GNG Monthly Discussion: NOVEMBER 2024

November was an interesting learning month. Many discussions took place, and various papers covering more expansive areas of neuropsychiatry were shared.

Neuropsychiatry of Epilepsy was the most discussed and read topic for this month.

We had 22 new editions to our Global Neuropsychiatry Community.

We hope you are finding our monthly roundups helpful. If you wish to add anything to them, please feel free to contact us.

We thank Jen for being a great organiser and for all her help.

We also take this opportunity to wish you and your family a Merry Christmas and A Wonderful New Year.

Thank you for being part of the community and the mutual learning process.

Warmest regards

Jas

Papers Shared

ADDICTIONS

Repurposing Semaglutide and Liraglutide for Alcohol Use Disorder
https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2825650?guestAccessKey=ac876998-5a25-4ae7-9ae7-d80237e767af&utm_source=silverchair&utm_medium=email&utm_campaign=jama_network&utm_content=network_highlights&utm_term=112424&adv=000002330134

According to the World Health Organization, the harmful use of alcohol is accountable for 5.1% of the global burden of disease.

In humans, genetic variation in GLP-1R is associated with an increased risk of AUD.

This cohort study was an observational study conducted nationwide in Sweden using data from January 2006 to December 2023.

Among patients with AUD and comorbid obesity/type 2 diabetes, the use of semaglutide and liraglutide was associated with a substantially decreased risk of hospitalisation due to AUD.

This risk was lower than that of officially approved AUD medications.

Semaglutide and liraglutide may effectively treat AUD, and clinical trials are urgently needed to confirm these findings.

This finding aligns with a recent study showing that semaglutide use is linked to lower incidence and relapse of cannabis use disorder.
Given the role of the GLP-1 receptor in craving and reward pathways, GLP-1 agonists may be effective for various addictions.

A recent review suggested that GLP-1 agonists may exert a centrally mediated effect to reduce addictive behaviour, at least partly via dopamine modulation.

COGNITION

Hearing Loss, Hearing Aids, and Cognition
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2824287#:~:text=The%20proportion%20of%20global%20cognitive,CI%2C%200.83%2D1.07).

This is just a refresher following Prof Griffiths's talk on Hearing and Cognition earlier this year. If you missed it, the video is available on the INA website.

To evaluate the relationship between measured hearing loss (HL), cognitive functions, and hearing aid (HA) use.

This cross-sectional analysis of the CONSTANCES cohort included adults aged 45 to 69 years from 21 preventive health centers in France, using data collected from January 1, 2012, to December 31, 2020.

Cognition was assessed at the start using five standardised tests administered by neuropsychologists. A global cognitive score was calculated, with scores at or below the 25th percentile indicating cognitive impairment.

The study involved 62,072 participants, average age 57.4 years (52% women). Among them, 38% had mild HL, 10% had disabling HL, and 3% used hearing aids. Mild HL increased the odds of cognitive impairment (odds ratio [OR], 1.10), while disabling HL had a greater impact (OR, 1.24). The odds of cognitive impairment were similar for hearing aid users and those with disabling HL without aids (OR, 0.94). However, hearing aid use was linked to lower odds of cognitive impairment in participants with depression (OR, 0.62).

The study found a connection between hearing loss severity and cognitive impairment, with hearing aids not significantly reducing cognitive issues overall. These findings emphasise the importance of monitoring cognitive function in middle-aged individuals with hearing loss.

Hearing aids slow cognitive decline in people at high risk.
https://www.nih.gov/news-events/nih-research-matters/hearing-aids-slow-cognitive-decline-people-high-risk

The study population included 573,088 individuals (298,006 women [52%]; mean age 60.8 [SD 11.3] years), with 23,023 dementia cases and a mean follow-up of 8.6 (SD 4.3) years.

Hearing loss increased dementia risk, shown by an adjusted hazard ratio (HR) of 1.07 (95% CI, 1.04-1.11) versus no hearing loss. Severe hearing loss in either ear correlated with higher risk: HR 1.20 (95% CI, 1.09-1.32) for the better ear and 1.13 (95% CI, 1.06-1.20) for the worse ear.

Compared to those without hearing loss, individuals with hearing loss not using aids faced greater dementia risk (HR 1.20 [95% CI, 1.13-1.27]) than those using aids (HR 1.06 [95% CI, 1.01-1.10]).

Overall, hearing loss was linked with a 7% higher dementia risk. Users of hearing aids showed lower dementia risk than non-users.

The findings indicate that hearing aids may help prevent or delay dementia progression.

Treating Auditory impairment and CogniTion (TACT) pilot trial
https://www.ucl.ac.uk/psychiatry/research/mental-health-older-people/tact-trial

TACT is a pilot trial where a computer randomly assigns MCI and hearing loss participants to receive either our new hearing aid intervention or a healthy ageing intervention.

This trial will determine if participants find the hearing aid intervention acceptable and helpful. We will assess whether the intervention increases hearing aid usage compared to the healthy ageing group.

Additionally, the pilot will help identify and resolve any issues with the interventions.

Ultimately, this work will inform us whether a larger, longer trial is feasible, aiming to discover if our intervention can delay or prevent dementia over time.

Clinical assessment of parietal lobe function
https://pn.bmj.com/content/23/5/404

The parietal function can be tested rapidly at the bedside with three simple tests, of visual inattention, constructional apraxia (visuosconstructive deficits) and limb apraxia.

More detailed or follow-up testing might incorporate visual cancellation (for neglect), visual localisation (dot counting), visual working memory (tapping out sequences of locations) and graphesthesia.

Bilateral parietal dysfunction may be associated with the triad of Bálint's syndrome: simultanagnosia (attending to only one item at a time), optic ataxia (misreaching to peripheral visual targets) and gaze apraxia (difficulty in making saccades to peripheral visual targets), all readily elicited at the bedside.

Meso-cortical pathway damage in cognition, apathy and gait in cerebral small vessel disease.
https://academic.oup.com/brain/article/147/11/3804/7665612

The study revealed that cognitive impairment, apathy, and gait dysfunction in small vessel disease (SVD) are closely interrelated, suggesting that damage to the mesocortical pathway may underlie these features.

DELERIUM

Delirium risk and mortality in people with pre-existing severe mental illness: a retrospective cohort study using linked datasets in England
https://pmc.ncbi.nlm.nih.gov/articles/PMC11578903/

Delirium risk and mortality in people with pre-existing severe mental illness: a retrospective cohort study using linked datasets in England

The authors found an association between SMI and delirium.

Individuals with SMI may be more susceptible to delirium in hospitals than those without SMI.

Limitations exist in using electronic health records, and further studies are needed to confirm these findings.

DEMENTIA

Alzheimer Disease—What's in a Name?
https://jamanetwork.com/journals/jamaneurology/article-abstract/2825807

In this issue of JAMA Neurology, the International Work Group (IWG) responds to the 2024 Alzheimer Association (AA) Diagnostic Framework for Alzheimer Disease (AD).

In 2018, the National Institute on Aging (NIA)–AA group biologically defined AD by the presence of brain amyloid (A) and tau (T) biomarkers, regardless of symptoms.

The 2024 update keeps this definition but adds new biomarkers.

They define AD based on core amyloid thresholds detected via PET, cerebrospinal fluid, or plasma biomarkers.

The necessity of tau for diagnosis is questioned, noting that most amyloid-positive PET scans also show tau pathology.

A clinical staging scheme is proposed to explain discrepancies between biomarker positivity and clinical symptoms, often due to mixed pathologies or resilience.

The AA group advises against testing asymptomatic individuals in clinical settings despite the emphasis on biomarker positivity for AD diagnosis.

EEG

Electroencephalography in encephalopathy and encephalitis
https://pn.bmj.com/content/24/1/2

Electroencephalography (EEG) is a valuable tool that enhances clinical neurological examinations by detecting subtle disturbances in brain function and allowing continuous monitoring of cerebral activity.

Although EEG is rarely definitive for diagnosing encephalopathy or encephalitis, it can reveal specific patterns that suggest underlying pathophysiologies, such as lateralized periodic discharges in HSV-1 or extreme delta brushes in autoimmune encephalitis.

Additionally, EEG is essential for confirming non-convulsive seizures and ***understanding concepts like epileptic encephalopathy*** and the ictal–interictal continuum, especially in critically ill patients.

EPILEPSY

Neuropsychiatry revisited: epilepsy as the borderland between neurology and psychiatry
https://pmc.ncbi.nlm.nih.gov/articles/PMC11466751/

Recent evidence indicates a bidirectional relationship between epilepsy and psychiatric symptoms.

Specific psychiatric symptoms can occur both before and after the onset of epilepsy, and their presence may impact the effectiveness of seizure treatment.

The lifetime prevalence of psychiatric symptoms among individuals with epilepsy is reported to be 35%, with an odds ratio of 2–5 times higher than that of people without epilepsy.

Psychiatric symptoms can influence epileptic seizures in a bidirectional manner. For example, depression and anxiety may precede epilepsy onset, and depression can worsen seizure outcomes.

Psychiatric Comorbidities in Persons With Epilepsy Compared With Persons Without Epilepsy
A Systematic Review and Meta-Analysis
https://jamanetwork.com/journals/jamaneurology/fullarticle/2827126?guestAccessKey=c8550c0c-9d3e-485a-a5df-32b61bdcb7f5&utm_source=silverchair&utm_medium=email&utm_campaign=article_alert-jamaneurology&utm_content=olf&utm_term=112524&adv=000002330134

Systematic reviews have shown a high prevalence of psychiatric comorbidities, such as anxiety and depression, in individuals with epilepsy (PWE).

However, the prevalence of other psychiatric disorders in PWE compared to those without epilepsy is less understood.

This study identified the prevalence of specific psychiatric disorders in PWE, revealing that many patients also have multiple comorbidities, including mood disorders, ADHD, and substance use disorders.

Recognizing these co-occurring disorders is critical, as they can complicate management and increase the risk of severe complications, such as suicidality.

Out of a systematic search of 10,392 studies, 27 met eligibility criteria, involving 565 participants with epilepsy and 13,434,208 without.

