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Cognitive function in older adults with major depression: effects of mineralocorticoid receptor stimulation

Christian Otte, Katja Wingenfeld, Linn K. Kuehl, Steffen Richter, Francesca Regen, Dominique Piber, Kim Hinkelmann



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**Abstract**

Memory and executive function are often impaired in older adults with major depression. Mineralocorticoid receptors (MR) are abundantly expressed in the hippocampus and in the prefrontal cortex, brain areas critical for memory and executive function. In both aging and depression, MR expression in the brain is reduced. Therefore, diminished MR function could contribute to impaired cognition in older adults with depression and might be a promising target for pharmacological intervention.

Twenty-three older adults with major depression (mean age 61.6 yrs.  $\pm$  8.1,  $n = 13$  women) without medication and 24 age-, sex- and education-matched healthy participants received the MR-agonist fludrocortisone (0.4 mg) or placebo in a randomized, double-blind, within-subject cross-over design. We measured psychomotor speed, executive function, verbal learning and memory, and visuospatial memory.

Compared to controls, depressed patients performed worse in psychomotor speed (group effect  $p = 0.01$ ), executive function (group effect  $p < 0.01$ ), verbal learning (group effect  $p = 0.02$ ), and verbal memory (group effect  $p < 0.01$ ) but not in visuospatial memory. There were no significant treatment effects. However, we found a group  $\times$  treatment interaction in verbal learning ( $p = 0.04$ ) and visuospatial memory ( $p = 0.02$ ) indicating that depressed patients performed worse after fludrocortisone whereas controls performed better after fludrocortisone.

Our data suggest that –in contrast to younger depressed patients- older adults with depression do not benefit from MR stimulation but deteriorate in cognitive function.

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