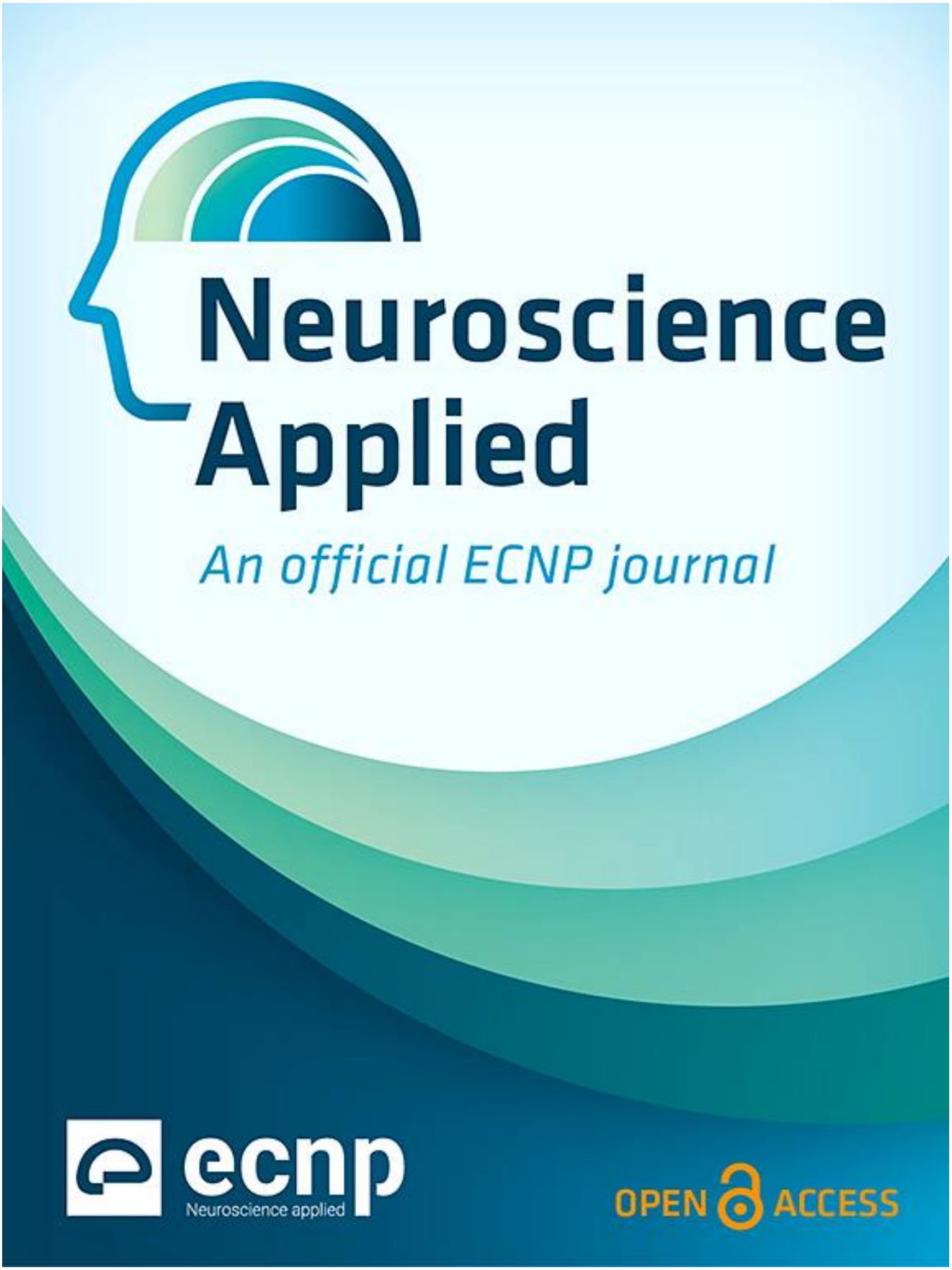
Neuroscience
Applied
An official ECNP journal
ecnp
Neuroscience applied
OPEN ACCESS