Results indicated that PWE had significantly higher odds of experiencing various psychiatric disorders, including anxiety, depression, and bipolar disorder, but not suicide attempts.

Other increased disorders included psychotic disorders, schizophrenia, PTSD, eating disorders, alcohol dependence, and ADHD.

The bidirectional relationship between epilepsy and psychiatric comorbidities necessitates further research.

It is important to determine if epilepsy is more prevalent in individuals with specific comorbidities and to explore potential common etiological factors.

Guidelines recommend routine screening for psychiatric comorbidities in PWE, as they tend to have a poorer quality of life and face greater adverse events.

De novo psychosis after left temporal lobectomy: a case of forced normalization?
https://pubmed.ncbi.nlm.nih.gov/34796883/

Forced normalisation is a clinical condition where psychiatric disturbances occur after controlling previously uncontrolled epileptic seizures, first described by Landolt in 1953.

Initially, psychosis was the main issue, but further studies suggested that any behavioural disturbance with seizure control could fall under this definition.

The authors reported a 65-year-old right-handed Caucasian patient from the Epilepsy Centre of Marseille who had left temporal drug-resistant epilepsy with one seizure per month before surgery.

Left anterior temporal lobectomy was performed, and the patient was seizure-free post-surgery but experienced acute psychosis three months later.

An EEG revealed rare left temporal epileptiform activity, mainly triggered by hyperventilation and breach rhythm over the left temporal surgical site.

The onset of psychosis following seizure cessation and decreased epileptiform activity raised questions about forced normalisation in this case.

Alternatively, the surgery itself might have contributed, as there is a risk of psychiatric disturbances unrelated to seizures during recovery.

In conclusion, the psychosis likely resulted from multiple factors, including surgery effects and seizure cessation, highlighting the need for targeted psychiatric support during the perioperative period for epilepsy patients.

Prevalence, patterns, service needs, and assessment of neuropsychiatric disorders among people with epilepsy in residential care: Validation of the Neuropsychiatric Inventory as a caregiver-rated measure of neuropsychiatric functioning in epilepsy
https://www.sciencedirect.com/science/article/abs/pii/S1525505008000607

The authors assessed 228 people with epilepsy in residential care using the Neuropsychiatric Inventory (NPI) and Brief Psychiatric Rating Scale (BPRS).

About half scored positive on at least one instrument, indicating a significant burden of psychopathology. Scores were higher in cognitively impaired subjects than those with intact function.

The NPI effectively identified four factors: psychosis, interictal dysphoric disorder, depression, and anxiety.

Significant mental health service needs reveal a hidden burden of psychiatric comorbidity, necessitating further research.

Forced normalization: A systematic review
https://onlinelibrary.wiley.com/doi/10.1111/epi.16276

Forced normalisation (FN) primarily affects patients with long-term uncontrolled epilepsy.

Psychosis is the most common behavioural symptom of FN. Antiepileptic drugs

(AEDs) and epilepsy surgery are the frequent triggers of FN.

The use of antipsychotics does not indicate a positive outcome. Most patients who discontinue the problematic AED show complete resolution of FN.

Screening for epilepsy-specific anxiety symptoms: French validation of the EASI
https://pubmed.ncbi.nlm.nih.gov/35180578/

Epilepsy-specific anxiety symptoms affected about 60%.

The French EASI performed well.

The French 8-item brEASI screens all DSM anxiety disorders more effectively than the GAD-7 but is less suitable for epilepsy-specific anxiety.

The authors propose the "Epilepsy-Specific Anxiety" (ESA) 10-item instrument, derived from dimension 2 of the EASI, as a complementary clinical and research tool.

Design and validation of two measures to detect anxiety disorders in epilepsy: The Epilepsy

The EASI and brEASI are the first reliable epilepsy-specific anxiety instruments. The EASI comprehensively assesses anxiety in PWE, while the brEASI offers quick insights for diagnosing anxiety disorders in busy neurology settings.

Given the prevalence of anxiety in PWE, these tools enhance the understanding and detection of anxiety in epilepsy.

Anxiety Survey Instrument and its brief counterpart

Psychiatric Comorbidities in Persons With Epilepsy Compared With Persons Without Epilepsy. A Systematic Review and Meta-Analysis
https://jamanetwork.com/journals/jamaneurology/article-abstract/2827126#:~:text=Significantly%20higher%20prevalence%20of%20psychiatric,Cochran%20Q%20P%20value%20for%20heterogeneity%20%3D%20.

The search identified 10,392 studies; 27 met eligibility criteria.

Meta-analyses included 565 and 13,434,208 without epilepsy.

The odds of various psychiatric disorders were significantly higher in PWE compared to those without epilepsy: anxiety (OR, 2.11; 95% CI, 1.73-2.58), depression (OR, 2.45; 95% CI, 1.94-3.09), bipolar disorder (OR, 3.12; 95% CI, 2.23-4.36), suicidal ideation (OR, 2.25; 95% CI, 1.75-2.88), but not suicide attempt (OR, 3.17; 95% CI, 0.49-20.46); psychotic disorder (OR, 3.98; 95% CI, 2.57-6.15); schizophrenia (OR, 3.72; 95% CI, 2.44-5.67); OCD (OR, 2.71; 95% CI, 1.76-4.15); PTSD (OR, 1.76; 95% CI, 1.14-2.73); eating disorders (OR, 1.87; 95% CI, 1.73-2.01); alcohol misuse (OR, 3.64; 95% CI, 2.27-5.83) and dependence (OR, 4.94; 95% CI, 3).

Antidepressants for people with epilepsy and depression.
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010682.pub3/full
https://pubmed.ncbi.nlm.nih.gov/31560136/

Managing depression in epilepsy can be challenging due to its diverse nature and factors like seizure type, antiepileptic medications, and anxiety as a comorbidity.

From experience, SSRIs and SNRIs can be effective , though it's best to avoid bupropion and tricyclic antidepressants. Start low and increase slowly , as interactions between antidepressants and antiepileptics should be considered. Cognitive Behavioral Therapy (CBT) and psychoeducation for patients and caregivers are also beneficial. I welcome you to share your experiences in this area.

Highlights of this review. Published in 2021. Not aware of any new data since then?

Depressive disorders are the most common psychiatric comorbidity in individuals with epilepsy, affecting about one-third and significantly reducing quality of life.

This review aimed to evaluate the efficacy and safety of antidepressants in managing depressive symptoms and their effects on seizure recurrence in those with epilepsy and depression.

They analysed 10 studies , including four randomised controlled trials (RCTs) and six non-randomized studies (NRSIs), involving 626 participants.

One RCT was deemed to have a low risk of bias, three had an unclear risk, and all six NRSIs had a serious risk of bias. Treatment heterogeneity prevented them from conducting a meta-analysis.

Results indicated that venlafaxine improved depressive symptoms by over 50% compared to no treatment (mean difference of -7.59; low-certainty evidence).

Comparisons between SSRIs and cognitive-behavioural therapy yielded inconclusive results regarding the complete remission of depressive symptoms.

There was no evidence of increased seizure risk associated with antidepressants.

Adverse event rates were comparable between antidepressants and controls , but non-randomized studies showed higher withdrawal rates due to adverse effects.

Reported side effects included nausea, dizziness, sedation, headaches, gastrointestinal issues, insomnia, and sexual dysfunction.

In summary, the evidence for antidepressant effectiveness in treating depressive symptoms in people with epilepsy is limited and variable. However, the use of antidepressants did not appear to worsen the seizures.

There is some low-certainty evidence that venlafaxine may be beneficial. Still, more research is needed to explore other antidepressants and more prolonged treatment durations to assess their impact on seizure control and treatment sustainability.

Personalised music as a treatment for epilepsy.
https://www.epilepsybehavior.com/article/S1525-5050(24)00210-5/fulltext

Music and epilepsy are intriguing areas of study. Prof. Trimble highlights the correlation between music and epilepsy management. What do you think?

Music universally makes us move and evokes emotional responses.

Research has focused on using music to treat psychiatric disorders like depression, anxiety, and PTSD, as well as conditions like dementia and post-stroke aphasia.

Music acts as a non-invasive brain stimulation technique, with therapeutic approaches differing by diagnosis.

The neurophysiological changes from music activate key brain structures, including subcortical, cortical, basal ganglia, and limbic areas, suggesting music may help synchronize our brains with external rhythms.

A meta-analysis of the Mozart Effect and epilepsy analyzed over 50 articles from PubMed, Medline, and the Cochrane Library (1998-2022) for cross-study comparisons.

In summary, 45% to 84% of subjects experienced significant reductions in Interictal Epileptiform Discharges (IEDs) after musical treatment, while 33% did not respond to the Mozart Effect.

Mozart's music features long-term periodicity, possibly influencing how the brain processes information. This characteristic is likely common to various musical forms.

Key factors include frontal theta activity (3-8 Hz), linked to drowsiness or meditation, and parasympathetic activity tied to the "rest-and-digest" response. These could involve Bayesian inference for shifts in cognitive connectivity.

Music may affect seizures by altering dopaminergic circuits or competing cognitive inputs, potentially serving as an anticonvulsant by enhancing spatial cognition areas and inhibiting adjacent motor regions. The Mozart Effect may relate to acoustic resonance, mirror neurons, and pathways involving dopamine and parasympathetic activation.

Concerns about music-induced seizures are minimal, with an annual incidence of about 1 in 10,000,000. Of those with musicogenic epilepsy, about 60% to 78% have temporal lobe epilepsy with a right-sided focus.

The X-System's MODA playlists, with varied music, are more effective than standard Mozart playlists. Using this music overnight may impact Electrical Status Epilepticus during slow-wave sleep (ESES) and enhance REM sleep, which is significant as sleep disturbances are common in seizure disorders. REM sleep offers anticonvulsant benefits while non-REM sleep is more likely to experience inter-ictal discharges.

The initial results using audification showing entrainment of cerebral activity of the EEG, with effects on seizure activity and the emotional state of patients, offer

therapeutic possibilities which are currently being explored.

