



Abstract Highlights

The following highlights have been selected from the European Academy of Neurology (EAN) Tournament Finals, a special session format featuring 6-minute presentations by participants. The abstract topics include novel approaches to communication in brain injury, predicting atrial fibrillation in cardioembolic stroke, and genetic testing for early onset Parkinson's disease.

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Novel Bedside-Approach to Communication in Brain Injury: Tongue-Based Motor Imagery

"Functional near-infrared spectroscopy (fNIRS) offers a non-invasive approach by measuring variations in cortical blood oxygenation levels."

PATIENTS with severe brain injuries face significant challenges in verbal and motor communication, as emphasised by Pardis Zarifkar, Department of Neurology, Copenhagen University Hospital, Denmark, during the 9th Congress of the European Academy of Neurology (EAN). In turn, these challenges present obstacles in conducting cognitive assessments.

In the context of evaluating motor cortex activation in the absence of physical movement, functional near-infrared spectroscopy (fNIRS) offers a non-invasive approach by measuring variations in cortical blood oxygenation levels. The proof-of-concept study by Zarifkar and colleagues investigates the feasibility of utilising tongue-based commands as a novel method of motor imagery communication using fNIRS.

The study included a cohort of 20 healthy staff volunteers from the Copenhagen University Hospital. They underwent fNIRS measurements targeting the frontoparietal and primary motor cortices, while performing tasks related to tongue motor and tongue motor imagery. To distinguish between tongue motor imagery and

a relaxed state, the researchers employed a support vector machine classifier to classify the brain activation patterns.

The results revealed that all participants successfully elicited activation in the tongue motor homunculus through tongue motor imagery, showing similar activation responses to those observed during actual physical tongue movement. The activation was specifically localised to the left hemisphere in both the tongue motor and tongue motor imagery tasks. Furthermore, tongue motor imagery specifically activated the frontoparietal regions that are associated with cognitive processing. The classifier achieved a high accuracy of 92% in successfully distinguishing motor imagery from the relaxed state.

Zarifkar underscored the significance of their study as a proof-of-concept for the application of a novel tongue motor imagery paradigm in healthy individuals. This highlights the potential of fNIRS to facilitate cognitive assessments, and enable meaningful interactions in patients with severe brain injury. ●

Pathogenetic Mechanism Underlying Concomitant Continuous Pain in Trigeminal Neuralgia

TRIGEMINAL neuralgia is characterised by the presence of continuous, burning pain, in addition to the characteristic electric shock-like paroxysmal pain. Typically, this pain responds less effectively to available treatments, so it is thought to be caused by a different pathogenetic mechanism. Gianfranco De Stefano, Sapienza University of Rome, Italy, therefore sought to investigate the pathogenetic mechanism underlying trigeminal neuralgia in patients with a definite diagnosis.

Presented during the 9th Annual Congress of the European Academy of Neurology (EAN), participants were subclassified according to the presence or absence of concomitant continuous pain. Both groups then underwent high resolution 3T MRI with a volumetric study of the trigeminal nerve, laser-evoked potentials, and quantitative sensory testing, according to the Network of Neuropathic Pain (DFNS) protocol.

"A total of 73 patients with a definite diagnosis of trigeminal neuralgia were enrolled in the study."

A total of 73 patients with a definite diagnosis of trigeminal neuralgia were enrolled in the study, with 28 reporting concomitant continuous pain (38%). Analysis of MRI data suggested patients with concomitant continuous pain showed a more severe trigeminal root atrophy ($p < 0.05$).

Overall, De Stefano concluded that the multimodal findings converged in showing that concomitant continuous pain is associated with axonal loss and the impairment of small trigeminal fibres. Furthermore, it is hypothesised that the axonal loss may trigger hyperexcitability in the second order neurone, as indicated by the correlation between the volume of the affected nerve with the wind-up ratio. This abnormal activity could underlie the development of concomitant continuous pain in trigeminal neuralgia. ●





Multiple Acute Ischaemic Lesions in Secondary Prevention with Dual Antiplatelet Treatment

FINDINGS from an ongoing, prospective, nationwide, multicentre, observational study show evaluating the efficacy of dual antiplatelet treatment (DAPT) for secondary prevention of transient ischaemic attack (TIA) or minor non-cardioembolic ischaemic stroke were presented at the 9th Congress of the European Academy of Neurology (EAN).

