to MCIs GG. Finally, all AG carriers exhibited a hypersynchronization between the RSC and the FMC, and a hyposynchronization between the RSC and the ACC.

CONCLUSIONS
Carriage of the Met allele (A) produces a special regional vulnerability within the RSC, both in MCIs and elderly controls. Furthermore, it seems to cause a harmful effect in the FC between different brain areas of the DMN, particularly in those subjects with MCI.