in Individuals With Mood and Other Common Mental Disorders in Ontario, Canada. JAMA Network Open. 2020;3(10):e2020213. doi:10.1001/jamanetworkopen.2020.20213 [2] Grillault Laroche D, Godin O, Dansou Y, et al. Influence of childhood maltreatment on prevalence, onset and persistence of psychiatric comorbidities and suicide attempts in bipolar disorders. Eur Psychiatry. Published online January 21, 2022:1-32. doi:10.1192/j.eurpsy.2022.7 [3] Nanni V, Uher R, Danese A. Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. Am J Psychiatry. 2012;169(2):141-151. doi:10.1176/appi.ajp.2011.11020335 [4] Teicher MH, Samson JA, Anderson CM, Ohashi K. The effects of childhood maltreatment on brain structure, function and connectivity. Nature Reviews Neuroscience. 2016;17(10):652-666. doi:10.1038/nrn.2016.111 [5] Pfaltz MC, Halligan SL, Haim-Nachum S, et al. Social Functioning in Individuals Affected by Childhood Maltreatment: Establishing a Research Agenda to Inform Interventions. PPS. Published online April 5, 2022:1-14. doi:10.1159/000523667

Conflict of interest

Disclosure statement:
This work was financially supported by a Spanish grant FIS PI17/00941 from Instituto de Salud Carlos III (ISCIII).

doi: https://doi.org/10.1016/j.nsa.2022.100229

P.0127

NEUROSCIENCE APPLIED 1 (2022) 100112 100230

Impact of COVID-19 on german treatment numbers of patients with depression – a gap in care for the mentally ill?

M. Aichholzer [1], C. Schiweck [1], A. Reif [1], S. Edwin Thanarajah [1]. [1] *University Hospital Frankfurt- Goethe University, Department for Psychiatry- Psychosomatic Medicine and Psychotherapy, Frankfurt am Main, Germany*

Background: The Covid-19 pandemic and the restrictions of daily life have been a major challenge for mental health. The number of newly diagnosed cases of depression and anxiety has increased worldwide [1,2] and patients with known psychiatric conditions experienced a worsening of symptoms [3]. At the same time, psychiatric care was limited by safety regulations and constraints of the health care system, that became more evident during the pandemic.
Aims: With this study we aimed to investigate whether in- and outpatient care of patients with first depressive episode and major depressive disorder (MDD) was impacted during the Covid-19 pandemic in Germany.
Methods: Nationwide data was extracted from the database of the German Institute for Hospital Remuneration System, a state agency that registers anonymized inpatient numbers and provide public access for the years 2020 and 2021. We tested changes in inpatients numbers (children and adults) for theses two years in relation to the nationwide Covid-19 incidence rate retrieved from the Robert-Koch-Institute. Since these data neither allow a comparison with pre-covid years nor give an insight into outpatient care, we investigated the cases at our department for the same period in comparison to 2019. The change in patient numbers in Frankfurt across all months for 2020 and 2021 in comparison to 2019 were tested in a one-way ANOVA after checking for normal distribution. The Dunnett's multiple comparisons test was conducted post-hoc.
Results: The nationwide numbers of Covid-19 cases and depressive inpatients showed opposing courses throughout 2020 and 2021 for both children and adults. During the first Covid wave in April 2020, the number of treated patients with 1) a first-time depressive episode decreased by 57.5% and 2) a recurrent depressive disorder decreased by 56.3% in comparison to January 2020. In our department, the number of inpatients with MDD significantly decreased in 2020 (adj. $p<0.0001$, 95% CI 12.20-29.30) as well as 2021 (adj. $p<0.0001$, 95% CI 12.54-29.63) compared to the pre-covid year 2019. The average numbers of patients treated with first episode depression remained the same across the years, but we saw a clear drop during every Covid-19 wave. The average number of outpatients treated for MDD and first episode remained unchanged during the pandemic. However, while MDD numbers declined during every wave, the number of first episode patients raised in parallel to the Covid incidence rate.
Conclusion: Our data exhibit that depressive patients, especially at times of high covid-19 infection rates, are less frequently tended for as inpatients. The data from Frankfurt demonstrates, that particularly MDD patients were significantly less often treated on a psychiatric ward during the pandemic, while the numbers of first episode patients remained the same. MDD patients seem to have withdrawn themselves more instead of seeking adequate help, which was facilitated by the safety regulations. These data highlight a disadvantage for people with depression during the pandemic and show the immense need for an improved care structure.