interventions. Mean differences (MD) and 95% confidence intervals (CIs) will be calculated for continuous outcomes. While for dichotomous data, odds ratios (OR) and 95% CIs will be calculated instead. Heterogeneity will be examined among the studies using tests for homogeneity (Cochran's Q test and I^2); $p \leq 0.10$ or $I^2 > 50\%$ is suggested as showing significant heterogeneity. Types of study included were comparative studies, which were designed as randomized controlled trials (including randomized cross-over studies, and cluster randomized trials) or quasi-experiment studies, or non-experimental observational studies (cohort, case-control). Y-BOCS version II (≥18 years) or CY-BOCS (6-17 years) were used as assessment instruments. A total of 15 studies were included (n=7 randomised controlled trials and n=8 open-label trials). The T-CBT group received interventions such as psycho-education, ERP, psychosocial interventions and cognitive restructuring. Interventions were technology-derived which can provide an online interaction (synchronous or asynchronous) for patients with OCD, including mobile apps, websites, computers, software, virtual reality application, video gaming. The comparison is the in-patient CBT in clinic/outpatient or another variant face-to-face setting.

Results: No significant differences emerged between T-CBT vs. CBTc in terms of efficacy. The heterogeneity of the methodologies of the selected studies as well as of the target population and the lack of complete data for each study did not allow a comparison of all study outcomes.

Conclusions: T-CBT could represent a valid alternative and/or complementary therapeutic option to CBTc. The amount of therapist assistance provided with T-CBT is a fraction of that provided in traditional face-to-face CBT, leading to significant cost-effectiveness.

No conflict of interest

doi: https://doi.org/10.1016/j.nsa.2022.100761

P.0734

NEUROSCIENCE APPLIED 1 (2022) 100112 100762

Working memory among children following acquired head injuries: parents' and teachers' reports and performance-based test

I. Aberdam [1], Y. Stukalin [1], A. Granat [2]. 1Tel Aviv-Yaffo Academic College, Behavioral Sciences, Tel-Aviv, Israel; 2Loewenstein Hospital Rehabilitation Center, The psychology and Neuropsychology, Raanana, Israel

Introduction: Collecting information from parents, teachers and performance-based tests following acquired brain injury (ABI) provides significant clinical value for rehabilitation plans and diagnostic processes. However, there is a lack of knowledge regarding the differences between the various types of assessment tools in examining working memory among children following ABI. The main purpose of the current study was to compare different measurement tools in the evaluation of working memory among children following acquired brain injury. The study focused on working memory functions given the importance of this function in childhood learning and social processes. Previous studies suggest that working memory difficulties after acquired brain injury are common [1, 2]. However, most of the studies focused on only one measurement method. It is important to understand if objective tools such as performance-based tests differ from subjective tools such as caregivers' reports such that each provides a unique perspective for a more comprehensive evaluation. To the best of our knowledge, no study has been conducted yet comparing parents' and teachers' reports with performance-based tests for working memory among children following acquired brain injury. Hence, the current study was designed to explore Working memory of children following acquired brain injury using several assessment tools. This comparison may yield new information compared with studies using one single tool.

Methods: A sample of 66 triads of child (after ABI), parent and teacher were studied. Parents and teachers completed the Behavior Rating Inventory of Executive Function (BRIEF) and children completed a performance-based test of Working Memory Index from the WISC-IV. A Pearson correlation test was conducted to assess the relationship between parents' and teachers' reports and the child's score. In addition, a one-way ANOVA with repeated measures was conducted to determine whether the WM differed between the rating and performance-based test.

Results: Working memory of children following acquired brain injury is lower compared to population norms according to parents' reports (M=62.77, SD=11.761), teachers' reports (M=65.48, SD=14.464) and Working Memory Index scores (M=89.39, SD=16.002). In addition, a significant relationship was found between Working Memory Index scores and both teachers' reports ($r(64)=0.283$, $p<0.05$) and parents' reports ($r(64)=0.261$, $p<0.05$), such that the more problems teachers and parents reported, the more children exhibited working memory problems according to a performance-based test. In addition, working memory is found to be more impaired when measured by the parents' reports and teachers' reports compared to a performance-based test. No such differences were observed between parents' and teachers' reports.

Conclusions: The current study underscores the importance of collecting information from both questionnaires and performance-based measures when evaluating working memory among children following ABI. The working memory of children following ABI is better on structured environment as reflected by performance-based test than on real-world settings, as reflected in the reports. Diagnostic processes should be sensitive to the differences that arise from the method of measurement.

