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The Relationship Between Associative Learning, Transfer Generalization, and Homocysteine Levels in Mild Cognitive Impairment

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Introduction and Objectives: Previous studies have shown that high total homocysteine levels are associated with Alzheimer's disease (AD) and mild cognitive impairment (MCI).

Aims: In this study, we test the relationship between cognitive function and total homocysteine levels in healthy subjects (Global Dementia Rating, CDR = 0) and individuals with MCI (CDR = 0.5).

Methods: We have used a cognitive task that tests learning and generalization of rules, processes that have been previously shown to rely on the integrity of the striatal and hippocampal regions, respectively.

Results: We found that total homocysteine levels are higher in MCI individuals than in healthy controls. We conducted further analysis after dividing MCI subjects in two groups, depending on their Global Deterioration Scale (GDS) scores: individuals with very mild cognitive decline (vMCD) and mild cognitive decline. There was no difference among the two MCI and healthy control groups in learning performance. However, we found that individuals with MCD make more generalization errors than healthy controls and individuals with vMCD. In addition, interestingly, we found that total homocysteine levels correlate positively with generalization errors, but not with learning errors.

Conclusions: Our results are in agreement with prior results showing a link between hippocampal function, generalization performance, and total homocysteine levels. Importantly, our study is perhaps among the first to test the relationship between learning (and generalization) of rules and homocysteine levels in healthy controls and individuals with MCI.