TMS-EEG indexes abnormal GABAergic signalling in patients with schizophrenia

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Aims. Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation tool designed to probe the strength of inhibitory and excitatory neurotransmission in the cortex. Combined with electromyography, paired-pulse TMS paradigms have revealed a deficit in inhibition mediated by GABA-A receptors in patients with schizophrenia. Combined TMS-electroencephalography (TMS-EEG) provides a more detailed examination of cortical excitability and may shed more light into the pathophysiology of schizophrenia. Of the various peaks of the TMS-evoked EEG signal, responses at 45 (N45) and 100 ms (N100) likely reflect GABA-A and GABA-B receptor-mediated inhibition, respectively. Responses at 25 ms (P25) are affected by voltage-gated channel ligands, whereas glutamatergic processes may be related to the P70 component. We here aim to systematically investigate the role of these neural processes in patients with schizophrenia by using TMS-EEG.
Method. TMS-evoked EEG potentials (TEPs) were recorded in patients with schizophrenia (n = 19) and in age-matched healthy controls (n = 17). 150 TMS pulses at 90% of resting motor threshold were applied over the left primary motor cortex during EEG recording. Differences in TEPs between the two groups were analysed for all electrodes and for time windows corresponding to each TEP (P25: 0.015-0.035 ms; N45: 0.035-0.06 ms; P70: 0.035-0.06 ms; N100: 0.09-0.14ms) by applying multiple independent sample t-tests. Further, a cluster-based permutation analysis approach was implemented to correct for multiple comparisons.
Result. Compared to controls, patients showed amplitude reduction for the P25 (negative and positive cluster; $p < 0.001$ and $p = 0.04$, respectively), N45 (negative and positive cluster; $p < 0.001$ and $p = 0.001$, respectively) and P70 component (negative and positive cluster; $p = 0.04$ and $p = 0.004$, respectively).
Conclusion. There results extend on previous literature about impairment of GABA-A receptor mediated inhibition in schizophrenia, as demonstrated by the N45 amplitude reduction, whereas no significant differences in GABA-B index (i.e., N100) were revealed. Our results also showed that, although specific mechanisms underlying P25 and P70 have not been fully elucidated yet, excitatory neurotransmission is altered in this clinical population. To conclude, TMS-EEG may provide a more comprehensive view of the inhibitory and excitatory mechanisms involved in the pathophysiology of schizophrenia.

Anxiety levels during COVID 19 pandemic in primary and secondary doctors in UK

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Aims. The study aims to examine the severity of anxiety in primary and secondary doctors in the UK during first wave of COVID-19 pandemic.
Method. An online General Anxiety Disorder-7 (GAD7) survey was distributed during the first wave of COVID-19 pandemic (April-May 2020) to doctors in primary and secondary care in the UK. Seven closed-ended questions were included in the questionnaire. Respondents were to indicate how frequently they experienced specific issues in the previous fortnight: Feeling nervous, anxious, or on edge; being unable to stop or control worrying; worrying too much generally; trouble relaxing; being so restless that it's hard to sit still; becoming easily annoyed or irritable, feeling afraid of something awful happening. Participants were required to tick one of four choices for each of the seven parameters - not at all (0), several days (1), more than half the days (2) and nearly every day (3). A person with minimal or no anxiety will score less than 5. The survey was anonymous and circulated in professional online doctors' forums. Participation was voluntary and no incentives were given.
Result. 273 completed surveys were received; 120 doctors were in primary care and 153 were in secondary care. Average GAD7 score was 6.4 in primary care and 7.9 in secondary care. 57% of primary care doctors and 66% of secondary care doctors reported score of 5 or more, representing at least mild anxiety symptoms. 22% doctors in primary care and 31% doctors in secondary care reported GAD7 score of 10 or more, indicating moderate to severe anxiety. One in ten doctors in both primary and secondary care reported severe anxiety due to the ongoing COVID-19 pandemic.
Conclusion. The finding of more anxiety in secondary care doctors might be because general practitioners could resort early in the pandemic to remote consultations along with inadequacy of resources, greater exposure to suffering/deaths of patients and colleagues in hospital and perceived risk of catching COVID-19 infection.

Results are limited due to relatively low numbers and it would be useful to replicate this study on a larger scale. Doctors are less likely to acknowledge their mental health difficulties due to stigma associated with mental health.

Many employers have psychological support systems in place for their staff, but it is questionable if affected individuals are willing to receive this support. This paper; therefore, calls for creating open anonymous platforms for professionals to get access to appropriate support to address their anxiety.

Cardiovascular risk quantification using QRISK-3 score in people with intellectual disability