Epilepsy and cognition – A bidirectional relationship?
https://www.sciencedirect.com/science/article/pii/S1059131117301541

In chronic epilepsies, cognitive deficits are observed in about 70-80% of patients.

Cognitive and behavioural issues in epilepsy should be viewed through a multifactorial and neurodevelopmental lens that includes patient demographics, epilepsy type, structural aspects, seizure activity, treatments, psychiatric comorbidities, and individual capacities.

Kraepelin observed that over 50% of epilepsy patients may experience a distinct form of dementia characterized by general slowness and clumsiness in mental functions.

The concept of an "epileptic personality" has been identified, marked by traits such as irritability, viciousness, hopelessness, religious ideation, subservience, and stilted courtesy.

Currently, there is limited evidence that seizures alone lead to significant mental decline or permanent cognitive impairment in chronic epilepsy. Instead, cognitive deficits are often present at epilepsy onset, with their progression influenced by underlying causes, treatment effects, and overall treatment success.

The authors concluded that there appears to be a bidirectional relationship between epilepsy and cognition.

Seizures can negatively affect cognition in both temporary and reversible ways. This includes cognitive dysfunction during and after seizures (known as ictal and postictal cognitive dysfunction). Additionally, interictal epileptic discharges can impact cognitive performance.

Seizures and cognitive deficits may indicate distinct symptoms of a shared underlying brain pathology, such as limbic encephalitis.

Currently, there is no convincing evidence in humans that recurrent seizures or the accumulation of lifetime seizures, taken alone, lead to a progressive and irreversible decline in previously developed cognitive functions.

The authors recommend a practical approach: A neuropsychological assessment should evaluate 1) the relationship between cognitive, behavioral issues, and active epilepsy or its treatment; 2) if impairments show early or late-stage brain pathology; and 3) if they indicate developmental delays or accelerated decline. If cognitive or behavioral functions worsen, physicians should investigate the causes.

Depression is a significant comorbidity of epilepsy that requires diagnosis and treatment.

Patients experiencing cognitive and behavioural issues should receive additional education, training, occupational therapy, or psychotherapy.

Believing that seizures are the only issue in epilepsy leads to treatments focused solely on controlling them. However, this narrow focus may overlook underlying conditions that, if addressed, could improve the patient's overall cognitive and behavioural health.

While seizures are the primary concern in epilepsy, other symptoms can also significantly burden patients and should be treated, particularly when seizures cannot be fully controlled.

The complex relationship between seizures and behaviour: an illustrative case report
https://pubmed.ncbi.nlm.nih.gov/17197245/

Epilepsy and behaviour have a complex relationship.

The authors presented the case of Mrs. A, who suffered from depression and later developed seizures and ictal psychosis after taking a selective serotonin reuptake inhibitor.

She exhibited forced normalisation with affective somatoform and hysterical symptoms.

Norman Geschwind's contribution to the understanding of behavioral changes in temporal lobe epilepsy: The February 1974 lecture
https://www.sciencedirect.com/science/article/abs/pii/S1525505009003138

Norman Geschwind ignited interest in interictal behavioral changes in temporal lobe epilepsy through 11 articles from 1973 to 1984.

This article summarizes his contributions and opinions. A previously unpublished 1974 lecture, "Personality Change in Temporal Lobe Epilepsy," reflects his views.

His observations indicated a keen interest in how temporal lobe epilepsy exemplifies behavioral change from limbic system lesions, resulting in increased emotionality, religious interests, hypergraphia, aggression, moral concerns, viscosity, and seriousness, with hyposexuality as an exception.

Geschwind defended the limbic syndrome's validity against conflicting views.

Associations between neurolinguistic deficits and personality traits in people with epilepsy
https://www.frontiersin.org/journals/neurology/articles/10.3389/fneur.2024.1416713/full

Associations between neurolinguistic deficits and personality traits in epilepsy have drawn attention in cognition and personality research.

Psychiatric and behavioral disorders (PBDs) significantly impact epilepsy, with 30–50% of people with epilepsy (PWE) experiencing anxiety, mood, psychotic, and personality disorders at rates two to three times higher than those without epilepsy.

Comorbid personality disorders remain controversial. Prevalence of Axis II disorders is 6% to 13% in the general population, compared to 4% to 35% in PWE, higher than in other neurological disorders.

Temporal lobe epilepsy (TLE) may exhibit "Gastaut–Geschwind syndrome," characterised by changes in sexual behavior, irritability, increased religiosity, hypergraphia, and circumstantiality due to limbic dysfunction.

This study included 72 participants: 23 with juvenile myoclonic epilepsy (JME), 29 with mesial temporal lobe epilepsy (MTLE), and 20 healthy controls, matched for sociodemographic profiles.

Personality and cognitive profiles, EEG, MRI, and clinical data were compared between groups.

The Personality Dimensions Questionnaire (PDQ4) assessed personality styles and social functioning, supplemented by

Brain Networks for Cortical Atrophy and Responsive Neurostimulation in Temporal Lobe Epilepsy
https://jamanetwork.com/journals/jamaneurology/fullarticle/2824204?guestAccessKey=6b668168-4d2b-4416-9955-dc32739c0c94&utm_source=twitter&utm_medium=social_jamaneur&utm_term=151939659820&utm_campaign=article_alert&linkId=649236921

Two brain networks were identified that showed functional connections to areas of hippocampal atrophy.

The first network was characterized by positive correlations with temporolimbic, medial prefrontal, and parietal regions, while the second network displayed negative correlations with frontoparietal regions.

White matter changes were found in the positive network, while cortical atrophy occurred in the negative network.

In patients receiving Responsive Neurostimulation (RNS), connectivity between the stimulation site and atrophied regions of the negative network was linked to fewer seizures.

These findings suggest that temporal lobe epilepsy (TLE) involves distributed pathology in networks linked to the hippocampal epicentre, highlighting potential therapeutic targets beyond the hippocampus.

NEUROMODULATION

Slowing Cognitive Decline in Major Depressive Disorder and Mild Cognitive Impairment: A Randomized Clinical Trial
https://pubmed.ncbi.nlm.nih.gov/39476073/

Transcranial Direct Current Stimulation (tDCS) + brain training slows cognitive decline with aging. Expansive JAMA Psychiatry RCT: 375 subjects, 5 centers, 10+ years planning/recruitment, 6+ years follow up.

Study shows that cognitive remediation + neuromodulation (tDCS) slowed cognitive decline by ~3 years compared to sham in a group of older adults with MCI or remitted MDD, with more pronounced effect in MDD irrespective of whether they also had MCI or not.

NEUROSCIENCES

Anterior insula as a gatekeeper of executive control
https://www.sciencedirect.com/science/article/pii/S0149763422002251?via%3Dihub

Executive control is a high-level cognitive function reliant on diverse brain circuits.

The authors suggest that the anterior insular cortex plays a crucial role in executive processes, acting as a gatekeeper to various brain regions through its connectivity.

Its flexible profile makes it a key hub in the midcingulate-insular salience network, driving activity in other major brain networks, like the medial frontoparietal default mode and lateral frontoparietal central executive networks.

The insular cortex's microanatomy and extensive connectivity position it to integrate multisensory stimuli for higher-order control functions.

Evidence supports the hypothesis that the anterior insula is a critical gatekeeper for executive control.

NEUROIMMUNOLOGY

Catatonia in anti-NMDA receptor encephalitis: a case series and approach to improve outcomes with electroconvulsive therapy*
https://neurologyopen.bmj.com/content/6/2/e000812?utm_source=alert&utm_medium=email&utm_campaign=BMJ%20Neurol%20Open&utm_content=latest&utm_NEUROIMMUNOLOGY

Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is a rare and potentially life-threatening autoimmune disorder characterized by antibodies targeting NMDA receptors in the brain, leading to neuronal dysfunction.

Psychiatric symptoms occur in 65% to 80% of cases, often preceding neurological issues, and the condition can present with catatonia.

In a case series of eight patients treated with electroconvulsive therapy (ECT), seizures were the most common presenting symptom (n=6), followed by psychosis (n=5) and mood symptoms (n=4), including features of mania.

Three patients exhibited catatonia symptoms, which worsened during hospitalization. Benzodiazepines (BZDs), particularly lorazepam, were utilized, with doses ranging from 24 mg to 156 mg daily as patients received an average of 29.9 ECT treatments.

Although two patients experienced seizures after ECT initiation, both had confirmed seizures prior to starting ECT. The underlying mechanisms of catatonia may involve dysfunctions in dopamine, GABA, and glutamate systems.

There is a significant risk of complications related to malnutrition and immobility in catatonia, which affects a substantial percentage of patients with anti-NMDAR encephalitis.

Dysautonomia prompted earlier initiation of ECT in this cohort, and the treatment is believed to enhance GABAergic response, potentially effective in reducing symptoms.

While there are concerns about ECT-inducing seizures in active encephalitis, it has been shown to have a neuroimmune effect and can be safely applied in similar conditions.

Despite two spontaneous seizures occurring post-ECT, six of the patients had EEG-confirmed seizures before treatment.

ECT is recognized as a safe and effective option for managing seizure disorders alongside antiepileptic medications.

NEUROINFLAMMATION

Inflammatory Biomarkers and Risk of Psychiatric Disorders
https://jamanetwork.com/journals/jamapsychiatry/fullarticle/2822344?guestAccessKey=7f3c046b-b418-496c-b485-68300c002030&utm_source=twitter&utm_medium=social_jamapsyc&utm_term=15161429334&utm_campaign=article_alert&linkId=643700960

In this cohort study, inflammatory biomarkers such as leukocytes, haptoglobin, C-reactive protein (CRP), and immunoglobulin G (IgG) were linked to an increased risk of developing psychiatric disorders.

The study found that individuals with higher-than-median leukocyte and haptoglobin levels, or lower-than-median immunoglobulin G (IgG) levels, faced an increased risk of psychiatric disorders.

Over the 30 years before diagnosis, those with psychiatric disorders had consistently higher leukocyte and haptoglobin levels and lower IgG levels compared to controls. Furthermore, elevated leukocyte levels were linked to a higher likelihood of depression, indicating a possible causal relationship.

