14 PERIPHERAL BLOOD MONONUCLEAR CELLS FROM PATIENTS WITH *SPAST* HEREDITARY SPASTIC PARAPLEGIA (HSP-*SPAST*) SHOW DISEASE-ASSOCIATED EFFECT OF REDUCED ACETYLATED α-TUBULIN

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Objectives HSP-*SPAST* is the most common form of hereditary spastic paraplegia (HSP). In vitro studies using HSP-*SPAST* patient-derived neurons have shown that reduced levels of acetylated α-tubulin in patient neurons leads to downstream effects of reduced microtubule-dependent axonal transport, increased oxidative stress and increased vulnerability to axonal degeneration. We investigate if non-neuronal peripheral blood mononuclear cells (PBMCs) show reduced levels of acetylated α-tubulin as previously seen in patient-derived neurons.

Methods We use flow cytometry to measure the levels of acetylated α-tubulin in PBMCs collected from 9 HSP-*SPAST* patients and 11 healthy controls. We compared the levels of acetylated α-tubulin in all viable PBMCs and PBMC subtypes – T cells, B cells and monocytes.

Results AAT levels in HSP-*SPAST* patient PBMCs were significantly lower than in control PBMCs ($p<0.01$). Analysis of PBMC subtypes revealed that acetylated α-tubulin levels were a) significantly lower in T cells from HSP-*SPAST* patients compared to healthy controls ($p<0.01$) and b) not significantly different in B cells and monocytes between patient and control groups. The significant difference seen in the T cell subpopulation is likely due to T cells being a much greater percentage (80%) of the PBMC population compared to B cells or monocytes.

Conclusions Non-neuronal cells, PBMCs, from patients with HSP-*SPAST* show the disease-associated effect of reduced acetylated α-tubulin, similar to previous findings in patient-derived neurons. These results show that the easily accessible PBMCs could be useful to study disease pathology and potentially develop biomarkers.

15 TAS TEST CLINICAL VALIDATION: AUTOMATED HAND MOVEMENT ANALYSIS HELPS DISCRIMINATE SUBJECTIVE COGNITIVE DECLINE, MILD COGNITIVE IMPAIRMENT AND DEMENTIA

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Objectives New brief cognitive screening tools that are not language-specific are required. Motor function declines across the dementia continuum and may aid screening. We evaluated the accuracy of TAS Test, a new automated online hand movement assessment, to discriminate healthy controls (HC) from adults with Subjective Cognitive Decline (SCD), Mild Cognitive Impairment (MCI) and Dementia.

Methods Participants attending the Tasmanian ISLAND Cognitive Clinic completed >2 hours of neuropsychological and medical assessments and a consensus diagnosis was formulated. They also completed TAS Test keyboard tapping tests (5 minutes duration). Motor features of frequency, rhythm, accuracy, and dwell time were extracted. Cognitively asymptomatic HCs with normal cognition completed TAS Test. Discriminatory accuracy of TAS Test motor features, adjusted for age, in multiple regression models was assessed using area under ROC curves (AUC) and compared to a null model comprising confounding variables only.

Results 205 participants were recruited (mean [SD] age 69.0 [8.9] years): 16 SCD, 40 MCI, 35 Dementia and 114 HCs. TAS Test discriminated better than null models with AUCs [95% CI]: SCD vs HC: 0.82 [0.73–0.91], MCI vs HC: 0.78 [0.69–0.86], Dementia vs HC: 0.91 [0.86–0.97], MCI vs SCD: 0.7 [0.63- 0.92], Dementia vs MCI: 0.82 [0.82–0.97], all p <0.01. Hand movements were progressively slower, less rhythmic and more inaccurate across the dementia continuum, especially for the dominant hand.

Conclusions Brief keyboard tapping tests aided stratification of diagnostic groups. This novel hand motor approach is accessible and opens new opportunities for objective motor measure in cognitive clinics and research applications.

16 IS TAU PET A ROBUST BIOMARKER FOR CHRONIC TRAUMATIC ENCEPHALOPATHY?

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Objective Chronic traumatic encephalopathy (CTE) is a post-mortem diagnosis. We previously reported a frontotemporal predominant tau ^{18}F-MK6240 PET pattern resembling the distribution of CTE in a retired Australian Rules Football player, in the context of a moderate amyloid-β plaque burden.[1] This study investigated ^{18}F-MK6240 as a potential CTE biomarker in contact sports players with exposure to repetitive head impacts (sRHI).

Methods 33 sRHI and 32 age-matched healthy controls (HC) completed amyloid and tau (^{18}F-MK6240) PET scans. Amyloid PET was quantified in Centiloids. ^{18}F-MK240 standardized uptake value ratios (SUVRs) were generated for the dorsolateral prefrontal cortex and composite regions of interest (ROI) (frontal; mesial-temporal; temporoparietal).

Results For sRHI, the primary contact sport was Australian Rules Football (n=17), boxing/kickboxing/martial arts (n=11), rugby (n=4) and soccer (n=1); 36.4% played professionally. sRHI had a mean age of 54.2 (±9.2) (vs HC 53.0±9.5, p=0.61). sRHI did not differ from HC in years of education (p=0.46) but had more impaired MMSE (28.1±1.9 vs 29.3 ±0.8, p=0.006, d=-0.80) and Clinical Dementia Rating scores (0.21±0.3 vs 0±0, p<0.001, d=1.25). sRHI and HC did not differ in mean Centiloids or ^{18}F-MK6240 SUVRs across all ROIs.