Some patients with a diagnosis of non-cardioembolic ischaemic stroke or high-risk TIA experience recurrent ischaemic events, despite receiving optimal treatment and secondary prevention with DAPT. Research by Eleonora De Matteis, Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, Italy, and colleagues sought to evaluate the effectiveness of secondary prevention with short-term DAPT in this patient cohort.

"These lesions occurred in different vascular territories in 20.3%."

The team enrolled patients from 62 different centres with non-cardioembolic ischaemic stroke or high-risk TIA receiving secondary preventive DAPT since February 2021. Whilst the recruitment and 90-day follow-up is ongoing, as of 8th January 2023, a total of 1,578 patients had been included in the study. Of these patients, 1,153 (73.1%) had undergone an MRI scan.

Upon evaluation of these scans to look for evidence of multiple acute ischaemic lesions, an indicator of occult cardioembolism, the team found that 251 patients (21.8%) displayed no acute ischaemic lesions, 558 patients (48.4%) displayed a single acute ischaemic lesion, and 344 patients (29.8%) displayed multiple acute ischaemic lesions. Cardiac monitoring for >24 hours was performed in 79.0% of patients who displayed multiple acute lesions.

Further analysis of those with multiple acute ischaemic lesions on MRI revealed that these lesions occurred in different vascular territories in 20.3%. Further to this, the researchers found that 106 out of 344 (30.8%) were caused by large vessel occlusion, 35 out of 344 (10.2%) were due to other defined causes, and the cause was undetermined in 203 out of 344 patients (59.0%).

The authors concluded that in their real-life prospective study, approximately one-third of patients receiving secondary prevention with short-term DAPT for minor non-cardioembolic ischaemic stroke or high-risk TIA displayed multiple acute ischaemic lesions on MRI, which is a radiological hallmark of cardioembolism. They found that these were mainly caused by arterial stenosis, or an undetermined cause. The ongoing results of this study could help to determine the real-life efficacy of short-term DAPT in secondary prevention of minor non-cardioembolic ischaemic stroke and high-risk TIA. ●

Novel Findings in Bi-allelic *PRKN* Gene Associated with Parkinson's Disease

MUTATIONS in the *PRKN* gene, coding for the protein parkin, are the most common cause of early-onset Parkinson's disease. New research, presented in the form of an abstract at the 9th Congress of the European Academy of Neurology (EAN), has provided the first proof that missense variants and variants located in the N-terminal of the protein are associated with a more benign progression of Parkinson's.

A total of 644 patients were included in the analysis reported, with age at onset 31.40 ± 11.38 years, and a disease duration 18.00 ± 12.50 years. These patients all had bi-allelic pathogenic mutations in *PRKN*, and no pathogenic mutations in other genes known to result in monogenic Parkinson's disease. Over 140 different mutations spanning the entire gene can be attributed to autosomal recessive inherited Parkinson's diseases; therefore, these research findings are all the more impressive. The type of mutation was analysed for an association with the age at onset and motor severity, considering disease duration as a covariant.

"Missense variants and variants of the N-terminal are associated with a less sinister progression of the disease."

Mean unified Parkinson's disease rating scale (UPDRS) score at the time of disease onset was 12.60 ± 1.40 , increasing by 3.85 ± 0.60 every 10 years ($n=310$; $p=3.6e-09$). Average initial L-dopa equivalent daily dose among those participants who had never received deep brain stimulation was 320 ± 71 mg, and this increased by 118 ± 30 mg every 10 years ($n=94$; $p=0.0013$). Patients with two missense variants had a later age of onset (36.4 ± 12.3 years) compared with those that had two structural variants (31.2 ± 10.8 years; $p=0.004$). Variants located at the N-terminus of the protein, more specifically exons 1–3, were associated with an earlier age at onset of Parkinson's disease (30.9 ± 10.3 years) when compared with variants located at the C-terminus, exons 7–12 (34.9 ± 12.5 ; $p=0.05$).

Demonstrating for the first time that missense variants and variants of the N-terminal are associated with a less sinister progression of the disease, the researchers were proud to present their findings at EAN 2023. The conclusions from this study will certainly provide a springboard for honing the specifics of future study, delving deeper into the complexities of mutations that cause Parkinson's disease, and also opening the door for potential early lifestyle changes, and/or treatment via genetic screening of patients. ●



Plasma Biomarkers: Predicting Atrial Fibrillation in Cardioembolic Stroke

BIOMARKERS found in patient plasma display use in predicting atrial fibrillation (AF) and early identification of cardioembolic stroke, according to researchers from the Neurology Department, Centro Hospitalar Entre Douro e Vouga, Santa Maria da Feira, Portugal, presented at the 9th Congress of the European Academy of Neurology (EAN).

