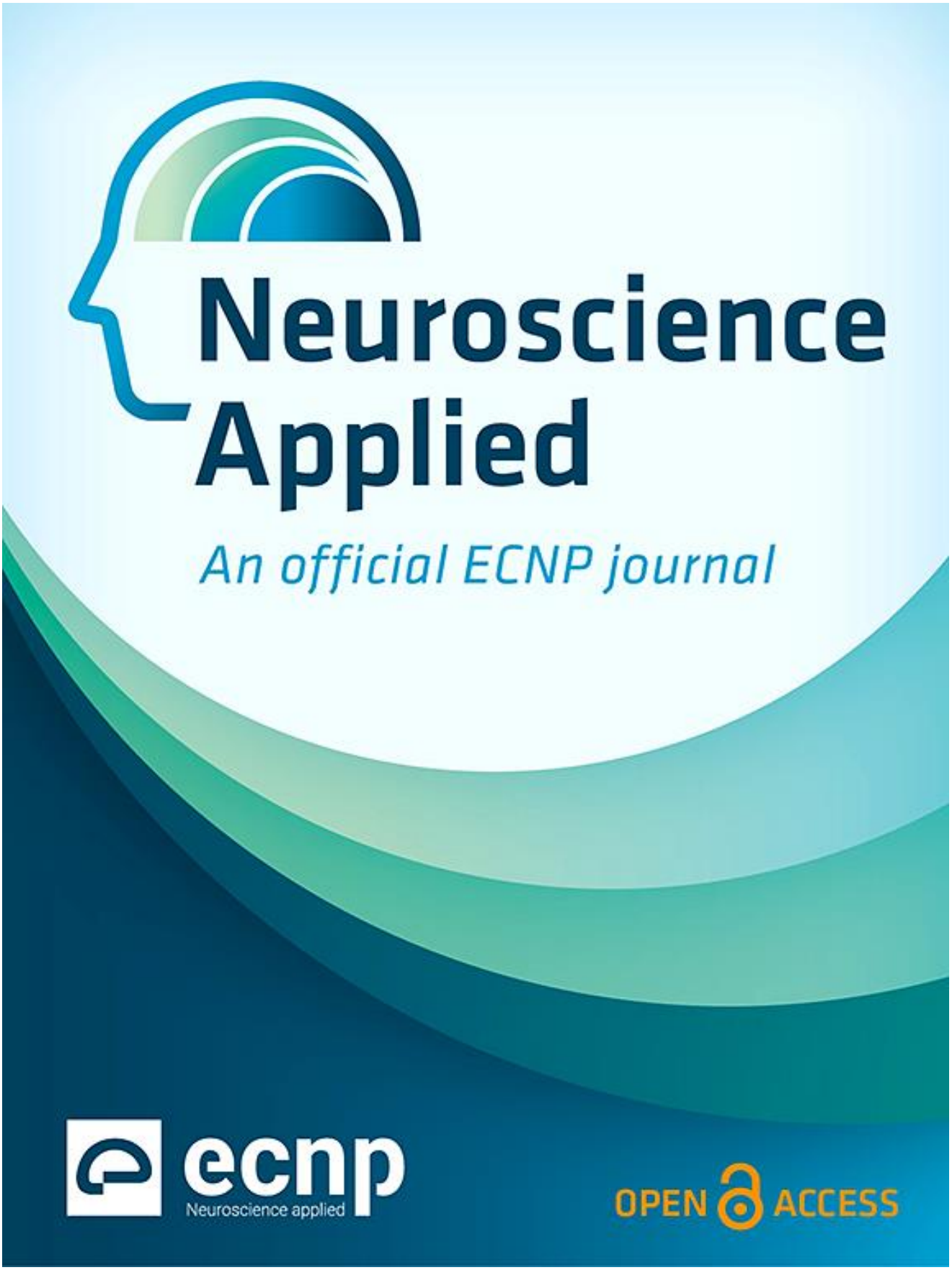
Neuroscience
Applied
An official ECNP journal
ecnp
Neuroscience applied
OPEN ACCESS

and Thalamus (patients, $\beta = 0.0007$, $p = 0.34$; controls, $\beta = 0.0003$, $p = 0.57$). We also did not see a group (MDD vs healthy) interaction effect (all p-values >0.44) nor a sex interaction effect for either patients (all p-values >0.24) or controls (all p-values >0.42).

Conclusions: We replicate our previous finding that 5-HT4R and trait Neuroticism are unrelated in healthy controls and further show no association in patients with MDD. Lastly, we find no evidence for a sex effect on the association between Neuroticism and 5-HT4R.