These markers could be useful for identifying high-risk populations.

The potential causal relationship between leukocytes and depression highlights the significant role inflammation may play in the development of psychiatric conditions.

The underlying mechanisms for the associations of serum leukocytes, haptoglobin, CRP, and IgG with psychiatry disorders remain unclear.

Possible explanations mainly include blood-brain barrier disruption, microglia activation, neurotransmission impairment, and other interactions between inflammations and neuropathology.

MOVEMENT DISORDERS

Parkinson's Disease

Impulse control disorders in Parkinson's disease: a national Swedish registry study on high-risk treatments and vulnerable patient groups
https://pubmed.ncbi.nlm.nih.gov/39084861/

The longitudinal study analysed records of all Parkinson's disease in the Swedish National Patient Registries and the Prescribed Drug Register (n=55,235). MAO-B inhibitor as a risk factor for ICD was somewhat surprising!

The study highlights key risk factors for developing impulse control disorders (ICDs) in Parkinson's Disease (PD) patients,
- male sex
- younger onset age
- poor mental health
- and treatment with dopamine agonists.

The study found an increased risk of gambling disorders (GD) associated with MAO-B inhibitors and that ropinirole may pose greater risks than pramipexole.

Overall, individual risk assessments for ICDs in PD patients are crucial.

Medications like dopamine agonists, especially ropinirole, and possibly MAO-B inhibitors should be avoided when possible, and at-risk patients should be monitored closely and offered timely support for managing ICDs.

PSP

Advances in progressive supranuclear palsy: new diagnostic criteria, biomarkers, and therapeutic approaches
https://www.sciencedirect.com/science/article/abs/pii/S1474442217301576

Progressive supranuclear palsy (PSP) is recognised as a group of motor and behavioural syndromes associated with 4-repeat tau neuropathology rather than solely as a common cause of atypical parkinsonism.

Reviews have identified various phenotypes of PSP, with language and behavioural symptoms often meeting the criteria for frontotemporal lobar degeneration.

Notable features include the presence of neurofibrillary tangles and tau protein aggregates in the basal ganglia and brainstem.

The MAPT gene is the most strongly associated genetic factor with the risk of developing PSP.

As a uniformly fatal disease, patients with PSP-P may initially respond to levodopa therapy; however, this benefit is usually temporary and does not extend the duration of the disease.

Physical therapy can enhance patient outcomes, and botulinum toxin injections may be beneficial for treating apraxia of eyelid opening.

HUNTINGTON DISEASE

Huntington's disease phenocopy syndromes revisited: a clinical comparison and next-generation sequencing exploration.
https://jnnp.bmj.com/content/early/2024/10/23/jnnp-2024-333602

The HDPC phenotype aligns with Huntington's disease (HD), but the genotype differs.

On average, patients with HD experience motor onset at a younger age and report more issues with dysphagia (difficulty swallowing), dysarthria (speech difficulties), and insomnia.

In contrast, patients with HDPC have a higher prevalence of tremor, dystonia, and disinhibition.

SLEEP

Assessing insomnia after stroke: a diagnostic validation of the Sleep Condition Indicator in self-reported stroke survivors.*
https://neurologyopen.bmj.com/content/6/2/e000768?utm_source=adestra&utm_medium=email&utm_campaign=usage&utm_content=bau_journal_monthly_email&utm_id=BMJ069

Research shows a bidirectional relationship between sleep and stroke. Insomnia affects 32.2% to 50.4% of stroke survivors and increases the risk of stroke by 30% before it occurs.

After a stroke, insomnia leads to poorer functional and cognitive outcomes, as well as heightened psychological distress.

Therefore, clinical guidelines recommend sleep assessments for stroke patients to improve management and reduce recurrence.

This study finds that the Sleep Condition Indicator (SCI) is a valid tool for diagnosing insomnia based on DSM-5 criteria after a stroke, though a lower threshold may be needed compared to the general population.

TRAUMATIC BRAIN INJURY

Apathy and Depression Among People Aging With Traumatic Brain Injury: Relationships to Cognitive Performance and Psychosocial Functioning*
https://psychiatryonline.org/doi/10.1176/appi.neuropsych.20230082

Apathy and depression are prevalent after moderate to severe traumatic brain injury (TBI), especially in older adults.

This study explored how these conditions relate to cognitive performance and psychosocial functioning in this group.

Apathy severity was significantly linked to cognitive performance, particularly executive functioning, even after adjusting for demographic and injury factors. In contrast, depression showed no significant correlation once corrections were made.

Both conditions independently affected health-related quality of life (HRQoL), but only depression influenced societal participation. About 50% of participants had neither condition, 25% had only apathy, and another 25% had both.

Having both conditions was associated with worse HRQoL and reduced social participation.

This study is the first to examine the relationship between apathy, depression, and cognitive functioning in older adults with a history of TBI, highlighting the need for targeted interventions for this vulnerable group.

Poor long-term outcomes and abnormal neurodegeneration biomarkers after military traumatic brain injury: the ADVANCE study
https://jnnp.bmj.com/content/early/2024/10/11/jnnp-2024-333777

About 17% of participants in the ADVANCE cohort with major combat trauma experienced a traumatic brain injury (TBI), one-third of which were moderate to severe.

Neurotrauma correlated with increased affective symptoms and poorer quality of life, motor function, and employment outcomes.

Plasma GFAP, a marker of glial activation, was significantly elevated, on average, eight years after injury. Higher levels are linked to a lower chance of employment.

RARE NEUROPSYCHIATRIC DISORDERS

SUSAC SYNDROME

The neurocognitive and neuropsychiatric manifestations of Susac syndrome: a brief review of the literature and future directions*
https://pmc.ncbi.nlm.nih.gov/articles/PMC11470906/

Susac syndrome is a rare condition affecting the brain, eyes, and ears, characterised by encephalopathy, branch retinal artery occlusions, and sensorineural hearing loss.

Its incidence is low, at 0.024 to 0.13 per 100,000 people, but it is an important differential diagnosis for multiple sclerosis and stroke.

Diagnosis can be challenging, as only 13% to 30% of patients show the full triad of symptoms.

A 2013 review found that 76% of patients presented with encephalopathy. Among these, 48% faced cognitive impairment, while others exhibited emotional disturbances, behavioural changes, apathy, or psychosis.

According to the European Susac Consortium (EuSaC) criteria, neuropsychiatric symptoms are crucial for diagnosis.

Prompt treatment is essential due to the frequent misdiagnosis of Susac syndrome.

Additionally, characteristic "snowball" lesions in the corpus callosum on MRI and elevated protein levels in cerebrospinal fluid are common findings.

Emerging research suggests that elevated serum neurofilament light chain and glial fibrillary acidic protein may be useful biomarkers for assessing disease activity and predicting clinical outcomes.

CADASIL

https://www.thelancet.com/journals/laneur/article/PIIS1474-4422(09)70127-9/abstract

Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) is the most common inherited cause of stroke and vascular dementia in adults.

It typically presents with early stroke onset, frequent migraines with aura, and variable ischemic white matter lesions on MRI.

CADASIL is linked to mutations in the NOTCH3 gene, which affects the accumulation of its protein in small arteries.

Symptoms include migraines, slurred speech, one-sided weakness, cognitive issues, and mental health concerns like depression and apathy.

This review highlights current insights into the disorder and its relation to common subcortical ischemic strokes and vascular dementia.

NEUROPHARMACOLOGY

Brexpiprazole for the Treatment of Agitation in Alzheimer Dementia
A Randomized Clinical Trial
https://jamanetwork.com/journals/jamaneurology/fullarticle/2811629

Interesting findings from this RCT exploring Brexpiprazole in treating agitation in AD. I found this very challenging area during my posting in an elderly dementia ward. According to this study, it looks like a good alternative option.

To evaluate the efficacy, safety, and tolerability of brexpiprazole for agitation in patients with Alzheimer's dementia.

A 12-week, double-blind, placebo-controlled clinical trial was conducted from May 2018 to June 2022 at 123 sites in Europe and the U.S., involving patients with agitation due to Alzheimer's dementia in care facilities or community settings.

Patients were randomly selected to receive oral brexpiprazole or a placebo in a 2:1 ratio for 12 weeks. Those in the brexpiprazole group were further randomized to 2 mg/day doses or 3 mg/day.

The primary outcome was the change in the Cohen-Mansfield Agitation Inventory total score from baseline to week 12. Safety was assessed by monitoring treatment-emergent adverse events.

A total of 345 patients were randomized (brexpiprazole: n=228; placebo: n=117), with completion rates of 86.8% and 88.9%, respectively. The mean age was 74 years (SD=7.5), and 56.5% of participants were female. Those receiving brexpiprazole group showed significant improvement in agitation scores compared to placebo (brexpiprazole: mean change −22.6; placebo: mean change −17.3; P=0.003). No adverse events occurred in more than 5% of brexpiprazole patients. Discontinuation due to adverse events was low (5.3% for brexpiprazole, 4.3% for placebo).

Brexpiprazole (2 mg or 3 mg) significantly reduced agitation in Alzheimer's dementia patients compared to placebo and was generally well tolerated.

Brexpiprazole acts as an antagonist at noradrenergic α1B and α2C receptors and serotonergic 5-HT2A receptors, while functioning as a partial agonist at 5-HT1A and dopaminergic D2 receptors, all with subnanomolar affinity.

It impacts brain functions related to agitation, aggression, impulsiveness, arousal, and psychosis, and its moderate affinity for histamine H1 receptors suggests its effects on agitation are not due to sedation .

Comparing the effectiveness of antipsychotics for treating agitation in Alzheimer's dementia is challenging due to differences in trial design, study populations, and outcome measures.

A Cochrane review found that atypical antipsychotics (such as olanzapine, quetiapine, and risperidone) have a small effect on agitation in dementia, with a standardized mean difference of −0.21.

Since 2005, there has been a boxed warning for atypical antipsychotics regarding the increased risk of cerebrovascular events and mortality in elderly patients with dementia-related psychosis.

