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Background: Low-grade inflammation is associated with an increased risk of depressive episodes in the general population[1]. The molecular links remain elusive but earlier studies suggest that pro-inflammatory cytokines gain access to the brain and modulate key pathophysiology of importance in Major Depressive Disorder (MDD), including serotonin signalling[2, 3]. Brain imaging with $[^{11}]$C-SB207144 Positron Emission Tomography (PET) of the serotonin 4 receptor (5-HT4R) has proven to be an interesting tool to assess serotonergic pathophysiology in MDD as we have shown that depressed patients have lower 5-HT4R non-displaceable binding level (BPND) compared to healthy controls[4]. So far, no studies have evaluated if low-grade inflammation is related to serotonin signalling, in terms of the 5-HT4R brain binding, in the healthy state.

Aims: The aim of this project is to determine if low-grade inflammation in terms of subtle elevation of high-sensitivity CRP (hsCRP) maps onto 5-HT4R brain binding in healthy individuals.

Methods: $[^{11}]$C-SB207145 PET imaging data were available from the Center for Integrated Molecular Brain Imaging (Cimbi) database[5] for 120 healthy individuals, of which 5 were excluded due to potentially acute infection defined as hsCRP$>$10mg/L or use of immunomodulating drugs. 115 individuals (66 women, 49 men) were eligible for the study with a mean age of 29.4(±12.6) years. HsCRP was determined from stored serum and analysed by a latex particle-based immunoassay turbidimetry method (detection limit 0.30-20mg/L). Coefficient of variance was maximum 4% for measurements of approximately 7mg/L and maximum 7% for lower measures of approximately 0.6mg/L. The association between hsCRP and log-transformed 5-HT4R BPND values in specific regions of interest (neostriatum, hippocampus, and neocortex) was evaluated using multiple linear regression models adjusted for age, BMI, serotonin transporter genotype variant status (5-HTTLPR L/L vs non-L/L), and injected $[^{11}]$C-SB207145 mass per kg bodyweight.

Results: We found no association between hsCRP and SHT-R BPND (log-scaled); neostriatum (-0.009, CI [-0.03:0.01], p=0.46), hippocampus (-0.02, CI [-0.04:0.003], p=0.10), neocortex (-0.002, CI [-0.03:0.02], p=0.86). In post hoc analyses, we observed a negative association between BPND and hsCRP only in the interval of hsCRP below 1.5mg/L (n=82), in all regions of interest: neostriatum (-0.16, CI [-0.27:-0.02], p=0.03), hippocampus (-0.13, CI [-0.25:-0.01], p=0.03), neocortex (-0.24, CI [-0.38:-0.10], p=0.001). P-values are uncorrected.

Conclusion: Overall, we found no statistically significant linear association between hsCRP and SHT-R BPND in neostriatum, hippocampus and neocortex in healthy individuals. Yet, in the very low span of hsCRP below 1.5mg/L, hsCRP appeared to be negatively associated with SHT-R brain binding in all three regions. We interpret this post hoc finding with caution. However, if replicated, we speculate if the lower end of the low-grade inflammation spectrum may reflect more stable levels of CRP, independent of recent transient dynamic changes in CRP, and therefore capture an association with serotonergic brain architecture, perhaps a coupling established early in brain development. Future studies must illuminate if low-grade inflammation is associated with serotonergic function (or treatment mechanisms) in the depressed state or in groups of particular high-risk for depression, e.g., individuals exposed to early life trauma.

No conflict of interest

References

[1] Wiium-Andersen, M.K., Ørsted, D.D., Nielsen, S.F., Nordestgaard, B.G., 2013. Elevated C-Reactive Protein Levels, Psychological Distress, and Depression in 73 131 individuals. JAMA Psychiatry 70, 176.

[2] Dhabhar, F.S., Burke, H.M., Epel, E.S., Mellon, S.H., Rosser, R., Reus, V.I., Wolfkowitz, O.M., 2009. Low serum IL-10 concentrations and loss of regulatory association between IL-6 and IL-10 in adults with major depression. Journal of Psychiatric Research 43, 962-969.