Conclusions Contact sports players with exposure to repetitive head impacts did not differ from controls in terms of brain tau burden. Limitations: sample size, heterogeneity in sports type and highest level of participation, and participants with relatively mild cognitive and functional impairments. Additionally, while ^{18}F-MK6240 has high affinity for 3R/4R tau in Alzheimer's disease, its affinity in CTE, particularly important at early stages, remains unclear.

REFERENCE

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17 BIOMARKER INTERPLAY BETWEEN CSF P-TAU AND ^{18}F-PI-2620 PET IN ALZHEIMER'S DISEASE AND 4R-TAUOPATHY

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Objectives Reliable biomarkers for detecting different abnormal tau protein isoforms between neurodegenerative diseases are currently missing. Phosphorylated tau (p-tau) in the cerebrospinal fluid (CSF) is acknowledged as a 3/4R tau biomarker in AD but not in other tauopathies. The positron emission tomography (PET) radiotracer ^{18}F-PI-2620 has the potential to detect abnormal 3/4R-tau in patients with Alzheimer's disease (AD) and 4R-tau in other tauopathies. This study investigates the interplay between tau-PET and CSF p-tau in AD and 4R-tauopathies.

Methods In this cross-sectional analysis, 52 patients with AD, 54 patients with PSP/CBS, and 11 controls underwent lumbar puncture and 0–60 min dynamic ^{18}F-PI-2620 PET scanning. Independent t-tests assessed group differences in standardized uptake value ratios for the 20–40min time window ($SUVr_{20–40}$) and p-Tau. Multiple regression analyses tested the association between $SUVr_{20–40}$ and p-tau and group interactions. ROC analyses evaluated biomarker performance in differentiating patient groups. Quantitative and voxel-wise analyses were performed with R, SPM, and VoxelStats, controlling for age and sex.

Results Patients with AD showed elevated p-tau levels ($p<0.05$; >61 pg/ml) and $SUVr_{20–40}$ in cortical regions, cingulate, insula, hippocampus, and amygdala ($p<0.05$). Patients with clinically suspected 4R-tauopathies showed low p-tau levels but demonstrated high $SUVr_{20–40}$ in the globus pallidus ($p<0.05$), compared to controls and AD. ROC analyses showed high performance at discriminating patients with 4R-tau from those with AD in mainly temporal and parietal regions $SUVr_{20–40}$(60–80%).

Conclusion The specific combination of CSF p-tau levels and ^{18}F-PI-2620 PET SUVR in disease-specific regions facilitates biomarker-guided stratification of AD and clinically suspected 4R-tauopathies.

18 MONASH STATUS EPILEPTICUS STUDY (MOSES): GLASGOW COMA SCORE, AGE AND INPATIENT ONSET, NOT TIME TO TREATMENT, PREDICT MORTALITY IN STATUS EPILEPTICUS

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Background There is ongoing controversy over the predictors of mortality and morbidity in status epilepticus (SE). As a result, many of the mortality prediction tools that have been introduced have failed to gain widespread acceptance.

Objectives To identify predictors of mortality and morbidity in SE in an Australian setting.

Methods We retrospectively reviewed medical records between January 2020 and December 2020 to identify patients diagnosed with SE. D ata regarding in-hospital mortality, modified Rankin Score (mRS), medical history, management and outcomes were collected from the electronic medical records.

Results We identified 157 patients. In-hospital mortality was 20.4% (32/157) and of the 125 that survived, 25.6%(32/125) had increased morbidity. Only 67(42.7%) of patients received first-line therapy, and of these only 35 were given within 20 minutes of first medical contact.

After adjusting for confounders, age, presenting Glasgow Coma Score (GCS), inpatient onset of SE, stroke and cardiac arrest were independently associated with in-hospital mortality. Using a predictive model with age, GCS and inpatient onset, we were able to predict in-hospital mortality with an area under the Receiver Operating Characteristic (ROC) curve (AUC) of 0.81.

Male sex and inpatient onset were independent predictors of increased morbidity. Time to treatment were not predictors of mortality.

Conclusion SE was associated with a high rate of mortality and morbidity in an Australian setting. Less than one-quarter of patients had timely provision of first-line SE treatment. Time to treatment was not associated with short-term mortality. A simple model comprising age, GCS and inpatient onset of SE was able to predict mortality.

19 FUNCTIONAL BRAIN MAPPING WITH TASK INDUCED GAMMA BAND ACTIVITY, DURING STEREOTACTIC-EEG: CURRENT STATE AND FUTURE DIRECTIONS

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Functional brain mapping with direct cortical stimulation (DCS) may be required for patients undergoing stereotactic-EEG (SEEG), as workup towards epilepsy surgery. DCS has several limitations. Task-induced gamma-band-activity (GBA) is an emerging mapping technique that may complement or replace, mapping with DCS. Experience with SEEG-GBA mapping is currently limited.

Objective Provide a comprehensive review of the literature exploring functional mapping during SEEG, with GBA.