

Conclusions Severe illness and more aggressive management were major risk factors for acute stroke. Traditional vascular risk factors and Caucasian ethnicity were risk factors for ischaemic stroke, while Hispanic or black ethnicity, higher PaO₂, and ECMO were significant risk factors for haemorrhagic stroke.

036

NERVE EXCITABILITY AND MOTOR UNIT NUMBER ESTIMATION: EARLY BIOMARKERS OF NERVE INVOLVEMENT IN HEREDITARY AMYLOIDOSIS (ATTRV)

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Objective Gene silencing treatments for hereditary transthyretin amyloidosis (ATTRv) have recently been developed with dramatic improvements observed in patient outcomes. However, the optimal time to initiate treatment is not yet known. The aim of this study is to explore the pathophysiological progression of neuropathic features of ATTRv using nerve excitability and motor unit number estimation.

Methods We prospectively recruited 14 symptomatic patients and 7 asymptomatic carriers and with varied TTR mutations and compared these to 21 healthy controls. Nerve excitability properties of ulnar motor and sensory axons, and ulnar-ADM motor unit number estimation was collected.

Results 'Fanning in' of threshold electrotonus was observed in the motor axons of symptomatic ATTRv patients, suggestive of membrane depolarisation. Motor unit number estimation demonstrated a significant reduction in mean unit number between symptomatic and asymptomatic ATTRv patients ($p=0.04$), with declines seen according to FAP stage and PND score. Significantly increased hyperpolarising current/threshold gradients were seen in sensory axons between symptomatic ATTRv patients and healthy controls ($p=0.002$), suggesting that upregulation of inwardly rectifying conductance may underlie sensory symptoms and neuropathic pain in ATTRv amyloidosis.

Conclusions These findings suggest that ulnar nerve excitability and motor unit number estimation could be used as a tool to identify early nerve disease in ATTRv and monitor progression.

037

THE GUT MICROBIOME IN PARKINSON'S DISEASE: LONGITUDINAL INSIGHTS INTO DISEASE PROGRESSION AND THE USE OF DEVICE-ASSISTED THERAPIES

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Objectives Previous studies have reported altered gut microbiome (GM) composition in association with motor and non-motor symptoms in Parkinson's disease (PD). Only a few prior studies considered the influences of PD medications, namely oral therapies, on the GM. We investigated the temporal stability of GM profiles from PD patients initiating device-assisted therapies (DAT) and in a separate cohort characterise GM influences on PD progression.

Methods Clinical data from validated questionnaires and stool samples from 74 PD patients and 74 healthy controls (HCs) were longitudinally evaluated, at $t=0$, 6 and 12 months. PD patients were sub-stratified as faster or slower progressors, inferred from levodopa equivalence dose and motor severity measures. Additionally, 19 PD patients receiving Deep Brain Stimulation or levodopa-carbidopa intestinal gel were longitudinally evaluated at $t=0$, 6 and 12 months post-therapy initiation.

Results Persistent underrepresentation of short-chain fatty-acid-producing bacteria, *Clostridium_XVIII*, *Butyrivibrio* and *Fusicatenibacter* was apparent in PD patients compared to HCs. No persisting GM profiles were recognised between faster and slower progressing patients, although predictive modelling supported the use of GM profiles to assist in defining PD progression. Our previous findings of acute GM changes in response to DAT initiation were not sustained at 6 and 12 months, although differing microbiota profiles persisted following DAT initiation.

Conclusions We present the largest longitudinal GM study in PD patients showing persistently altered GM profiles indicative of underrepresentation of short-chain fatty-acid-producing bacteria. DAT's were found to exert acute variable influence on the GM that didn't persist over time.

038

RESOLVING INFECTIOUS MENINGITIS IN UGANDA WITH METAGENOMICS AND HOST TRANSCRIPTOMICS

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Objectives Tuberculous meningitis (TBM) is a common cause of meningitis in sub-Saharan Africa. CSF PCR with GeneXpert RIF/MTB Ultra is only 70% sensitive for detection of definite/probable TBM. Many infections can mimic TBM. Metagenomic next generation sequencing (mNGS) can detect the whole diversity of infectious microbes, but can be insensitive to TB in CSF. We assessed whether leveraging CSF mNGS to identify infections combined with a machine learning classifier (MLC), based on host transcriptomic data generated by mNGS, could enhance diagnostic accuracy for TBM.

Methods Prospectively enrolled 347 HIV-infected Ugandan adults with subacute meningitis: RNA/DNA libraries were made from CSF and deep sequenced. Non-human sequences