

COGNITIVE AND PHYSICAL STIMULATION, GENETIC RISK AND COGNITIVE DECLINE



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A mio papà e a mia mamma.

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ABSTRACT

Physical Activity (PA) and Cognitive Activity (CA) are generally considered protective for Alzheimer's disease (AD) and Mild Cognitive Impairment (MCI), but the experimental evidence on the effectiveness of non-pharmacological treatments has been enigmatic, as rarely hypotheses based on principles of physiological processes and neuroplasticity have been put forward. Moreover, it is not known what impact the ϵ_4 allele of the Apolipoprotein E (ApoE) has on the effects of CA and PA. We hypothesised that benefits due to PA and CA can be detected using appropriate theoretical frameworks based on brain function.

We identified and tested two paradigms of study based on hierarchically high-order physiological mechanisms associated to PA and CA. We also hypothesised that the ϵ_4 allele would mediate any effect.

A single PA session caused a selective effect of exercise on prefrontal-dependent cognition in a sample of healthy untrained adults. We interpreted this finding in the light of the Transient Hypofrontality Theory. We speculated that a PA programme administered to old adults would be associated to similar processes, to account for the general trend that suggests that prefrontal regions benefit from exercise (evidence which cannot be fully accounted for by the current major hypotheses).

We then designed a CA programme based on exercises targeting more brain areas simultaneously in order to resynchronise the Default Mode Network, a brain neurobiological system which shows specific patterns of dysfunction in AD even at the preclinical MCI stage. We trained healthy and MCI adults, finding positive modulation of brain function in both groups. Structural and cognitive improvements were also detected.

The presence of the ϵ_4 allele mediated the effects of both PA and CA on brain function.

Non-pharmacological treatments can contrast the effect of ageing and AD, but it is necessary to identify appropriate paradigms based on evidence of brain function and connectivity.

