Conclusions Results show sustained treatment effect and continued benefit with AVAL beyond the PAP, and stabilization of treatment effect after switching from ALGLU to AVAL over 97 weeks, supporting long-term maintenance of clinically meaningful outcomes with AVAL.
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2287 THE IMPACT OF SLEEP ON THE PROGRESSION OF PARKINSON'S DISEASE: A MENDELIAN RANDOMIZATION STUDY

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Introduction Sleep disturbance is common in Parkinson's disease (PD) and significantly impacts quality of life. Although often considered a sequelae of PD, there is emerging evidence that sleep disturbance may itself play a causal role in neurodegeneration via altered clearance of pathological proteins. Whether sleep disturbance affects the pathological progression of PD is unknown.
Methods To elucidate the causality between sleep disorders and progression of PD, we performed two sample Mendelian randomization analysis using genetic variants identified from GWAS databases for sleep variables including insomnia, sleep duration, chronotype, napping and daytime sleepiness. Outcome measures were derived from a large collective GWAS of PD progression(N=4093 cases) including the Unified Parkinson's disease rating scale (UPDRS total and UPDRS- III), motor fluctuations, Age of onset of PD, Mini-mental state examination (MMSE) and Montreal Cognitive Assessment (MOCA). The robustness of results was examined using conventional Mendelian randomization sensitivity analyses.
Results Genetic liability to increased sleep duration was associated with a lower rate of progression of motor symptoms in PD using UPDRS-III score. Meanwhile insomnia was associated with increased rate of motor progression of PD. Predisposition to daytime sleep was associated with lower rates of progression of cognitive decline in PD measured using MMSE. No robust relationships were determined between markers of progression and chronotype or dayime napping. Statistical measures showed significant pleiotropy for the relationships identified.
Conclusion Sleep-related variables may have a deterministic role in the clinical progression in Parkinson's disease and may represent a modifiable target for altering the trajectory of neurodegeneration.

2289 DYNAMIC NETWORK IMPAIRMENTS UNDERLIE COGNITIVE FLUCTUATIONS IN LEWY BODY DEMENTIA

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Objective Cognitive fluctuations are a core clinical feature of Dementia with Lewy bodies (DLB), and although common and disabling, their pathophysiology is poorly understood. This work aimed to identify novel functional network signatures of cognitive fluctuations and investigate their underlying neurobiology by relating them to neuromodulatory systems.
Methods Patients with DLB and age-matched controls were assessed on both subjective and objective measures of fluctuations and attention. Resting state dynamic functional magnetic resonance imaging was used to identify the temporal and topological signatures of cognitive fluctuations. Abnormal patterns of activation were mapped onto established gene expression atlases to determine associations with specific neuromodulators.
Results DLB patients displayed more stationary brain-state configurations relative controls. This signature of reduced temporal variability correlated significantly with fluctuation-related measures using a sustained attention task (response time variability and drift rate). Topologically, patients with DLB demonstrated a less integrated (more segregated) functional network architecture compared to the control group. Regions of reduced integration were observed across dorsal and ventral attention, sensorimotor, visual, cingulo-opercular and cingulo-parietal networks. Relatively segregated networks correlated positively with subjective and objective measures of fluctuations. Regions of reduced integration and unstable regional assignments were significantly related to the pattern of expression of specific classes of noradrenergic and cholinergic receptors across the cerebral cortex.
Conclusions Cognitive fluctuations in DLB are related to specific dynamic functional network impairments that are linked to the noradrenergic and cholinergic systems. Such systems may be viable targets of future therapies.

2291 PLASMA NEUROFILAMENT LIGHT CHAIN AND CLINICAL DIAGNOSIS IN FRONTOTEMPORAL DEMENTIA SYNDROMES

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Objective To study plasma NfL levels in people with frontotemporal dementia (FTD) syndromes and determine if plasma NfL can distinguish between FTD syndromes and FTD phenocopy, whom are difficult to clinically distinguish from bvFTD.
Methods Plasma NfL was estimated using two independent Quanterix Simoa machines (a HD-X and SR-X). Participants referred to a tertiary national outpatient cognitive service were characterised into bvFTD, slowly progressive bvFTD (slow progressor), phFTD, motor neuron disease with FTD (FTD-MND), semantic variant FTD (svFTD) and non-fluent variant FTD (nfvFTD). Statistical comparisons were performed using non-parametric tests.
Results Fifty participants, mean age 67.2 (standard deviation 8.4) years and mean follow-up duration of 3.6 (2.4) years were analysed, and 49 patients had a final diagnosis of an

FTD syndrome. Plasma NfL was significantly higher in the FTD group compared to phFTD (p = 0.002). There was a trend towards a higher median NfL in bvFTD compared to phFTD (p = 0.14). NfL [median (interquartile range) pg/mL] was comparable in bvFTD [41.10 (50.72), n=20], semantic variant FTD [44.38 (16.61), n=11] and non-fluent variant FTD [42.61 (22.93), n=9]. It was highest in FTD with motor neuron disease [79.67 (45.32), n=4], and lowest in phFTD [13.99 (0.79), n=2] and 'slow progressors' [17.97 (3.62), n=3].