[3] Miller, A.H., Maletic, V., Raison, C.L., 2009. Inflammation and Its Discontents: The Role of Cytokines in the Pathophysiology of Major Depression. Biological Psychiatry 65, 732-741. doi:10.1016/j.biopsych.2008.11.029.

[4] Koehler-Forsberg, K., Jorgensen, A., Vinther, S., Poulsen, A., Landman, E., Florescu, A.M., Jorgensen, M.B., Frokjaer, V.G., Knudsen, G.M., 2020. P:310 Patients with major depressive disorder have lower cerebral serotonin 4 receptor binding than healthy controls. European Neuropsychopharmacology 31. doi:10.1016/j.euroneuro.2019.12.073.

[5] Knudsen, G.M., Jensen, P.S., Erritzoe, D., Baaré, W.F.C., Ettrup, A., Fisher, P.M., Gillings, N., Hansen, H.D., Hansen, L.K., Hasselbalch, S.G., Henningsson, S., Herth, M.M., Holst, K.K., Iversen, P., Kessing, L.V., Macoveanu, J., Madsen, K.S., Mortensen, E.L., Nielsen, F.A., Paulson, O.B., Siebner, H.R., Stenbæk, D.S., Svarer, C., Jennig, T.L., Strother, S.C., Frokjaer, V.G., 2016. The Center for Integrated Molecular Brain Imaging (Cimbi) database. Neuroimage 124, 1213-1219. doi:10.1016/j.neuroimage.2015.04.025.

P.0431 SARS-CoV-2 neuropsychiatric pathogenic mechanisms - a case report of delirium with psychotic symptoms as sole manifestation in SARS-CoV-2 positive patient

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Background: SARS-CoV-2 is a severe acute respiratory syndrome which generates a wide spectrum of clinical presentations. Fever, gastrointestinal and upper respiratory symptoms are among the most common initial manifestations reported [1]. However, neuropsychiatric symptoms are also frequent, and in some cases, these can remain as sole manifestation of the infection [2]. We report a case of a 53-year-old woman with delirium with psychotic component, comitant with SARS-CoV-2 infection, with no other associated symptoms. We aim to discuss the mechanisms through which SARS-CoV-2 affects the Central Nervous System (CNS), highlighting the heightened possibility of such occurrence, even in the absence of risk factors for neurological disease.

Methods: Description of a clinical case and review of the literature on the subject.

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Results: E. a married 53-year-old woman with no background of medical illness, was brought to the psychiatric emergency room for a case of disorganized behavior with acute onset. Mental state evaluation revealed altered level of consciousness, distractibility, incoherent speech, poorly structured persecutory delusional beliefs, auditory hallucinations and sleep maintenance insomnia. Clinical history and examination revealed no other neurological as well as gastrointestinal and respiratory symptoms or signs. Diagnosis of delirium was confirmed using Confusion Assessment Method (CAM) Diagnostic Algorithm. Laboratory investigation revealed leukocytosis and elevation of creatinine-kinase and lactate-dehydrogenase. Electroencephalogram exhibited an unspecified grade 1/5 encephalopathy. No significant changes were found in chest X-ray, brain CT-scan or lumbar puncture. Hospitalization was proposed, aiming diagnostic investigation and clinical stabilization. According to institutional norms at the time, prior screening for SARS-CoV-2 was performed, with the RT-PCR test result coming positive. Cerebral spine fluid was not tested for SARS-CoV-2. E. was medicated with olanzapine 5mg id and was discharged eight days later, fully recovered from her neuropsychiatric symptoms, and exhibiting no other clinical manifestations of SARS-CoV-2 in the meantime.