References

[1] Dunning, D. L., Westgate, B., & Adlam, A.-L. R., 2016. A meta-analysis of working memory impairments in survivors of moderate-to-severe traumatic brain injury. Neuropsychology, 30(7), 811–819. [2] Eve, M., O'Keeffe, F., Jhuty, S., Ganesan, V., Brown, G., & Murphy, T., 2016. Computerized Working-Memory Training for Children Following Arterial Ischemic Stroke: A Pilot Study With Long-Term Follow-Up. Applied Neuropsychology: Child, 5(4), 273–282.

No conflict of interest

doi: https://doi.org/10.1016/j.nsa.2022.100762

P.0735

NEUROSCIENCE APPLIED 1 (2022) 100112 100763

Association between CYP2C19 genotype and body weight with escitalopram exposure – a cross sectional study

A. Jeremic [1], P. Vukovic [1,2], M. Vezmar [2], D. Pesic [3,4], J. Drakulic [2], F. Milosavljevic [1], C. Miljevic [4,5], B. Markovic [6], N. Maric Bojovic [4,7], M. Jukic [1,8]. 1University of Belgrade - Faculty of Pharmacy, Department of Physiology, Belgrade, Serbia; 2Institute for Mental Health, Clinic for adults, Belgrade, Serbia; 3Institute for Mental Health, Clinic for children and adolescents, Belgrade, Serbia; 4University of Belgrade - Faculty of Medicine, Department of Psychiatry, Belgrade, Serbia; 5Institute for Mental Health, Department for pharmaceutical services and laboratory diagnostics, Belgrade, Serbia; 6University of Belgrade - Faculty of Pharmacy, Department of Pharmaceutical Chemistry, Belgrade, Serbia; 7Institute for Mental Health, Department for research and education, Belgrade, Serbia; 8Karolinska Institutet, Pharmacogenetics section- Department of Physiology and Pharmacology, Solna, Sweden

Background: Depression causes significant burden to the society world-wide. Escitalopram is a commonly prescribed antidepressant, predominantly metabolized by the polymorphic CYP2C19 enzyme; however, this drug isn't always effective [1]. The CYP2C19 genotype determines the CYP2C19 enzymatic capacity and CYP2C19*2 is the main loss-of-function (Null) allele [2]. In the most psychiatric clinics worldwide, escitalopram therapy usually starts with the standard recommended dose of 10 mg/day, regardless of CYP2C19 genotype [3]. The objective of this study was the quantification of difference in the escitalopram exposure among patients between genetically associated CYP2C19 slow and normal metabolizers, considering also the body weight [4].

Methods: In this ongoing prospective cross sectional study, the drug concentration was measured in 53 outpatients treated with 10 mg of escitalopram, 2 weeks after treatment initiation, 24 hours after the last dose. Measured plasma concentration was 25-50 ng/ml was considered the ideal drug exposure. [5] If the drug concentration was 5-25 ng/ml, patients were classified as underdosed/underexposed, while patients with drug concentration <5ng/ml were classified as non-compliers and excluded from the further analysis. Patients were genotyped by polymerase chain reaction–based assay for the CYP2C19*2 allele. All participants were included from the Institute for Mental Health in Belgrade outpatient clinic and daily hospital. The patients were classified based on their CYP2C19 genotype; those carrying CYP2C19*2 variant alleles were categorized into slow metabolizer group, while non-carriers were categorized into normal metabolizer group. Difference in body weight and age between slow and metabolizer groups was analysed by the Mann-Whitney's test. The effects of CYP2C19 metabolizer category (normal vs. slow metabolizer) and body weight on escitalopram plasma level were evaluated by the linear regression model.

Results: Out of 53 outpatients, who completed the study to date, 24 participants were slow metabolizers and 29 participants were normal metabolizers. After two weeks of treatment with 10mg of escitalopram, only 13 patients (24%) were

within the therapeutic range (25-50ng/ml), no patient was underexposed, while the remaining 40 patients were underexposed. Median age body weight in the slow metabolizers group were 41 years [IQR: 27-47] and 77kg [IQR: 65-88,5], while in normal metabolizers group age and body weight were 35 years [IQR: 22-49] and 66kg [IQR: 59-88]. The drug level increase due to lower body weight and due to occurrence of CYP2C19*2 allele observed in the regression equation did not reach statistical significance.