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Aims. The prevalence of cardiovascular diseases (CVD) in people with intellectual disability (ID) is around 14%, higher than the general population. However, CVD risk assessments are not consistently performed. Given the high risk of premature deaths in people with ID, it is important to identify preventable risk factors and follow evidence-based interventions. QRISK-3 is a validated risk-stratification tool, which calculates the 10-year risk of developing a heart attack or stroke (https://qrisk.org/three/index.php). There are no published studies on the use of QRISK-3 in people with ID. This project aimed to

understand the use of QRISK-3 in an ID clinic and to quantify individual CVD risks to recommend appropriate management options.
Method. A cross sectional study was performed on 143 patients open to an ID psychiatry clinic. Patients and carers were sent an accessible information leaflet on this study. Basic demographic data and information on psychiatric diagnoses were collected. Patients were grouped according to the presence of severe mental illness (SMI) defined as schizophrenia, bipolar disorder and other psychotic illnesses. QRISK-3 $\geq$ 10% was defined as elevated risk in accordance with NICE guidelines. Patients who had a high QRISK-3 score were advised to contact their GP.
Result. Of 143 patients, 73 (51.0%) had a mild ID and the remaining had a moderate to severe ID. The mean age was 43.3 years, 53.1% were male. Overall, 28 (19.6%) participants had an elevated CVD risk, of whom 16 (57.1%) were not on statins, which is the recommended treatment. The mean QRISK-3 score was 6.31 (standard deviation [SD] 8.95), and the relative risk is 3.50 (SD 7.13). The proportion of QRISK-3 $\geq$ 10% and mean score were not significantly different in those with SMI, but those with SMI were more likely to be prescribed statins than those without (14 [31.1%] vs 10 [10.2%], $p = 0.002$). Statins were given to 24 (16.8%) participants, of whom 12 (50%) had elevated CVD risk. 89% had a blood pressure recording within the past 5 years, 87% had height and 88% had weight recorded. 73% had lipid serology results recorded.
Conclusion. Elevated CVD risk was common in this ID study population, and more than half with elevated QRISK-3 were not on the medical treatment recommended by national guidelines. QRISK-3 could feasibly be implemented in the outpatient setting. Increased routine CVD risk assessment and management should be considered as another measure to reduce morbidity and mortality.

A case of olanzapine-associated rhabdomyolysis

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Aims. To describe the case of olanzapine-associated rhabdomyolysis in a 20-year-old patient with a suspected diagnosis of paranoid schizophrenia.
Method. A 20-year-old male Caucasian patient was admitted to the Psychiatric Department with a one-month history of irrational behavior, talking to himself, persecutory delusions, and poor sleep. He was prescribed oral olanzapine at a dose of 10 mg per day. After two days of olanzapine monotherapy, the patient experienced muscle jerks in the legs. Four days after the initiation of olanzapine treatment, he complained about fatigue and weakness in the lower extremities along with myalgia. Physical examination revealed decreased muscle power with no extrapyramidal symptoms. Blood chemistry showed serum creatine kinase (CK) and serum lactate dehydrogenase (LDH) of 9,725 U/L and 843 U/L, respectively, on day four of the therapy. The Naranjo algorithm score of 6 suggested that olanzapine was the probable cause of rhabdomyolysis. A diagnosis of drug-induced rhabdomyolysis was established from the background of blood tests (increased serum CK and LDH levels), clinical presentation (fatigue and weakness in the lower extremities, muscle jerks, and myalgia), and Naranjo algorithm score of 6 for olanzapine. On suspicion of its contribution to rhabdomyolysis, olanzapine was immediately withdrawn. The patient was referred to the intensive care unit. To prevent acute renal failure, high-volume alkaline diuresis was initiated. After consulting a clinical pharmacologist, the patient's primary physician decided to perform a pharmacogenetic test to develop an individualized treatment regimen. Pharmacogenetic test results were interpreted using the PGX2 software (Meditsina LLC, Moscow, Russia). The test revealed that the patient was a homozygous mutant for CYP2D6*4, which corresponds to CYP2D6 PM phenotype. With this in mind, trifluoperazine was prescribed at a daily dose of 10 mg instead of olanzapine as recent data indicate that trifluoperazine is metabolized by CYP1A2 and UGT1A4 instead of CYP2D6. Subsequently, the patient recovered well and was discharged without any nephrological sequelae.
Result. Recent research demonstrates that CYP2D6 is one of the most important isoenzymes implicated in drug metabolism because the CYP2D6 gene is highly polymorphic. Few reports on the association between olanzapine use and rhabdomyolysis have been published to date, and the present case report draws attention to pharmacogenetic testing which allowed the psychiatrist to prescribe another antipsychotic with no risk of rhabdomyolysis.
Conclusion. The presented case demonstrates that pharmacogenetic-guided personalization of treatment may allow selecting the best medication and determining the right dosage, resulting in the reduced risk of adverse drug reactions and pharmacoresistance.

Effects of tailored quality improvement programme for effective medication management in high dependency in-patient psychiatry rehabilitation unit

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Aims. To determine the effects of a tailored quality improvement programme for effective medication management including a reduction in prescription and administration errors in oral and depot psychotropic medication, patient education on medication and implementation of policies and guidelines.
Background. Medication errors are common in hospital admissions and pose a threat to patient safety (Buckley et al. 2013). Medication errors may occur in different stages of the patient treatment process such as during prescribing, transcribing, preparing, dispensing, administration, and monitoring (Wang et al. 2015). In addition to these, for the detained mental health patients, the Mental Health Act 1983 legislation requires up-to-date treatment certificate compliance (Wales. Welsh Assembly 2008). A Quality Improvement programme to improve safe medication prescription and administration was designed for the patients admitted in Delfryn House, a mental health high dependency rehabilitation unit.
Method. Using Plan-Do-Study-Act (PDSA) quality improvement methodology, a medication management committee was created under the leadership of Specialty doctor and Head of Care (HOC), and comprising of the consultant psychiatrists, specialty doctor, heads of care (ward managers), senior nurses,