

## Neopterin Acts as an Endogenous Cognitive Enhancer

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Neopterin is found at increased levels in biological fluids from individuals with inflammatory disorders. The biological role of this pteridine remains undefined; however, due to its capacity to increase hemoxygenase-1 content, it has been proposed as a protective agent during cellular stress. Therefore, we investigated the effects of neopterin on motor, emotional and memory functions. To address this question, neopterin (0.4 and/or 4 pmol) was injected intracerebroventricularly before or after the training sessions of the step-down inhibitory avoidance and fear conditioning tasks, respectively. Memory-related behaviors were assessed in Swiss and C57BL/6 mice, as well as in Wistar rats. Moreover, the putative effects of neopterin on motor and anxiety-related parameters were addressed in the open field and elevated plus-maze tasks. The effects of neopterin on cognitive performance were also investigated after intraperitoneal lipopolysaccharide (LPS) administration (0.33 mg/kg) in interleukin-10 knockout mice (IL-10<sup>-/-</sup>). It was consistently observed across rodent species that neopterin facilitated aversive memory acquisition by increasing the latency to step-down in the inhibitory avoidance task. This effect was related to a reduced threshold to generate the hippocampal long-term potentiation (LTP) process, and reduced IL-6 brain levels after the LPS challenge. However, neopterin administration after acquisition did not alter the consolidation of fear memories, neither motor nor anxiety-related parameters. Altogether, neopterin facilitated cognitive processes, probably by inducing an antioxidant/anti-inflammatory state, and by facilitating LTP generation. To our knowledge, this is the first evidence showing the cognitive enhancer property of neopterin.