References

[1] Frokjaer, V.G., Mortensen, E.L., Nielsen, F.Å., Haugbol, S., Pinborg, L.H., Adams, K.H., Svarer, C., Hasselbalch, S.G., Holm, S., Paulson, O.B., Knudsen, G.M., 2008. Frontolimbic Serotonin 2A Receptor Binding in Healthy Subjects Is Associated with Personality Risk Factors for Affective Disorder. Biol Psychiat 63, 569–576. https://doi.org/10.1016/j.biopsych.2007.07.009 [2] Vittengl, J.R., 2017. Who pays the price for high neuroticism? Moderators of longitudinal risks for depression and anxiety. Psychol Med 47, 1794–1805. https://doi.org/10.1017/s0033291717000253 [3] Haahr, M.E., Fisher, P.M., Jensen, C.G., Frokjaer, V.G., Mahon, B.M., Madsen, K., Baaré, W.F.C., Lehel, S., Norremolle, A., Rabiner, E.A., Knudsen, G.M., 2014. Central 5-HT4 receptor binding as biomarker of serotonergic tonus in humans: a [11C]SB207145 PET study. Mol Psychiatr 19, 427–432. https://doi.org/10.1038/mp.2013.147 [4] Köhler-Forsberg, K., Ozenne, B., Landman, E.B., Larsen, S.V., Poulsen, A.S., Dam, V.H., Ip, C.-T., Jørgensen, A., Meyer, M., Eiberg, H.R.L., Svarer, C., Jørgensen, M.B., Frokjaer, V.G., Knudsen, G.M., 2021. Evidence for a serotonergic subtype of major depressive disorder: A NeuroPharm-1 study. Medrxiv 2021.06.17.21258740. https://doi.org/10.1101/2021.06.17.21258740 [5] Stenbæk, D.S., Dam, V.H., Fisher, P.M., Hansen, N., Hjordt, L.V., Frokjaer, V.G., 2017. No evidence for a role of the serotonin 4 receptor in five-factor personality traits: A positron emission tomography brain study. Plos One 12, e0184403. https://doi.org/10.1371/journal.pone.0184403

No conflict of interest

doi: https://doi.org/10.1016/j.nsa.2022.100235

P.0133

NEUROSCIENCE APPLIED 1 (2022) 100112 100236

Humanized CYP2C19 transgenic mouse as an animal model of cerebellar ataxia

F. Milosavljević [1], I. Brusini [2,3], A. Atanasov [1], M. Manojlović [1], M. Vučić [1], Z. Oreščanin-Dušić [4], J. Brkljačić [5], P. Sitarica [1], Č. Miljević [6], A. Nikolić-Kokić [4], D. Blagojević [4], C. Wang [2], P. Damberg [7], V. Pešić [1], R. Tyndale [8,9,10], M. Ingelman-Sundberg [11], M. Jukić [1,11]. [1] *Faculty of Pharmacy- University of Belgrade, Department of Physiology, Belgrade, Serbia;* [2] *KTH Royal Institute of Technology, Department of Biomedical Engineering and Health Systems, Huddinge, Sweden;* [3] *Karolinska Institutet, Department of Neurobiology- Care Sciences and Society, Huddinge, Sweden;* [4] *Institute for Biological Research "Siniša Stanković" – National Institute of Republic of Serbia-University of Belgrade, Department of Physiology, Belgrade, Serbia;* [5] *Institute for Biological Research "Siniša Stanković" – National Institute of Republic of Serbia-University of Belgrade, Department of Biochemistry, Belgrade, Serbia;* [6] *Faculty of Medicine- University of Belgrade, Department of Psychiatry, Belgrade, Serbia;* [7] *Karolinska University Hospital, Karolinska Experimental Research and Imaging Center, Solna, Sweden;* [8] *Campbell Family Mental Health Research Institute, Centre for Addiction and Mental Health, Toronto- Ontario, Canada;* [9] *University of Toronto, Department of Pharmacology and Toxicology, Ontario, Canada;* [10] *University of Toronto, Department of Psychiatry, Ontario, Canada;* [11] *Karolinska Institutet, Section of Pharmacogenetics- Department of Physiology and Pharmacology, Stockholm, Sweden*

Background: Animal models are essential for understanding aetiology and pathophysiology of movement disorders. Previously, it had been found that mice transgenic for the human CYP2C19 gene, which is expressed in the liver and developing brain, exhibit altered neurodevelopment associated with impairments of their motor function and emotionality [1, 2]. The aim of this study was to characterize motoric phenotype of the CYP2C19 transgenic mouse and validate its potential usefulness as an animal model for ataxia.

Methods: Experiments were performed on CYP2C19 transgenic mice and control wild-type littermate mice. Body weight of mice was measured between the 21st and 42nd postnatal day. Mouse gait was analysed with footprint test [3] in young animals at four time points and once in adult mice. The maximal height of hindpaw elevation while walking was measured offline from the video footage of the footprint test. Motoric function was quantified by the rotarod and beam-walking tests. Structural differences in 20 brain regions of wild-type and transgenic mice were investigated with 9.4T gadolinium-enhanced postmortem neuroimaging. Antioxidative enzyme status was determined in the brain tissue in order to assess potential differences in the brain oxidative-antioxidative balance between wild-type and transgenic mice. When multiple brain regions or multiple antioxidant enzyme activities were analysed, p-values were FDR corrected for multiple comparisons.