While no cerebrovascular treatment-emergent adverse events (TEAEs) were reported in the current trial, both patients and clinicians should be aware of this potential risk

A systematic review on the efficacy of GLP-1 receptor agonists in mitigating psychotropic drug-related weight gain
https://www.cambridge.org/core/journals/cns-spectrums/article/systematic-review-on-the-efficacy-of-glp1-receptor-agonists-in-mitigating-psychotropic-drugrelated-weight-gain/48801F4A9CE25AE46D43F26B8847E8EB

Evidence indicates GLP-1RAs effectively reduce weight gain in those on psychiatric medications.

They may influence weight changes by affecting metabolism and cognitive processes tied to hunger and satiety.

Future studies should investigate the long-term safety, tolerability, and efficacy of different GLP-1RAs in managing abnormal weight and metabolic stability in psychiatric groups.

Psychedelic and MDMA-Related Adverse Effects—A Call for Action
https://jamanetwork.com/journals/jama-health-forum/fullarticle/2825777#:~:text=For%20example%2C%20there%20are%20concerns,and%20under%20what%20circumstances%20these

This is an interesting read about the adverse effects of psychedelics. Researchers are exploring the use of psychedelics for various conditions, including depression, PTSD, alcohol use disorder, and, more recently, functional neurological disorders (FND). The authors emphasize the need for a better understanding of these adverse effects as clinical trials are conducted.

Here are four key points related to research on the adverse effects of psychedelics and MDMA:

Adverse effects include hallucinogen-persisting perception disorder (HPPD), psychotic symptoms, mood disturbances (such as hypomania and depression), and anxiety among specific individuals.

Evidence regarding who is most affected and under what conditions remains limited. Additionally, research suggests that other impairing effects, such as existential struggles, depersonalisation, derealisation, and social disconnection, may occur but are poorly understood.

Identifying the individuals and situations in which the use of psychedelics and MDMA may pose risks is crucial.

Both pharmacological and non-pharmacological therapies must be developed to treat these adverse effects.

Increased funding for psychedelic research should ideally be accompanied by enhanced education for healthcare professionals about the adverse effects of psychedelics and MDMA.

Evaluation of akathisia in patients receiving selective serotonin reuptake inhibitors/serotonin and noradrenaline reuptake inhibitors.
https://pubmed.ncbi.nlm.nih.gov/39374042/

In conclusion, results suggest that akathisia is not a rare side effect of SSRI/SNRI in patients with mood disorders, especially in smokers and younger patients. In addition, akathisia may reduce treatment compliance owing to a reduction in QoL.

Practice guideline recommendations summary: Treatment of tics in people with Tourette syndrome and chronic tic disorders
https://pmc.ncbi.nlm.nih.gov/articles/PMC6537133/

Clinicians should inform patients and caregivers that watchful waiting is an acceptable approach for managing tics.

They may prescribe Comprehensive Behavioral Intervention for Tics (CBIT) as an initial treatment option.

It's important to assess and treat any co-occurring conditions, such as ADHD, OCD, and anxiety disorders.

Methylphenidate and guanfacine are likely to reduce tic severity and improve ADHD symptoms.

Patients should be made aware that treatments for tics seldom lead to their complete cessation.

For those with access to CBIT, it should be offered before medication.

Physicians can recommend α2 adrenergic agonists for patients with both tics and ADHD.

Haloperidol, risperidone, aripiprazole, and tiapride effectively reduce tic severity compared to placebo, while pimozide, ziprasidone, and metoclopramide may also help but with less certainty.

Topiramate can be prescribed when its benefits outweigh the risks.

If legally allowed, clinicians might consider cannabis-based medications for adults with TS who have successfully self-medicated with cannabis.

For patients with medication-resistant tics, a multidisciplinary evaluation involving a psychiatrist, neurologist, neurosurgeon, and neuropsychologist is necessary to assess the risks and benefits of Deep Brain Stimulation (DBS).

OTHERS

Remembering the Physician's Humanity—Physicians Are Humans Too. Great article by our esteemed member Thomas Pollok.
https://jamanetwork.com/journals/jamaneurology/article-abstract/2825845?utm_source=twitter&utm_campaign=content-shareicons&utm_content=article_engagement&utm_medium=social&utm_term=110424V

DISCUSSIONS

The relationship between hearing loss and cognition was examined. The two papers presented gave rise to differing perspectives. While hearing loss appears to be associated with cognitive decline, the effectiveness of hearing aids in preventing or delaying this decline remains a topic of debate.

TACT trial is being conducted to look into this relationship.

Discussion 2. The question was asked if prescribing AEDs are treating psychiatric illness or epilepsy, or both.

Krish replied both. But then there is forced normalisation.

Alexis Comment: Forced normalization is a rare phenomenon, though likely under-recognized. Calle-Lopez provides a clear review in Epilepsia 2019.

Epilepsy is a neuropsychiatric disorder with frequent comorbidities linked chronologically.

Historically, Hughling Jackson, Falret, and Ey proposed that psychosis and epilepsy arose from the same brain network disorder, manifesting as seizures or psychosis—leading to the concept of alternating psychosis, similar to forced normalization.

However, in France, neurology and psychiatry were separated in 1968, and care for people with epilepsy (PWE) was gradually abandoned by psychiatrists.

In contrast, in Japan, psychiatrists treat pharmacosensitive PWE, influenced by

Kraepelin's classification, which viewed epilepsy as a form of psychosis. I'm curious about how other countries approach epilepsy and psychiatry. Regardless, it is undoubtedly a neuropsychiatric disorder!

Comments made on interictal dysphoric disorder and epileptic personality.

Great article! I have a psych cl patient, who was admitted for full thickness burn of the hand leading to amputation, because she dipped her hand into boiling water during an absence seizure! We still feel puzzled about how this could have happened, please share your thoughts/ experiences on this if you can.

Alexis: The concept of "epileptic personality" is outdated and was studied by F. Minkowska and T. Lempérière during the era when ASM were barbiturates. These personality changes may have been due to iatrogenic effects and cognitive slowness, leading to the rejection of this concept.
In my practice with temporal epilepsy, I observe:

- Interictal Dysphoric Disorder (described by Blumer) which some authors find controversial. Patients often recover easily with SSRIs, suggesting it might not be a personality disorder.
- Mild paranoid ideas are often underrecognized and seem more related to deficits in social cognition seen in some temporal epilepsies rather than personality changes.

The original study by Bear & Fedio (1977) explored this topic in considerable detail. They administered a 100-item questionnaire to patients with epilepsy and their relatives, revealing noteworthy observations, particularly concerning laterality.

Patients with left temporal lobe epilepsy were more likely to exhibit ideational and philosophical traits and had a tendency to tarnish their own image, with their relatives holding a more favorable view of them than they did themselves. Conversely, patients with right temporal lobe epilepsy tended to be emotionally driven and polished their self-image, perceiving themselves more positively than their relatives did.

Dietrich Blumer revalidated this questionnaire and termed it the Neurobehavioral Inventory. In collaboration with Professor Trimble, Ludger van Elst conducted an MRI volumetric study on bilateral hippocampal atrophy, correlating the findings with the NBI. The personality characteristics associated with temporal lobe epilepsy were historically described best by Gastaut and subsequently by Geschwind, often referred to as the Gastaut-Geschwind syndrome. One element, "hyper-religiosity," was further examined by our group (Wuerfel et al., JNNP), which localized this trait (but not other aspects of the epilepsy personality) to the right hippocampus.
Thus, it is unlikely that these characteristics are entirely iatrogenic, as they persist into the 21st century even with newer antiepileptic drugs. I acknowledge that elements of social cognition may be involved and could constitute part of the epileptic process.

Alexis: Thank you for your precisions
I am really interested in classical clinical observations, and I agree that it is necessary to know the “old fashioned” works

Nonetheless, as medications, culture, comprehension of the brain change, we need to rethink the previous works according to the current practices, times, studies and new medications

So some I am questioning whether historical syndromes disappeared or changed. For example, I met only one patient that corresponds to the description of Geschwind syndrome

For sure, we need to know old studies, to have a comprehensive view of current research and patients.

Krish: The answer to this perhaps lies in history. Landolt who described forced normalisation was director of the Swiss Epilepsy Centre and followed patients for years pre and post ethosuximide. Kraeplin's observations of Schizophrenia were similarly gleaned in long follow up and close observation. We have centres like Bethel in Germany and Chalfont in UK where such long term follow up and monitoring is possible and happens. But today the vast majority of people even with difficult to treat epilepsy are in the community.

And our first response to difficult to diagnose or treat patients is to rely on technology for the solutions. Prof Trimble who so well described the Schizophrenia like Psychosis of epilepsy used to say (in response to the statement) "I don't see these patients in my practice" - "you need to see as many complicated patients with epilepsy as we do".

The problems of epilepsy related behavioural dysfunction are by no means common, but they exist and often are missed a. Lack of observation in community living patients b. Lack of an observer to report symptoms or changes c. Lack of aptitude in the medical community to spend time on history, focusing on the tests to be done instead.

In India we have the advantage of people living with their families and history taking remains a huge asset in making sense of what is going on in a person with epilepsy.

And of course I submit to your view that the course and character of illness may change with treatment over time. But there is that old adage in medicine "the eyes cannot see what the mind does not know" and that is where the clinical observations of a bygone era hold great promise especially for those in training.

Jas, we may need to consider different instruments in different populations. For example for patients with ID the NPI is useful as are other observer rated measures. For adults capable of giving a good account of themselves the GHQ or CIS-R may be considered (both quite short) or indeed the QoLIE or SF36 - both extensively used.

The BPRS is based on a physician interview and observation over 30 minutes and captures psychotic symptoms as well- hence expert observer rated. In patients with specific co morbidities like ADHD we may need to think of specific measures as you have suggested.

We compared a range of measures with the Schedule for Clinical Assessment in Neuropsychiatry (SCAN) interview and found many of the above to have fair sensitivity and specificity.

Kiri asked: Hi all. I am asking with my patients permission. In your experience what is the best management/ medication for frontal dysregulation syndrome in mixed mild dementia. 62 year of man. A combination of severe brain injury (PTA>1 month) with haemosiderin in the frontal and temporal lobes) and AD. Amyloid PEt scan positive with strong family history.