References

[1] Lakhan, R., Agrawal, A., Sharma, M., 2020. Prevalence of depression, anxiety, and stress during COVID-19 pandemic. Journal of Neurosciences in Rural Practice 11, 519–525. doi:10.1055/s-0040-1716442 [2] Salari, N., Hosseinian-Far, A., Jalali, R., Vaisi-Raygani, A., Rasoulpoor, S., Mohammadi, M., Rasoulpoor, S., Khaledi-Paveh, B., 2020. Prevalence of stress, anxiety, depression among the general population during the COVID-19 pandemic: A systematic review and meta-analysis. Globalization and Health 16. doi:10.1186/s12992-020-00589-w [3] Vindegaard, N., Benros, M.E., 2020. Covid-19 pandemic and Mental Health Consequences: Systematic review of the current evidence. Brain, Behavior, and Immunity 89, 531–542. doi:10.1016/j.bbi.2020.05.048

Conflict of interest

Disclosure statement:
Carmen Schiweck, Mareike Aichholzer, Sharmili Edwin-Thanarajah have no conflict of interest to declare. Andreas Reif received speaker's honoraria, and / or served on advisory boards, from Shire/Takeda, Medice, Janssen, Servier, and SAGE.

doi: https://doi.org/10.1016/j.nsa.2022.100230

P.0128

NEUROSCIENCE APPLIED 1 (2022) 100112 100231

eIF2α pathway underlies ketamine antidepressant action in an endoplasmic reticulum stress model

L. Miquel Rio [1,2,3], U. Sarriés-Serrano [1,2,3], V. Paz [1,2,3], L. Campa [1,2,3], A. Bortolozzi [1,2,3]. [1] *Institute of Biomedical Research of Barcelona- Spanish National Research Council, Neuroscience and Experimental Therapeutics, Barcelona, Spain;* [2] *August Pi i Sunyer Biomedical Research Institute, Clinical and experimental neuroscience, Barcelona, Spain;* [3] *Mental Health Networking Biomedical Research Centre, Systems Neuropsychopharmacology, Madrid, Spain*

Background: Depression is a devastating mood disorder that causes profound disability worldwide. Social and environmental stressors are essential factors involved in the underlying pathophysiology of depression. Moreover, neuroimaging studies reported both morphological and functional changes in susceptible brain regions of depressed patients, raising the possibility of altered cellular homeostasis whose mechanisms are not yet fully understood. The endoplasmic reticulum (ER), an indispensable sub-cellular component of eukaryotic cells, performs essential functions for organism survival. Indeed, the ER stress and unfolded protein response (UPR) represent a cellular response to environmental and/or emotional stress situations and have shown to be active in both depressive-like animal models as well as in post-mortem brains of depressed individuals [1,2]. Here we have tested the hypothesis that ER stress and UPR pathway overactivation in raphe serotonin (5-HT) neurons are involved in the cellular pathological mechanisms of anxiety and depression by causing altered protein homeostasis. We also propose the critical role of the eIF2α pathway for the antidepressant actions of ketamine.
Methods: Depressive-like mouse models were generated using lipopolysaccharide (0.83 mg/kg, i.p.) or a combination of chronic corticosterone exposure (7.5 mg/ml, oral) plus restraint (2 h/day). ER stress model was obtained by a single local application of tunicamycin (200 ng/μl) in the raphe nuclei of mice. 24 h after administration, tunicamycin-treated mice received a single dose of ketamine (10 mg/kg, i.p.), and its antidepressant effects were evaluated 30 min and 2 days later. Expression of ER markers and UPR pathway proteins, including BIP, GRP94, CHOP, p-eIF2a, and p-eEF2 were assessed by Western blot (WB). Moreover, we examined neuroplasticity gene expression (e.g. BDNF, TrkB) and the cellular activity marker Egr-1 in interconnected brain regions by in situ hybridisation. Anxiety- and depression-like behaviours, as well as serotonin function, were also assessed. Statistical analysis was performed by t-test and one-way or two-way ANOVA, as appropriate.
Results: Local infusion of tunicamycin into raphe nuclei rapidly and efficiently induced ER stress in 5-HT neurons, leading to a time-dependent increase in BIP protein level ($p<0.01$). Furthermore, CHOP protein level, which triggers apoptosis pathways, was increased 7 days after tunicamycin infusion. ER stress led to an increased eIF2α and eEF2 phosphorylation ($p<0.05$), suggesting activation of the PERK pathway in 5-HT neurons. Similar results were found in depressive-like mouse models based on acute LPS administration or chronic corticosterone exposure plus restraint, leaving significant increases in phosphorylation of eIF2α and eEF2 proteins in raphe nuclei. Tunicamycin-treated mice exhibited an anxious-depressive phenotype and showed impaired cortical