Conclusions: We report the case of a delirium as a sole manifestation of SARS-CoV-2 infection. The presence of symptoms such as delusional beliefs and hallucinations should be interpreted as features of delirium manifestation, instead of SARS-CoV-2-induced psychosis [3]. Direct and indirect mechanisms of SARS-CoV-2 CNS disturbance have been proposed in scientific literature, such as neuronal invasion and cytokine storm, respectively [4]. In our case, implication of SARS-CoV-2 in delirium etiology is suggested by the temporal relationship between the two and the absence of other possible causes found for this clinical presentation. E.’s absence of risk factors for delirium (such as old age or other medical conditions), as well as the absence of any other symptomatology during the course of this disease, both suggest that SARS-CoV-2 poses a particular risk of CNS damage when compared to other respiratory viruses. Thus, in current pandemic times, the sheer presence of delirium should encourage screening of a SARS-CoV-2 infection, even in the absence of other symptoms [1]. Further studies are needed to understand the mechanisms by which SARS-CoV-2 infection affects the CNS.

No conflict of interest

References

[1] Alkeridy, W.A., Almaghlouth, I., Alrashed, R., Alayed, K., Binkhamis, K., Alsharidi, A., Liu-Ambrose, T., 2020. A Unique Presentation of Delirium in a Patient with Otherwise Asymptomatic COVID-19. Journal of the American Geriatrics Society 68, 1382-1384.
[2] Ticinesi, A., Cerundolo, N., Parise, A., Nouvenne, A., Prati, B., Guerra, A., Lauretani, F., Maggio, M., Meschi, T., 2020. Delirium in COVID-19: epidemiology and clinical correlations in a large group of patients admitted to an academic hospital. Aging Clinical and Experimental Research 32, 2159-2166.
[3] Watson, C.J., Thomas, R.H., Solomon, T., Michael, B.D., Nicholson, T.R., Pollak, T.A., 2021. COVID-19 and psychosis risk: Real or delusional concern? Neuroscience Letters 741, 135491. doi:10.1016/j.neulet.2020.135491.
[4] Beach, S.R., Praschan, N.C., Hogan, C., Dotson, S., Meredeth, F., Kontos, N., Frichione, G.L., Smith, F.A., 2020. Delirium in COVID-19: A case series and exploration of potential mechanisms for central nervous system involvement. General Hospital Psychiatry 65, 47-53. doi:10.1016/j.genhospsych.2020.05.008.

do: 10.1016/j.euroneuro.2021.10.404

P.0432
Is neuroinflammation the missing link between depression and dementia?

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Background: Later life depression symptomatology differs from that seen in younger adults and the underlying pathology may also differ. The evidence for neuroinflammation playing a role in depression causation is building in younger adults. Aging has been associated with higher levels of plasma pro-inflammatory cytokines.

Depression has been identified as a potentially modifiable risk factor for the development of dementia, but whether it is a risk factor or an early sign of a developing dementia remains unclear. Neuroinflammation is increasingly recognised as a key part of Alzheimer’s Disease neuropathology.

Depression has been shown in several cohorts from mid-life onwards to affect performance on cognitive tests, but the mechanism of this and whether it is merely a state effect is unknown. It is possible that depression may exert its effect on increased risk of dementia via increased neuroinflammation.

Aims To investigate the link between depression, inflammation and dementia. We hypothesised that recurrent depression has adverse effects on performance in cognitive tests in middle to older age and that this effect is modified by anti-inflammatory medication.

Methods: We identified UK based cohort studies available via Dementia Platforms UK which included individuals aged over 50, medical history, details of prescribed medications, results from detailed cognitive testing and had used reliable measures to assess depression. No specific ethical approval was required for this secondary analysis of existing data.

In this abstract we report our results for UK Biobank which administered bespoke, non-standardised cognitive tasks. Individuals with recurrent depression had at least episodes of depression and had sought treatment. Controls had no history of depression. The presence/absence of inflammatory illness was assessed using a standardised list of inflammatory conditions.

Individuals with dementia, chronic neurological conditions and chronic psychotic disorders were excluded. A range of possible confounders e.g. age, gender, BMI, smok-