He is on donepiel and was on sertraline 75mg. He saw the local psychiatrist and Sertraline was stopped as he was experience vivid dreams and tried to strangle the dog at night (I wonder if that was donepizel so have changed it to morning). He was tried on epilim and has now been started on quetiapine 50/100mg.

The behaviour is causing significant distress to both my patients and his family. He has insight. But can't control himself. We have looked at behaviour modification. Your help knowledge and my ongoing education through discussion would be appreciated. Thank you.

Hetal Mehta: Vivid dreams and acting them out could be REMBD. I would do a PSG
Melatonin; if that doesn't work, clonazepam small doses
High conversion to synneucleinopathies.

Mohan Rathnaiah: Many thanks for sharing this complex case.
Bit more information might help chose the appropriate molecule please

- continued autonomic dysfunction ?
- premorbid personality and job please
- mobility? Sensory impairment ?
- atypical neurodevelopmental traits?
- pre-morbid impulsivity?
- current pain? Constipation?
- current medication list along with psychotropics already mentioned
- any pattern to BPSD - ?sundowning - this might help decide timing of dose

Few options worth considering based on comprehensive information:

- Propranolol 40 mg bd
- Melatonin-MR 4 mg nocte
- Clomipramine 25 mg nocte (instead of SSRI)
- Methylphenidate 5 mg mane if hyperactive thinking, apathy, brain fog and lack of impulse control
- Promethazine 25 mg

Kiri : No behav rem sleep disorder (formal sleep study only mild osa). Has DM type II. No PD. Fractured c1/2 from the accident age No autonomic features. No sundowning. Business man. Still trying to run his business I am trying to get him to retire. Driven man to succeed. Not FTD personality. Behavioural changes only recent. No neurodivergent issues

Baldev Singh: I'd get him back on SSRI. Sertraline is a great choice but other SSRI's can be tried as well. I'd also consider small dose Risperidone and potentially Carbamazepine/Oxcarbamazepine. Propranolol as suggested above would be an option too.

Krish: Very interesting conundrum - thank you. I agree with the many possibilities raised. I wonder if you have a recent EEG on him? The nocturnal event could be a seizure arising from the frontal lobes apart from REM sleep behaviour disorder as suggested.

A PSG and video EEG recording overnight may actually help clarify. In general for its thymoleptic properties one would consider carbamazepine or oxcarbazepine in these instances. I agree on both a SSRI and a Neuroleptic continuing.

In India we have olanzapine and fluoxetine coming as a combination drug - which I have found very useful in instances of emotional dyscontrol. I wonder also if the events turn out to be predominantly behavioural (ie no seizures etc) if rTMS would help. @Vivek Misra do comment.

Vivek Misra: Hi, as the patient is Positive on Amyloid PET - rTMS to the precuneus can slow cognitive decline and improve function. (https://academic.oup.com/brain/article/145/11/3776/6701823)

We do have a similar patient profile now, aged 74, who responded well with left DLPFC stimulation TMS.

Other modality, what we work with in behavioural disturbances post TBI is the use of anodal tDCS to L-DLPFC; given EEG is normal and no seizure event in last 18months.

Coming to most advanced NIBS, I have seen the primary data of tFUS (Storz Medicals) in Dementia and its promising.

Dhama: Hi Kiri, along with all the other excellent ideas and recommendations from others, I wonder if memantine could be another consideration. Given young-onset amyloid PET positive AD and family history, this would be suspicious for a monogenic cause and thus neurogenetics referral/genetic testing could be offered/considered.

Seizures/epilepsy would be more likely for this reason alone, especially if PSEN1/other genetic cause, but risk would be even greater with that severe TBI, so just to add more weight for EEG as previously recommended too.

Krish: Also should Memantine await the seizure diagnosis as it's known to provoke seizures?!

Kiri: We have discussed genetic testing and it has been declined by the whanau (family). I can revisit. None of his behaviour was stereotypic so I would assume seizure less likely. I will review to see if I have requested EeG. Thank you.

Memantine isn't funded in NZ. I haven't had much success with it in other patients. Do you think it works?

Srivasata: ChATs and NMDA Receptor antagonists are available in India both in the public sector and the private sector(Rivastigmine, Donepezil, Memantine and Galantamine:though I am not very sure whether Galantamine is available as much as the others in the public sector).

I have not had any experience in using Galantamine with those with neurodegeneration I work with. All the four are equally safe, effective and efficacious.

The side effect profile and the underlying clinical conditions is what decides the choice of the medication.

We have found Memantine to be very useful either as monotherapy or an accepted combination in India(Donepezil and Memantine) in those with added vascular involvement(AD+VCI) for example. For non AD dementias, it does not worknas much as Rivastigmine does. Have no experience with Galantamine.

Mohan: Hi Kiri
I have rarely seen Memantine working for BPSD like presentation.
Many thanks for providing additional detailed information.

Based on the information, Melatonin-MR in the night (with graded increase based on the response), Paracetamol 1 g QDS regular and Propranolol 40 mg bd might be worth trying.

If there is availability of DORA, Lemborexant is worth considering?

Antonio: I add a second vote for Memantine in this case. Memantine is finding a good space for itself in the emotion and fear regulation pathway particularly due to it hypocampal neuro genesis benefit(studies in ptsd). Plus it's benefit in the sleep and overall cognitive enhancement.

Avoid the antipsychotic for sure.

Mohammad: What's the function of paracetamol here Dr Babu?

Mohan: There is evidence for Paracetamol effective use in BPSD and this gentleman seems to have source of pain (fractured C1/2)

Kiri: Thank you for the discussion. It is really interesting. I am going to have to revisit memintine! The patient doesn’t have chronic pain. The injury was 43 years ago

Chaminda: can you describe some of the troubling behaviour? Sorry if you have mentioned this already

Kiri: Frightening Verbal outbursts. Short fuse. Rapid escalation. Causing fear in people around him. No physical violence to people . Insight into behaviour but unable to control it. One episode only of vivid dreams a nd behaviour - tried to strangle the dog. Caused a significant fright in the patient

I've had some good results with epilim at low doses. the other medications that come to mind is trazodone which I don't think is available in NZ(being a fellow kiwi). Chaminda Gunawardana: interesting he has insight into his behaviour. any particular things set him off? or is it spontaneous?

Kiri: Being interrupted. Driving past an address. Something going wrong. Being asked a question. Yet he can discuss them calmly in clinic. He is volatile with the unexpected.

Alice: Hi Kiri, Rowena Mobbs has a big cohort of TBI and TES patients and swears by lamotrigine for explosivity/rage attacks. I use it a bit as it's generally also well tolerated in our populations. Memantine would be another option.

Screening Tools
https://www.phqscreeners.com

Thanks Vivek for sharing this.

Here we can find PHQ, GAD, PHQ SADS etc in 24 Languages.

All PHQ, GAD-7 screeners and translations are downloadable from this website and no permission is required to reproduce, translate, display or distribute them.

Shared by Heiko - Patient Health Questionnaire PHQ might be an addition to the list. It includes PHQ-9 for depressive Symptoms, PHQ-15 for somatic symptoms and GAD-7 for anxiety.

The validated german version PHQ-D goes further I think and can be used to screen for somatoform disorders, depressive disorders, anxiety disorders, eating disorders and alcohol abuse. It also includes questions on psychosocial functioning, stressors, critical life events.

Screening tools for identifying psychiatric co-morbidity in Epilepsy.

1. NDDI-E
2. GAD-7
3. HADS
4. ESA
5. br EASI
6. French brEASI
7. NPI(ID population)
8. BPRS
9. GHQ
10. CISR
11. QoLIE
12. SF 36

WSR II (NOT USED)

Rafey: You may read Prof Gus Baker’s work on epilepsy, quality of life and impact of co-morbidities

@ Tim Nicholson compiled the outcome measures paper for the faculty few years ago and may be able to say more.
HADS is still widely used in this patient population.
@Rohit Shankar is writing on epilepsy in intellectual disability population and in people with neurodiversity - he will be able to advise on overlapping assessment areas and more

Monthly Webinar

Summary of talk from Dr Medford – Inpatient treatment outcomes in Severe FND. Add the link if you can.

Summary of talk from Dr Mosley – deep Brain Stimulation and Neuropsychiatry. Add the link if you can.

Surveys

Jai is a research fellow and neuropsychology registrar at Monash University in Melbourne, Australia. They are conducting a survey related to traumatic brain injury (TBI) and invite feedback from experienced mental health practitioners and researchers—those with over five years of expertise in dealing with acquired brain injuries—regarding a new transdiagnostic tool designed to evaluate mental health in this demographic.

Thanks to everyone who completed this. The survey is now closed. We will wait to receive the results.

Other Resources

Neuropsychiatric Aspects of Epilepsy: Our esteemed member, John Joska, from Cape Town, South Africa, has created a collection of electronic notes on common neuropsychiatric disorders. Here is one on epilepsy, which was co-edited by our esteemed member, Maria Oto. It's an easy read and a valuable resource. Please share it widely.

To access the entire collection, please follow the link provided. If you would like to contribute to the e-notes or co-edit, please contact John directly. This is a fantastic opportunity to contribute to the field of neuropsychiatry. Thank you, John, for all your hard work!

https://health.uct.ac.za/hiv-mental-health/notes-neuropsychiatry

Highlights of the clinical note

Epilepsy is a common neurological disorder that affects over 50 million people worldwide. It is marked by seizures and sudden bursts of electrical activity in the brain. These seizures can lead to emotional, cognitive, and social challenges.

Seizures are classified based on their origin (focal or generalised), movement involvement (motor or non-motor), and the individual's awareness during the event. Understanding these classifications helps doctors customize treatment.

The causes of epilepsy may include genetic factors, structural brain abnormalities, and metabolic issues. Many people with epilepsy also experience mental health challenges, with about one in three suffering from depression.

Additionally, individuals may have non-epileptic seizures triggered by psychological factors, which can occur in both confirmed and unconfirmed cases.

Diagnosis relies on clinical assessments and eyewitness accounts.