Conclusion: While the result directionality was in accordance with the previously published studies, the effects of body weight and CYP2C19*2 allele occurrence were not significant in the analysed cohort. The absence of significant effects was likely due to still limited power of the study. Since this interim analysis includes only approximately one third of patients compared with what had been originally planned, it is expected that firmer conclusions related to the combined effect of CYP2C19 genotype and body weight on escitalopram exposure will emerge after all planned patients are included.

References

[1] Jukic, MM., Haslemo, T., Molden, E., Ingelman-Sundberg, M., 2018. Impact of CYP2C19 Genotype on Escitalopram Exposure and Therapeutic Failure: A Retrospective Study Based on 2,087 Patients. Am J Pcychiatry. 175(5), 463-70. [2] Goldstein, JA., Blaisdell, J., 1996. Genetic tests which identify the principal defects in CYP2C19 responsible for the polymorphism in mephenytoin metabolism. Methods Enzymol. 272, 210–218. [3] Hicks, J. K., Bishop, J. R., Sangkuhl, K., Müller, D. J., Ji, Y., Leckband, S. G., Leeder, J. S., Graham, R. L., Chiulli, D. L., LLerena, A., Skaar, T. C., Scott, S. A., Stingl, J. C., Klein, T. E., Caudle, K. E., Gaedigk, A., 2015. Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2D6 and CYP2C19 genotypes and dosing of selective serotonin reuptake inhibitors. Clin Pharmacol Ther. 98, 127–134. [4] Jin, Y., Pollock, BG., Frank, E., Cassano, GB., Rucci, P., Müller, DJ., Kennedy, JL., Forgione, RN., Kirshner, M., Kepple, G., Fagiolini, A., Kupfer, DJ., Bies, RR., 2010. Effect of age, weight, and CYP2C19 genotype on escitalopram exposure. J Clin Pharmacol. 50(1), 62-72. [5] Heimke, C., 2019. Concentration-Effect Relationships of Psychoactive Drugs and the Problem to Calculate Therapeutic Reference Ranges. Ther Drug Monit. 41(2), 174-9.

No conflict of interest

doi: https://doi.org/10.1016/j.nsa.2022.100763

P.0736

NEUROSCIENCE APPLIED 1 (2022) 100112 100764

Differential effects of repeated treatment with DOI and psilocybin on the head-twitch response (HTR), locomotor activity and anxiety-like behaviour

E. Stojek [1], J. Prenderville [1], F. Dunphy-Doherty [1]. 1Transpharmation, Ireland, Dublin, Ireland

Serotonin 5-HT2A receptors are widely distributed in the central nervous system and are thought to mediate the effects of psychedelic drugs. The 5-HT2A receptor has been identified as a potential therapeutic target for a number of psychiatric disorders, including anxiety and major depressive disorder (MDD). The aim of the present study was to investigate the effects of repeated administration of the psychedelic drugs DOI and psilocybin at two different treatment timepoints; 0h and 48h. For this purpose, we examined the head twitch response (HTR) which is widely used as a behavioural assay for 5-HT2A activation associated with rapid side-to-side rotational head movement. Locomotor activity and anxiety-like behaviour were also assessed in the open field.

Male C57BL/6J mice (n=56) were habituated to an open field arena (29cm x 36cm x 16cm) 30 minutes prior to testing. The mice received a single i.p. injection of either saline, DOI (0.5 mg/kg or 1 mg/kg), or psilocybin (0.3 mg/kg, 1 mg/kg, 3 mg/kg or 5 mg/kg). Immediately post-treatment the mice were placed back in the test cage for 30 minutes. To assess HTR, the mice were observed for 20 minutes (n=4 per group). Mice were recorded using AnyMaze software for 30 mins to assess the effects of DOI and psilocybin on locomotor activity (m) and time (s) spent exploring the centre of the arena (n=7-8 per group). The above protocol was repeated 48h later to assess the effects of repeated treatment with either DOI or psilocybin on HTR, locomotor activity and time spent exploring the centre. One-way ANOVA was used for statistical analysis and an alpha level of 0.05 was used as a criterion for statistical significance.