Results: CYP2C19 transgenic (TG) animals exhibited approximately 5-10% reduced body weight (p=0.015) during 3rd and 4th postnatal week, while after postnatal day 31, the differences in the body weight were no longer statistically significant. The TG animals exhibited approximately two fold higher maximal hindpaw elevation in young (2.1-fold [CI95%: 2.0, 2.2], p<0.0001) and adult mice (1.9-fold [CI95%: 1.8, 2.1], p<0.0001), compared to wild-types. In the 5th postnatal week, all transgenic mice exhibited increase in elevation of both hindpaws, while after this point they gradually started exhibiting unilateral phenotype until almost all (49 of 51) animals became unilaterally affected in the adulthood. Footprint analysis and rotarod test did not detect significant differences (p>0.1) between TG and control mice in any of the analysed parameters, accounting for all examined time points. CYP2C19 transgenic mice exhibited 14% increase in beam crossing time (14%, [95%CI: 6.4, 22], p=0.0014) and 5.6-fold more paw-slips (p<0.0001, n=89) in the beam-walking test. CYP2C19 transgenic mice exhibited profound reduction in cerebellar volume (-11.8% [95%CI: -14.7, -9.0], q<0.0001, n=59) and moderate reduction in hippocampal volume (-4.2% [95%CI: -6.4%, -1.9%], q=0.015, n=59); compared to the corresponding volumes measured in WT mice. Superoxide dismutase activity was slightly increased (1.14-fold [CI95%: 1.06, 1.23], p=0.0010, q=0.023) in the cerebelli and moderately increased (1.3-fold, [CI95%: 1.18, 1.47], p<0.0001, q=0.0013) in the hippocampi of transgenic mice compared to wild-types, while glutathione reductase activity was significantly increased (1.2-fold [CI95%: 1.13, 1.35], p<0.0001, q=0.0021) in the hippocampi of TG mice.

Conclusions: Humanized CYP2C19 transgenic mice exhibit altered motoric function, functional motoric impairments and reduced cerebellar volume. CYP2C19 transgenic mice can be a useful tool for the studies focused on understanding the physiology of cerebellar development, as well as aetiology and pathophysiology of cerebellum-related disorders.

References

[1] Jukic, M.M., Opel, N., Strom, J., et al., 2017. Elevated CYP2C19 expression is associated with depressive symptoms and hippocampal homeostasis impairment. Mol. Psychiatry 22(8), 1155-1163. [2] Persson, A., Sim S.C., Virding, S., Onishchenko, N., Schulte, G., Ingelman-Sundberg, M., 2014. Decreased hippocampal volume and increased anxiety in a transgenic mouse model expressing the human CYP2C19 gene. Mol. Psychiatry 19(6), 733-741. [3] Wertman, V., Gromova, A., La Spada, A.R., Cortes, C.J., 2019. Low-Cost Gait Analysis for Behavioral Phenotyping of Mouse Models of Neuromuscular Disease. J. Vis. Exp. 149.

No conflict of interest

doi: https://doi.org/10.1016/j.nsa.2022.100236

P.0134

NEUROSCIENCE APPLIED 1 (2022) 100112 100237

Catatonia in Parkinson disease due to withdrawal of antiparkinsonian medications: a case report

Z. Uçar Hasanlı [1], E. Aslanbaba Bahadır [2], M.C. Akbostancı [2], E.T. Özel Kızıl [1]. [1] *Ankara University Faculty of Medicine, Department of Psychiatry, Ankara, Turkey;* [2] *Ankara University Faculty of Medicine, Department of Neurology, Ankara, Turkey*

Introduction: Catatonia is a neuropsychiatric syndrome with motor, cognitive, affective and autonomic symptoms. Catatonia is important because it is life-threatening and can improve dramatically with treatment. Parkinson's Disease (PD) is a disorder in with symptoms such as bradykinesia, tremor and rigidity due to dopaminergic neuron degeneration. In addition, psychiatric symptoms such as depression, anxiety, apathy, and impulsivity are also common. However, catatonia is quite rare in PD. We present a patient who developed catatonic symptoms after discontinuation of antiparkinsonian drugs (AD).

Case: A 58-year-old, male, deaf-mute patient who had PD applied to the emergency department with complaints of negativism, mutism, immobility, and to reject his medications. He had PD for about seven years. The treatment was levodopa+ carbidopa+entacapone combination 125/31.25/200 mg 4 times daily, rasagiline 1 mg/day, amantadine 200 mg/day, pramipexole 3 mg/day,