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BEHAVIORAL CHARACTERIZATION OF YOUNG AND OLD MICE WITH A TARGETED MUTATION OF THE P66<sup>shc</sup> GENE.

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Targeted mutation of the mouse p66<sup>shc</sup> gene has been reported to induce resistance to oxidative stress and to result in longer life span in animal models. In this study we compared the behavioral phenotype of p66<sup>shc-/-</sup> mice of the 129 /Sv(ev) strain with their wild type controls (p66<sup>shc+/+</sup>). Forty animals were used, divided into 4 groups of 10 mice each: a) transgenic old (11 months) mice (KO-O); b) wild type old mice (WT-O); c) transgenic young (4 months) mice (KO-Y) and d) wild type young mice (WT-Y). All subjects underwent a battery of behavioral tests (Hot plate, Open field (OF), Elevated plus maze, Morris water maze (MWM) and social/aggressive behavior test) to assess nociception, exploratory activity, emotionality, and spatial navigation ability. Overall, results indicate that age-dependent differences, present in wild type subjects, were less pronounced in KO animals, particularly in the OF and in the Hot plate tests which revealed an increase in pain threshold in both KO groups. In the spatial memory task there was an overall genotype *per* age effect, with the KO-Y group showing better retention compared to all others. More in detail, results from the MWM test indicate that young and old KO mice employ different strategies when dealing with a spatial learning test, particularly in the reversal phase, while wild type groups show a more homogeneous performance as well as a clear age-dependent decline in spatial ability. Studies aimed to correlate behavioral differences with selected changes in neurochemical parameters in these mice are currently in progress.

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