DOCTORAL THESIS

Relating brain signal complexity, cognitive performance and APOE polymorphisms: the case of young healthy human adults

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Abstract

Human brain is a complex dynamical system, whose complexity could be highly functional and characterize cognitive abilities or mental disorders. The APOE ε4 allele is a well-known genetic risk factor for the development of Alzheimer's Disease and cognitive decline in later human life. However, there are no robust conclusions about the APOE genotype-phenotype association among young healthy adults. The main goal of this study is to investigate the bridges between brain signal complexity, APOE genotype and cognitive performance among young adults under the framework of individual difference.

Before going deeper to the main topic, the first study assessed the reliability of Residue Iteration decomposition (RIDE), a method for analysis brain signals that was applied in the main parts of my thesis. Using a dataset independent from the main topic, I demonstrated that as compared with conventional analysis method, the RIDE-reconstructed event-related-potentials (ERPs), including the N400 component reflecting the evaluation of semantic incongruities during social communication, could more sensitively characterize people across a spectrum of autistic level.

The second study investigated how individual differences in APOE genotypes are associated with 1) brain signal complexity measured with Multiscale Entropy (MSE) and 2) cognitive ability in specific domain, especially, working memory capacity. Using Structural Equation Modelling (SEM) we showed that APOE ε4 is associated with higher entropy at scale 1-4 and lower entropy at scale 5 and above, especially at frontal scalp regions and in an eyes open condition; in addition, we showed a stronger drop in MSE from closed to open eyes condition among ε4 carriers than non-carriers. The ε4 association with cognitive performance was complex, but basically ε4 seems to be associated with worse cognitive performance among lower educated people, whereas no such association appeared among the higher educated.

The third study connected MSE with a different cognitive domain – face and object cognition abilities We showed that 1) increased MSE at all scales is associated with better cognitive performance from the view of both diffusion process during perceptual decision making and task performance accuracy. However, the association was only consistent for a closed eyes condition. 2) Increased MSE at higher scales (7 or 8) was associated with tighter coupling between RIDE-extracted single trial stimulus evaluation speed at the neural level and reaction time at the behavior level.

To summarize, the results of my doctoral study connected brain signal complexity, APOE genotype and cognitive behavior among young healthy adults, providing a deeper understanding of brain-behavior relationships and - potentially – for early AD diagnosis when cognitive decline is not yet evident.

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