

Name of Sponsor: Charité Universitätsmedizin Berlin	EudraCT results post synopsis: 2014-005239-15	(For National Authority Use only)
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Title of Study: Effects of mineralocorticoid receptor stimulation on cognitive bias and social cognition in patients with major depression and healthy controls: what's the role of NMDA receptors?	
EudraCT-Number: 2014-005239-15	
Principal Investigators: Christian Otte	
Study centre(s): Charité Universitätsmedizin Berlin, Klinik für Psychiatrie und Psychotherapie, Hindenburgdamm 30, 12203 Berlin	
<p>Publication (reference):</p> <p>Nowacki, Wingenfeld, Kaczmarczyk, Chae, Salchow, Abu-Tir, Piber, Hellmann-Regen, & Otte (2020). Steroid hormone secretion after stimulation of mineralocorticoid and NMDA receptors and cardiovascular risk in patients with depression. <i>Translational Psychiatry</i>, 10(1): 109.</p> <p>Nowacki, Wingenfeld, Kaczmarczyk, Chae, Abu-Tir, Deuter, Piber, Hellmann-Regen, & Otte (2020) Cognitive and emotional empathy after stimulation of brain mineralocorticoid and NMDA receptors in patients with major depression and healthy controls. <i>Neuropsychopharmacology</i>, 45(13), 2155-2161.</p> <p>Nowacki, Wingenfeld, Kaczmarczyk, Chae, Salchow, Deuter, Piber, Hellmann-Regen, & Otte (in press). Selective attention to emotional stimuli and emotion recognition in patients with major depression: the role of mineralocorticoid and glutamatergic NMDA receptors. <i>Journal of Psychopharmacology</i>.</p>	
<p>Studied period (years): 3</p> <p>21.09.2016 (date of first enrolment)</p> <p>11.02.2019 (date of last completed)</p>	Phase of development: Early 2016
Objectives: To examine the effects of mineralocorticoid receptor (MR) stimulation and simultaneous MR and NMDA receptor (NMDA-R) stimulation on selective attention to facial emotional stimuli, facial emotion recognition, cognitive and emotional empathy and visuospatial memory in patients with major depression (MDD) and healthy controls (HC).	
Methodology: Prospective, monocentric, randomized, double-blind, placebo-controlled study with parallel-group design and single administration of fludrocortisone and/or D-cycloserine.	
Number of patients (planned and analyzed): 232 participants planned and analyzed (116 MDD patients, 116 HC).	

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Diagnosis and main criteria for inclusion:

- Age 18-65 years
- Depressed male and female patients according to DSM-V & minimum of 17-items Hamilton Depression Score of 18
- healthy controls
- informed consent signed

Test product, dose and mode of administration, batch number:

- Fludrocortisone 0.4 mg: Astonin H 0,1 mg, single dose, oral administration, batch number 6105265.00.00
- D-Cycloserine 250 mg: Cycloserine 250 mg, single dose, oral administration, batch number PL 14385/0005

Duration of treatment: Single administration

Reference therapy, dose and mode of administration, batch number:

- Placebo pill, single dose, oral administration

Criteria for evaluation:

Efficacy: Emotional dot probe (selective attention to emotional stimuli), Facial recognition task (facial emotion recognition), Multifaceted Empathy Test (MET; cognitive and emotional empathy), Virtual Water Maze (visuospatial memory).

Safety: Blood pressure, heart rate, measures of subjective well-being (Visual Analogue Mood Scales, VAMS), adverse events (AE), serious adverse events (SAE), serious adverse reactions (SAR)

Statistical methods: ANOVA and t-tests

Summary - Conclusions

Efficacy Results:

- Emotional dot probe (selective attention to emotional stimuli): MR stimulation and simultaneous MR and NMDA-R stimulation showed no (additional) effect on selective attention to emotional stimuli in MDD patients and healthy controls.
- Facial recognition task (facial emotion recognition): MR stimulation and simultaneous MR and NMDA-R stimulation showed no (additional) effect on facial emotion recognition. Separate NMDA-R stimulation increased emotion recognition in MDD patients and healthy controls.
- Multifaceted Empathy Test (cognitive and emotional empathy): MR stimulation increased cognitive empathy but not emotional empathy in MDD patients and healthy controls. Simultaneous MR and NMDA-R stimulation showed no (additional) effect on cognitive and emotional empathy. Separate NMDA-R stimulation decreased cognitive empathy in MDD patients only.
- Virtual Water Maze (visuospatial memory): MR stimulation and simultaneous MR and NMDA-R stimulation showed no (additional) effect on visuospatial memory in MDD patients and healthy controls.

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Safety Results: No AE, SEA SAR reported.

Conclusion: Our study found some evidence for an involvement of MR in social cognition. Stimulation of MR increased cognitive empathy in MDD patients and healthy controls but showed no effect on the other examined (social) cognitive processes. Simultaneous MR and NMDA-R stimulation showed no (additional) effect on selective attention to emotional stimuli, facial emotion recognition, cognitive and emotional empathy, and visuospatial memory. Furthermore, the research emphasizes that NMDA-R might be involved in cognitive empathy and emotion recognition, but these results need to be replicated by future studies before definite conclusions can be drawn.

Date of the report: 28. of April 2021