20 cases, zolpidem was found to be useless or potentially detrimental, even delaying other more useful interventions. A successful "Zolpidem Test" to confirm diagnosis was reported in 11 cases.
Conclusions: Given its lack of significant side effects and short half-life, zolpidem emerges as a possible diagnostic tool for catatonia, in the so-called "Zolpidem Test". In selected cases of catatonia associated with a variety of etiologies, it may be a useful therapeutic option, with efficacy ranging from a few hours of lucidity to complete restoration of consciousness. Information on the effect of GABA-A PAMs in this area are lacking. Further research is needed to clarify the role of zolpidem in the treatment of catatonia, especially to identify clinical features of patients that could predict outcome.
[1] AN Edinoff, SE Kaufman, JW Hollier, CG Virgen, CA Karam, GW Malone, EM Cornett, AM Kaye, AD Kaye (2021), Catatonia: clinical overview of the diagnosis, treatment, and clinical challenges. Neurology international 13:570-586. [2] R Tandon, S Heckers, J Bustillo, DM Barch, W Gaebel, RE Gur, D Malaspina, MJ Owen, S Schultz, M Tsuang (2013), Catatonia in DSM-5. Schizophrenia research 150:26-30. [3] SR Beach, F Gomez-Bernal, JC Huffman, GL Fricchione (2017), Alternative treatment strategies for catatonia: A systematic review. General Hospital Psychiatry 48:1-19. [4] A. D'Agostino G. Broglia, A. Masserini, M. Marchetti, S. Scaravaggi, C. Ossola, The effect of Zolpidem and other Z-compounds in Catatonia: A Systematic Review. PROSPERO, 2024.
No conflict of interest

https://doi.org/10.1016/j.nsa.2024.105146

P3438
NEUROSCIENCE APPLIED 3 (2024) 105145
NEUROMODULATION IN A PRECLINICAL MODEL OF TREATMENT-RESISTANT DEPRESSION: NEUROBEHAVIOURAL EFFECTS OF A STANDARD PROTOCOL

M. Boffa [1,2], F. Martella [3], S. Spalletti [1], L. De Risio [4], G. Di Lorenzo [5,6], S.L. Sensi [2], G. Martinotti [2,7,8], C. D'Addario [3], M. Pettorruso [2,7], F. Zoratto [1]. [1] *Istituto Superiore di Sanità, Centre for Behavioural Sciences and Mental Health, Rome, Italy;* [2] *"G. d'Annunzio" University of Chieti-Pescara, Department of Neuroscience Imaging and Clinical Sciences, Chieti, Italy;* [3] *University of Teramo, Department of Bioscience and Technology for Food Agriculture and Environment, Teramo, Italy;* [4] *ASL Roma 5, Department of Mental Health and Addiction, Rome, Italy;* [5] *University of Rome Tor Vergata, Laboratory of Psychophysiology and Cognitive Neuroscience - Department of Systems Medicine, Rome, Italy;* [6] *IRCCS Fondazione Santa Lucia, n/a, Rome, Italy;* [7] *ASL 2 Abruzzo Lanciano-Vasto-Chieti, Department of Mental Health, Chieti, Italy;* [8] *University of Hertfordshire, Psychopharmacology- Drug Misuse and Novel Psychoactive Substances Research Unit- School of Life and Medical Sciences, Hatfield, United Kingdom*

