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Neuromodulatory property of standardized extract Ginkgo biloba L. (EGb 761) on memory: behavioral and molecular evidence.

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Abstract

Although it has been suggested that the standardized **Ginkgo biloba** leaf extract (Egb 761) may have a beneficial effect on **memory**, the cellular and molecular changes that underlie this process are not yet well defined. The present study evaluated the effects of acute (one dose) or subacute treatments (one daily dose/seven days) with EGb 761 (0.5 g kg(-1) and 1.0 g kg(-1)) on rats submitted to a conditioned emotional response (CER) in comparison with positive (4 mg kg(-1) Diazepam) and negative (12%Tween 80) control groups. To this end, eighty (n=10/group) adult, male, Wistar rats (+/-250-300 g) were used in an off-baseline CER procedure. We here observed that the rats submitted to an acute and subacute EGb 761 treatments had acquisition of fear conditioning. Additionally, we investigate if the expression of genes previously associated with classical conditioning (CREB-1 and GAP-43) and new candidate genes (GFAP) are modulated following EGb 761 acute treatment. CREB-1, GAP-43 and GFAP mRNA and protein expressions were evaluated using both quantitative PCR (qPCR) and immunohistochemical analysis, respectively. We here show, for the first time, that EGb 761 modulated GAP-43, CREB-1 and GFAP expression in the prefrontal cortex, amygdala and hippocampus. We observed an underexpression of GAP-43 in all structures evaluated and over-expression of GFAP in the amygdala and hippocampus following acute G. **biloba** treatment when compared to control group (Tween; $p<0.01$). GAP-43 expression was decreased in prefrontal cortex and hippocampus in the subacute treatment with EGb 761. Subacute treatment with EGb 761 lead to a decreased CREB-1 in mPFC ($p<0.001$) and increased in the hippocampus to 1.0 g kg(-1)G. **biloba** group ($p<0.001$). The results obtained from immunohistochemical analysis support our aforementioned findings and revealed that the changes in expression occurred within specific regions in the areas evaluated. All together, our findings not only provide new evidence for a role of EGb 761 on **memory** but also identify molecular changes that underlie the fear **memory** consolidation.

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