Treatment usually involves medications and therapy, which can help manage symptoms and improve quality of life.

However, some anti-epileptic drugs can cause neuropsychiatric side effects, making careful evaluation essential for effective treatment.

Welcome New Members

1. Helen Murray – Research Fellow
2. Chaminda Gunawardhana – Geriatrician, Australia
3. Shereen Brifcani – Neurospychologist, UK
4. Jo Wang – Old Age Psychiatrist, NZ
5. Shereen Brifcani
6. Rosamund Hillfuffyfo
7. Susan Yates
8. Chinwe Obinwa
9. Jik – NZ
10. Clelia Galmiche
11. W Curt LaFrance Jr
12. Keith Woods -Neuropsychologist, NZ
13. Rory Hutchinson

14. Tejas Gohler
15. Eike Jakob Spruth
16. Tornike
17. Huda
18. Fiona Hinchliffe
19. Montse
20. Joshua Tam
21. Prof Karl Bechter

22. Jayaraj K
23. Lauren

Table 10.5 *(Continued)*

Safety in epilepsy	Drug	Comments
Antipsychotics		
Low risk – good choices	Amisulpride/ sulpiride	Considered to be safe in PWE.[43] Renally excreted, so low risk of pharmacokinetic interactions with antiseizure medications. Seizures uncommon in overdose[44]
	Aripiprazole	Rarely lowers seizure threshold.[5] Incidence of seizures similar to placebo in RCTs[24]
	Ziprasidone	
	High potency FGAs	For example, fluphenazine, haloperidol, trifluoperazine, flupentixol. Low risk of lowering the seizure threshold[5]
	Risperidone	Unlikely to lower the seizure threshold.[5] Incidence of seizures similar to placebo in RCTs.[24] Has been recommended for PWE.[32,45] Evidence of safety in a case series of adolescents with epilepsy[46]
Probably low risk – use with caution (limited evidence)	Asenapine	Seizure rate similar to placebo in RCTs.[47] Data and clinical experience of use in PWE is extremely limited
	Brexpiprazole	
	Cariprazine	
	Lurasidone	
Moderate risk – care required	Olanzapine	Olanzapine and quetiapine both associated with seizures in RCTs.[24] However, olanzapine causes more EEG abnormalities.[44] Overall risk of reducing the seizure threshold is considered to be low[5] and olanzapine has been recommended by some for PWE.[32] Data relating to olanzapine are difficult to interpret. EEG changes are seen in some but not all studies[48] and it has been reported to be both anticonvulsant[49] and proconvulsant.[50] Quetiapine has a high risk of drug interaction in PWE[45]
	Quetiapine	
Higher risk – care required	Clozapine	Most epileptogenic antipsychotic.[32] However, has been used successfully in PWE stable on antiseizure medications without worsening seizures[51] and even in treatment-resistant epilepsy.[52] Note, should not be used with carbamazepine (risk of blood dyscrasias and reduced clozapine levels). Valproate or lamotrigine are the antiseizure medications of choice
Higher risk – avoid	Low potency FGAs (e.g. chlorpromazine)	Best avoided in PWE.[31] Doses of chlorpromazine above 1g/day have a 9% incidence of seizures
	Loxapine	Highest rate of seizures amongst the FGAs[53]
	Depot antipsychotics	None of the depot preparations currently available are thought to be epileptogenic, however: ■ The kinetics of depots are complex (seizures may be delayed) ■ If seizures do occur, the offending drug may not be easily withdrawn Depots should be used with extreme care

Table 10.5 Psychotropics in epilepsy

Safety in epilepsy	Drug	Comments
Antidepressants		
Low risk – good choices	SSRIs	Recommended in PWE.[14,18] SSRIs may be anticonvulsant at therapeutic doses[13] but pro-convulsant in overdose.[31] SSRIs with the lowest risk of interactions with antiseizure medications are generally preferred (citalopram/escitalopram, followed by sertraline).[14,18,32,33] Escitalopram is preferred over citalopram in PWE (lower risk of seizures in overdose).[34] Others have low risk of seizures (e.g. fluoxetine[34]) but drug interactions with antiseizure medications should be considered.[14,18] Fluoxetine may be less likely to provoke seizures in older people than escitalopram or citalopram.[35] Some evidence that sertraline is safe and effective in PWE[36]
	Mirtazapine	Recommended in PWE.[18,37] Not known to be proconvulsive[34]
	Duloxetine	Recommended for PWE.[11,18] Risk of seizures is probably negligible[34,35]
Probably low risk – use with caution (limited evidence)	Agomelatine	Not known to be proconvulsive.[38] Anticonvulsant in animal models[34]
	MAOIs	Not known to be pro-convulsive at therapeutic doses.[34] Low risk of seizures in overdose[17]
	Moclobemide	Not known to be proconvulsive.[34] Anticonvulsant in animal models[34]
	Reboxetine	Small open label study suggests no problems in PWE[39]
	Vortioxetine	Not known to be proconvulsive[34,40] but no experience in PWE[34]
Moderate risk – care required	Lithium	Low risk of seizures.[34] Anticonvulsant in animal models.[34] However, limited data showing increases or decreases in seizures frequency in PWE.[34] For bipolar, consider anticonvulsant mood stabilisers[41]
	Trazodone	Limited data suggest some risk of seizures[34,42]
	Venlafaxine	Effective in PWE[11] and has been recommended[18] but mixed evidence on seizure risk[34]
	Vilazodone	Limited data. Seizure exacerbation in a patient with epilepsy has been reported[34]
Higher risk – avoid (pro-convulsive at therapeutic doses[13])	Amoxapine	Several reports of seizures at therapeutic doses[42]
	Bupropion	Dose-related risk of seizures (particularly with instant-release formulations).[34] Risk is less with slow-release formulations at doses under 300mg/day[34]
	Maprotiline	Several reports of seizures at therapeutic doses[42]
	TCAs	Most TCAs are epileptogenic at higher doses (particularly clomipramine and amitriptyline[10,24,42]). Doxepin possibly lower risk (one small study in PWE).[34] SNRIs are preferred over TCAs in PWE[17]

Daniel Mille

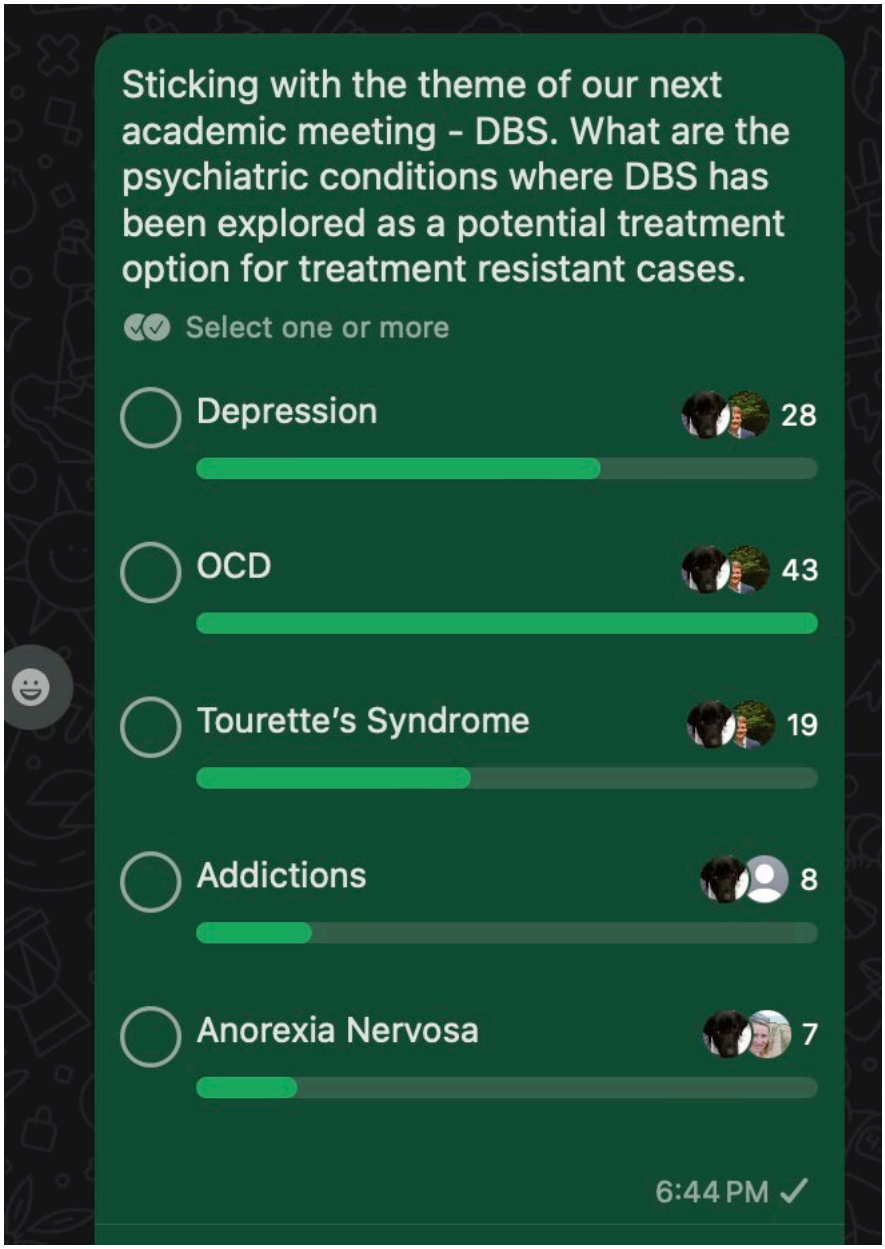
Table 10.5 *(Continued)*

Safety in epilepsy	Drug	Comments
Drugs for ADHD		
Low risk	Methylphenidate	Three RCTs support safety and efficacy in children with epilepsy at therapeutic doses (0.3–1mg/kg/day).[10] Two single dose RCTs and one open label extension study demonstrated no effect on seizures in adults.[54,55] A large case control study found an increased rate of seizures after the start of methylphenidate but not in the longer term.[56] This is difficult to interpret but suggests caution would be appropriate
Probably low risk[57,58] – use with caution (limited data)	Amfetamines	Data are limited to one small retrospective study in PWE.[10] No patients who had well controlled epilepsy experienced an increase in seizure frequency.[59] Of note, dexamfetamine was historically used as an adjunctive antiseizure agent[60]
	Atomoxetine	Data are limited to one small retrospective study in PWE.[10] Discontinuation rates were high (though none due to seizure exacerbation[61]). Seizure rate similar to placebo for patients without epilepsy[62]

This table contains information about the pro-convulsive effects of antidepressants and antipsychotics when used in therapeutic doses. See section on psychotropics in overdose for information about supra-therapeutic doses.