Administration of DOI and psilocybin at all doses resulted in a significant increase in the number of head twitches at both time points (0h and 48h). DOI (0.5 mg/kg) significantly increased locomotor activity after the first treatment ($p < 0.05$) but not at subsequent 48h treatment. Furthermore, the 5 mg/kg dose of psilocybin reduced mobility after the first treatment ($p < 0.05$) but not at subsequent 48h treatment. It was observed that after the first treatment psilocybin at 3 mg/kg ($p < 0.01$) and 5 mg/kg ($p < 0.0001$) resulted in a significant reduction in time spent exploring the centre of the arena. After the second treatment (48h) DOI 0.5 mg/kg ($p < 0.05$), 1 mg/kg ($p < 0.05$) and psilocybin 1 mg/kg ($p < 0.01$), 3 mg/kg ($p < 0.01$) and 5 mg/kg ($p < 0.0001$) resulted in a significant reduction in the time spent exploring the centre.

A significant increase in HTR was observed following treatment of DOI and psilocybin at the 0h and 48h time points, indicating that repeated exposure to the compounds at these doses did not decrease the 5HT2A receptor response. Conversely, there were differences in locomotor activity and anxiety-like behaviour between first and second exposure to DOI and psilocybin. Taken together, this data suggest that prior exposure to DOI and psilocybin influences behavioural changes induced by the subsequent administration, which may have implications for clinical use.

No conflict of interest

doi: https://doi.org/10.1016/j.nsa.2022.100764

P.0737

NEUROSCIENCE APPLIED 1 (2022) 100112 100765

Effects of personalized dosing based on drug plasma level quantification on effectiveness and safety of escitalopram treatment

P. Vuković [1,2], A. Jeremić [1], M. Vezmar [2], D. Pešić [3,4], J. Drakulić [2], F. Milosavljević [1], Č. Miljević [4,5], N. Marić Bojović [4,6], M. Jukić [1,7]. 1University of Belgrade - Faculty of Pharmacy, Department of Physiology, Belgrade, Serbia; 2Institute of Mental Health, Adult Clinic, Belgrade, Serbia; 3Institute of Mental Health, Clinic for children and youth, Belgrade, Serbia; 4University of Belgrade - Faculty of Medicine, Department of Psychiatry, Belgrade, Serbia; 5Institute of Mental Health, Clinical Studies Cabinet, Belgrade, Serbia; 6Institute of Mental Health, Service for scientific research and educational activities, Belgrade, Serbia; 7Karolinska Institutet, Pharmacogenetics section - Department of Physiology and Pharmacology, Solna, Sweden

Background: Considering the negative impact of anxiety and depression on society and lack of emergence of new antidepressants, it is of paramount importance to utilize the available treatment options in the best manner possible. Escitalopram is a commonly prescribed antidepressant that is predominantly metabolized by the polymorphic CYP2C19 liver enzyme and consequently, CYP2C19 genotype affects escitalopram metabolism. Previous report showed a strong association between CYP2C19 genotype and escitalopram exposure [1]; therefore, CYP2C19 genotype is a potentially clinically relevant feature in escitalopram treatment, since underdosed patients exhibit lower escitalopram treatment effectiveness [2] and since escitalopram adverse drug reactions (ADR) are dose dependent [3]. Objective of this prospective cohort clinical trial is to evaluate the impact of escitalopram dose adjustment based on escitalopram exposure on treatment efficacy and safety.

Methods: In this prospective cohort study patients suffering from depression were assessed for potential clinical benefits of a personalized dosing regimen for escitalopram, which is based on therapeutic drug monitoring of escitalopram plasma level. Treatment effectiveness was evaluated based on Hamilton depression rating scale (HAM-D), which was performed one day prior to escitalopram treatment initiation (Baseline, Visit 0), as well as after four (Visit 1) and eight (Visit 2) weeks of follow-up. Side effect assessment was based on Scandinavian UKU Side effects rating scale, which was performed at V1 and V2. In case of need, dose adjustment was performed at V1 and was guided by the measured steady state drug plasma level using HPLC two weeks after treatment initiation, with the aim to achieve the optimal exposure to escitalopram in every patient at V2. Relative change in HAM-D and UKU scale readouts from V1 to V2, were compared between comparator (dose was adjusted) and control (dose was not adjusted) groups by independent samples t-test and Chi-square test, respectively. The study protocol in full detail is available on clincaltrials.gov [4]

Results: To this day, 25 participants completed the study, and out of these, 19 participants required dose adjustment between visits. There were no statistically significant differences in the change in HAM-D scores from V1 to V2 between groups ($p>0.1$). In the comparator group, 11/19 patients reported ADRs, compared to 2/6 patients in control group. Appearance of new, or worsening of