Background. Repetitive transcranial magnetic stimulation (rTMS), a focal neuromodulation technique, is currently recommended for treatment-resistant depression (TRD) [1]. rTMS preclinical application has long been problematic; however, recent optimization has laid the foundations for improved translational studies [2]. Nonetheless, available results have limited predictive value for TRD patients treated with TMS, as only antidepressant-sensitive preclinical models were used [3].
Objective. To overcome this issue, we evaluated rTMS effects on the recovery of the depressive-/anxiety-like phenotype and the expression of key genes in a recently validated rat model of TRD[4,5].
Methods. As a TRD model, we applied chronic mild stress (4 weeks) to socially-isolated Wistar-Kyoto rats, an endogenous MDD model [4,5]. An antidepressant-responsive model (prolonged social isolation in Wistar rats; SI) and a control group (socially-housed Wistar rats; CON) were also included in the study. TRD, SI, and CON animals were exposed to standard rTMS, targeting the frontal cortex bilaterally, for eight consecutive days (10 Hz, 40 pulses/train, 1600 pulses/session). Corresponding TRD, SI, and CON sham groups were exposed to the same manipulation and acoustic effect. We then evaluated the short-term (after the last rTMS session) and long-term (after two weeks) effects through behavioural tests investigating motivational/apathy-like state, helplessness, and altered emotionality. We also assessed plasma corticosterone as well as short- and long-term variations in the expression of genes encoding for BDNF and CB1 receptor. Statistical analyses were performed using t-test or rm-ANOVA, as appropriate.
Results. SI rats receiving active rTMS showed reduced helplessness in the short-term forced-swim test (model×treatment: $F(2,92)=5.47$, $p=0.005$, $p<0.05$ in Tukey posthoc) and decreased anxiety-like behaviour in the short-term open-field (model×treatment: $F(2,92)=2.72$, $0=0.071$, $p<0.05$ in Tukey posthoc) and long-term plus-maze (model×treatment: $F(2,70)=2.15$, $p=0.124$, $p<0.05$ in Tukey posthoc) tests than sham SI animals. They also showed reduced plasma corticosterone concentrations (model×treatment: $F(2,70)=5.08$, $p=0.008$, $p<0.05$ in Tukey posthoc). By contrast, active (vs. sham) rTMS in TRD rats normalized the greater anxiogenic response in the novelty-suppressed feeding test (group×treatment: $F(2,90)=3.16$, $p=0.047$, $p<0.05$ in Tukey posthoc) and contributed to the recovery of the motivational/apathy-like state in the splash test ($\chi^2_{(1)}=4.51$, $p=0.034$). No significant behavioural changes were observed in the CON group following active rTMS. In the long-term assessment, the TRD active group had significantly higher BDNF and CNR1 mRNA levels in the prefrontal cortex than the TRD sham group ($p=0.024$ and $p=0.042$, respectively). A similar trend was evidenced for BDNF mRNA levels in active SI rats ($p=0.07$). No significant changes were observed in the hippocampus or in the short-term assessment.
Conclusion. Results obtained in the SI model confirmed available evidence on the efficacy of standard rTMS in ameliorating the neurobehavioural phenotype in an antidepressant-responsive model. The marked rTMS-induced variations in gene expression also suggested responsiveness in TRD rats, although the effects on the behavioural profile were more circumscribed. In the TRD model, deep brain stimulation reversed anhedonic, anxiogenic, and dyscognitive effects[4,5], whilst rTMS, to our knowledge, has not been previously tested. Further preclinical investigations in this model are deemed necessary to help identify optimal stimulation protocols and shed light on new neurobiological-based rationales for rTMS use.
References
[1] Voineskos, D., Daskalakis, Z.J, Blumberger, D.M., 2020. Management of Treatment-Resistant Depression: Challenges and Strategies. Neuropsychiatr Dis Treat. 16, 221- 234. [2] Parthoens, J., Verhaeghe, J., Servaes, S., Miranda, A., Stroobants, S., Staelens, S., 2016. Performance Characterization of an Actively Cooled Repetitive Transcranial Magnetic Stimulation Coil for the Rat. Neuromodulation 19(5), 459-68. [3] De Risio, L., Borgi, M., Pettorruso, M., Miuli, A., Ottomana, A.M., Sociali., A., Martinotti, G., Nicolò, G., Macrì, S., di Giannantonio, M., Zoratto, F., 2020. Recovering from depression with repetitive transcranial magnetic stimulation (rTMS): a systematic review and meta-analysis of preclinical studies. Transl Psychiatry 10(1), 393. [4] Willner, P., Gruca, P., Lason, M., Tota-Glowczyk, K., Litwa, E., Niemczyk, M., Papp, M., 2019. Validation of chronic mild stress in the Wistar-Kyoto rat as an animal model of treatment-resistant depression. Behav Pharmacol. 30(2-3), 239-250. [5] Papp, M., Gruca, P., Lason, M., Niemczyk, M., Willner, P., 2019. The role of prefrontal cortex dopamine D2 and D3 receptors in the mechanism of action of venlafaxine and deep brain stimulation in animal models of treatment-responsive and treatment-resistant depression. J Psychopharmacol. 33(6), 748-756.
Conflict of interest
This abstract is financially supported by a "Ricerca Finalizzata, Young Researchers" grant from the Italian Ministry of Health (to MP, FZ, and LDR grant code GR-2019-12370173).

https://doi.org/10.1016/j.nsa.2024.105145

P3439
NEUROSCIENCE APPLIED 3 (2024) 105146
GALANTAMINE AND MEMANTINE FOR TREATMENT IN MILD COGNITIVE IMPAIRMENT: AN OBSERVATIONAL-PROSPECTIVE STUDY IN 824 PATIENTS FOR 3 YEARS

J. Zarra [1], L. Schmidt [2], F. Zarra [3]. [1] *Centro Médico San Lucas and the Foundation ALEA Asociación de Lucha en la Enfermedad de Alzheimer. ORCID: 0009-0003-3124-9386, Department of Neurosciences and Psychiatry Service, Gualeguaychú, Argentina;* [2] *Centro Médico San Lucas, Servicio de Psiquiatría, Gualeguaychú, Argentina;* [3] *Universidad de Buenos Aires, Facultad de Medicina, Buenos Aires, Argentina*

Introduction: During the last decades, specialists in Alzheimer's Disease (AD) have begun to perceive the close relationship between the development of Mild Cognitive Disorder as an indicator of two aspects: on the one hand the progression to dementia and on the other as a "clue "which reveals a probably effective therapy that delays the evolution and progression to dementia. Galantamine is a competitive and reversible cholinesterase inhibitor and an allosteric modulator of nicotinic receptors. Reduced levels of acetylcholine in the brain are thought to be responsible for some of the symptoms of Alzheimer's disease. Galantamine increases the concentration of acetylcholine in the brain and this increase is believed to be responsible for improved thinking, along with memantine: a