1:55 PM

2


Sticking with the theme of our next academic meeting - DBS. What are the psychiatric conditions where DBS has been explored as a potential treatment option for treatment resistant cases.
Select one or more
Depression
28
OCD
43
Tourette's Syndrome
19
Addictions
8
Anorexia Nervosa
7
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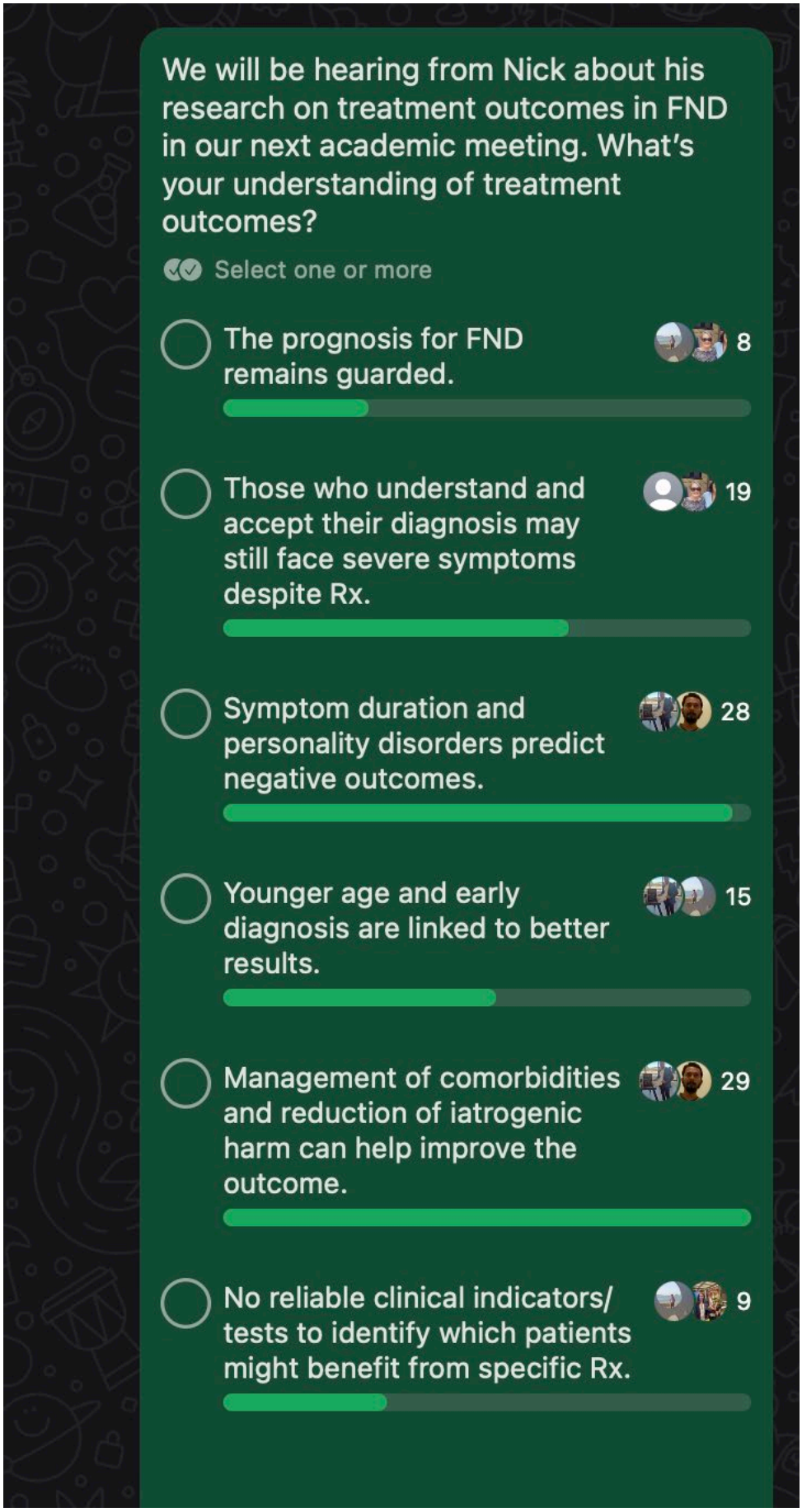
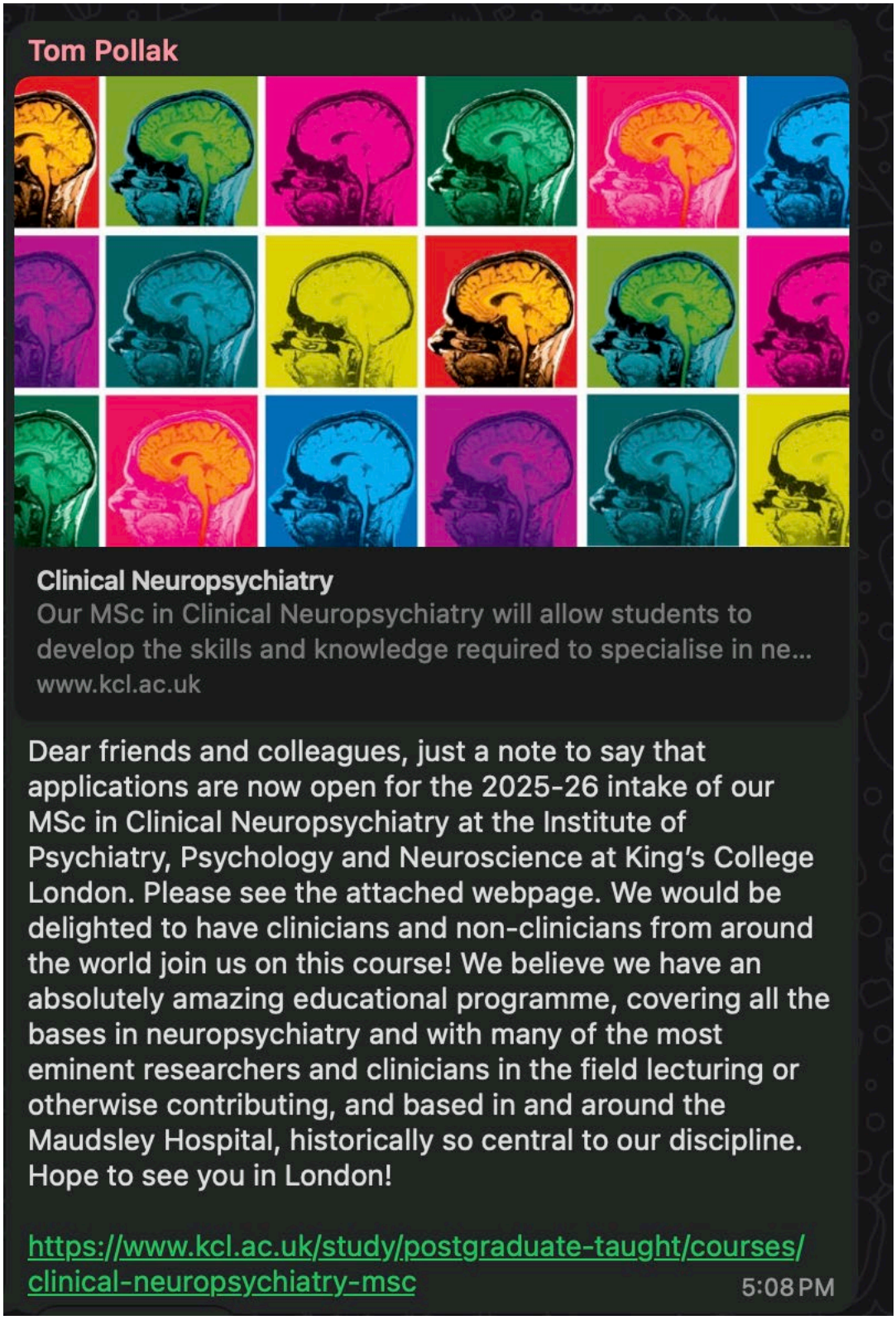

We will be hearing from Nick about his research on treatment outcomes in FND in our next academic meeting. What's your understanding of treatment outcomes?
Select one or more
The prognosis for FND remains guarded.
8
Those who understand and accept their diagnosis may still face severe symptoms despite Rx.
19
Symptom duration and personality disorders predict negative outcomes.
28
Younger age and early diagnosis are linked to better results.
15
Management of comorbidities and reduction of iatrogenic harm can help improve the outcome.
29
No reliable clinical indicators/ tests to identify which patients might benefit from specific Rx.
9



Courses

https://www.eventbrite.com/e/istdp-for-functional-neurological-disorders-dr-allan-abbass-tickets-917999680757?utm-campaign=social&utm-content=attendeeshare&utm-medium=discovery&utm-term=listing&utm-source=cp&aff=ebdsshcopyurl

For anyone interested in FND treatment there is a good course on use of Intensive Short Term Dynamic Psychotherapy being offered by Dr Abbass.

Conferences

Hi folks,

Come one come all - the RANZCP congress 2025 will be on the beautiful GC in Queensland. It's one of the biggest psychiatry conferences in the southern hemisphere and I see that quite a few of the members in this group will be presenting. Registration now open:

https://congress.ranzcp.org/

We hope you are finding our monthly review helpful. Any feedback on how to improve them would be highly appreciated. Have a lovely festive time with your family and friends

Warmest regards

Jen and Jas