The results of this study show a remarkable similarity between the receptor complex with a positive cooperative effect on the (negative) modulation of the in vitro curves and the in vivo curves, concerning both the effect of STREP treatment with ALCAR in the middle-aged STREP-treated rat. Spatial discrimination learning in the Morris task was affected after STREP treatment and this cognitive impairment was related to hippocampal choline acetyl transferase (Chat) activity in the frontal cortex, stratum and septum was not affected after STREP treatment. Chronic treatment with ALCAR attenuated the STREP-induced impairment in spatial bias during the probe trial and attenuated the STREP-induced decline in hippocampal Chat activity. These findings suggest that, in this animal model, chronic treatment with ALCAR had a beneficial effect on the behavioral as well as on the biochemical level. Presently histological, neurochemical, and behavioral studies are in progress to elucidate the effect of STREP on the neurodegeneration of certain brain structures and transmitter systems.

Treatment of middle-aged rats with an i.c.v. injection of streptozotocin (STREP) may provide a relevant model of neurodegeneration that could be induced by a decrease in the mitochondrial metabolism of glucose. Acetyl-L-carnitine (ALCAR) has been found to enhance the utilization of alternative energy sources, such as lipid substrates or ketone bodies. Via such a mechanism of action ALCAR could antagonize the effects of STREP treatment. This study was designed to evaluate the behavioral and biochemical effects of chronic treatment with ALCAR in the middle-aged STREP-treated rat. Spatial discrimination learning in the Morris task was affected after STREP treatment and this cognitive impairment was related to hippocampal ChAT activity in the frontal cortex, stratum and septum was not affected after STREP treatment. Chronic treatment with ALCAR attenuated the STREP-induced impairment in spatial bias during the probe trial and attenuated the STREP-induced decline in hippocampal ChAT activity. These findings suggest that, in this animal model, chronic treatment with ALCAR had a beneficial effect on the behavioral as well as on the biochemical level. Presently histological, neurochemical, and behavioral studies are in progress to elucidate the effect of STREP on the neurodegeneration of certain brain structures and transmitter systems.