Conclusion Plasma NfL appears to be able to differentiate subtypes of true FTD from phFTD in this exploratory analysis. Further studies should be undertaken with larger samples of patients from all clinical groups to confirm these findings and establish cut-points for each syndrome.

2294 NON-FATAL CEREBRAL ARTERY AIR EMBOLISM DUE TO PULMONARY BAROTRAUMA FROM A PNEUMATOCELE DURING COMMERCIAL AIR TRAVEL

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Cerebral air embolism is a catastrophic phenomenon described in trauma, vascular intervention, barotrauma related to positive pressure ventilation, SCUBA diving and rarely air travel.[1] A 71-year-old woman was found unrousable at the end of an uneventful three-hour flight on a small aircraft. On examination, she was obtunded, without lateralising or brainstem signs, and a possible seizure was witnessed. She was loaded with antiseizure medication and intubated for airway protection.

Initial CT stroke protocol showed bilateral frontal lobe attenuation without perfusion deficit or vessel occlusion. Lumbar puncture revealed elevated protein with normal cell count, and EEG showed generalised, bifrontal predominant asymmetric slowing. The clinical impression was of acute encephalopathy; infective, toxic and metabolic screens were unremarkable, no further seizures were observed. Antibiotics and antivirals were discontinued, autoimmune aetiology was considered, and IVIG commenced. Serial MRI Brains demonstrated progressive bilateral cortical and thalamic T2 changes with initial areas of enhancement and progressive milary cortical susceptibility foci on SWI. Despite treatment, there was minimal initial recovery. Autoimmune markers in blood and CSF were negative. CT chest to exclude malignancy revealed a right pneumatocele. We concluded diffuse ischaemic injury had occurred secondary to air embolism. No intravascular gas was seen on imaging review. Our patient was outside the time frame for hyperbaric oxygen therapy. She slowly recovered but was discharged with significant deficits to a nursing home.

This case highlights a rare phenomenon due to atmospheric pressure changes during flight in patients with pulmonary pneumatoceles/cysts. Timely recognition is essential to facilitate treatment.[2]

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2296 COGNITION, ADAPTIVE SKILLS AND EPILEPSY DISABILITY/SEVERITY IN PATIENTS WITH LENNOX-GASTAUT SYNDROME UNDERGOING DEEP BRAIN STIMULATION FOR EPILEPSY

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Objective We describe the properties of six cognitive tests and their utility in young adults with Lennox-Gastaut syndrome (LGS) undergoing a deep brain stimulation (DBS) treatment trial ('ESTEL': Electrical Stimulation of Thalamus in Epilepsy of the Lennox-Gastaut phenotype), assessing for changes in outcomes after 3-months of treatment.

Methods Twenty ESTEL patients with LGS (17–37 years;13 females) were studied; one participant was not randomised due to device removal, with outcomes of 19 remaining participants reported. All had cognitive/behavioural testing administered at baseline (i.e., pre-DBS implantation), end of the blinded phase and study exit. Testing batteries measured cognition (NIHTB-CB), adaptive skills (ABAS-3), epilepsy severity (GASE)/disability (GAD), quality of life (QOLIE-31) and depression (PHQ-9). Changes in test scores after 3-months of DBS-treatment were compared to baseline (Wilcoxon signed rank test).

Results No deterioration in tests scores was observed after 3-months of DBS treatment, and epilepsy severity (GASE) improved (P=0.03). Testing that relied on participants, rather than caregivers could only be completed only by higher-functioning individuals (NIHTB-CB, n=13; QOLIE-31, n=3; and PHQ-9, n=6), with behavioural and physical limitations further adding to difficulties with test administration. Standardised scores were hindered by a 'floor effect', with use of raw scores revealing variability amongst participants in order to assess for changes post-treatment.

Conclusion DBS treatment is associated with reduced epilepsy severity and disability in young adults with LGS. Performing neuropsychological outcome testing in patients with cognitive impairment is challenging but possible and requires careful selection of testing batteries and modifications of test interpretation to avoid floor effects.