Over a 2-year period, between January 2020–January 2022, Barbara Teixeira, Centro Hospitalar Entre-Douro e Vouga, and colleagues consecutively recruited a total of 717 patients admitted to the Stroke Unit with an ischaemic stroke diagnosis, with the aim of evaluating the accuracy of three plasma biomarkers: brain natriuretic peptide (BNP), N-terminal-proBNP (NT-proBNP), and troponin I, in predicting AF. Medical records were retrospectively reviewed to ascertain plasma BNP, NT-proBNP, and troponin I levels in the acute phase, and ≥ 48 -hour ECG monitoring was also reviewed. Of the 717 enrolled patients, 583 had no previous AF diagnosis.

The results showed for patients without a previous diagnosis of AF, 120 out of 507 (23.7%) patients had a high troponin I on admission, 164 out of 432 (38.0%) had a high BNP, and 24 out of 68 (35.5%) had a high NT-proBNP.

Further analysis showed that of the 120 patients with a high admission level of troponin I, 35.8% had AF (risk ratio [RR]: 2.2, 95% confidence interval [CI]: 1.6–3.0). The AF detection sensitivity and specificity were 40.1% and 81.0%, respectively, with an area under the receiver operating characteristic curve (AUC) of 0.69.

AF was identified in 41.5% of patients with an elevated BNP (RR: 4.8; 95% CI: 3.1–7.4). The sensitivity and specificity for AF detection were 74.7% and 71.8%, respectively, and AUC was 0.73. Similarly, in patients with a high NT-proBNP, 47.5% had AF (RR: 4.5; 95% CI: 1.6–12.8), with a detection sensitivity of 71.8%, specificity of 73.6%, and AUC of 0.72.

The authors concluded that BNP, NT-proBNP, and troponin I can be helpful for early identification of cardioembolic stroke. The study highlighted that of these plasma biomarkers, troponin I displayed greater specificity but lower sensitivity in detection of AF than BNP and NT-proBNP, whereas BNP and NT-proBNP exhibited higher sensitivity but lower specificity in AF detection than troponin I. ●

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Harmonising Genetic Testing for Early Onset Parkinson's Disease

NOVEL results from the PARKNET multicentre study have highlighted the importance of correctly interpreting genetic testing from multiple different laboratories, for patients with early-onset Parkinson's disease (EOPD). Patients with EOPD often submit to diagnostic genetic testing based on next-generation sequencing (NGS). However, frequently, the subsequent interpretation of the NGS results can be challenging in a diagnostic setting, with an additional lack of research/ literature currently addressing this challenge.

This study, presented at the 9th Congress of the European Academy of Neurology (EAN), retrospectively collected the data of 648 patients with EOPD (age of onset: >55 years), who had undergone NGS of a minimal panel of 15 PD-related genes, as well as a PD Multiplex Ligation-dependent Probe Amplification's (MLPA) from eight Italian genetic diagnostic laboratories. The patients were additionally analysed to look at the very-EOPD subgroup of patients with an age of onset of >40 years. All variants were classified according to the latest American College of Medical Genetics (ACMG) criteria, and the diagnostic outcomes pre- and post-harmonisation were compared.

The researchers found that in 186 of the 648 patients with EOPD (29%), and in 71 of the 167 patients with very-EOPD (45%), the diagnostic report listed at least one single nucleotide variant or copy number variation. In 105 of the patients with EOPD (16%) the testing outcome was considered diagnostic. After harmonisation, the genetic diagnosis changed in 20 out of 186 patients with EOPD, with six reporting shifts from non-diagnostic to diagnostic, and 14 diagnostic reports being reclassified as inconclusive. A definite diagnosis was reached in 97 patients with EOPD (15%), and 39 patients with very-EOPD (25%), the majority of whom carried either GBA variants or bi-allelic *PRKN* single nucleotide variants or copy number variations (17 EOPD [3%]; 12 very-EOPD [8%]). In 89 EOPD (14%) cases and 32 very-EOPD cases (20%), the genetic report was inconclusive.

The study represents a successful attempt to harmonise diagnostic reporting of PD genetic testing across several different laboratories, underlining the current challenges in the interpretation of genetic variants emerging from NGS multigene panels, and highlighting the relevant implications in terms of counselling. ●

"Patients with EOPD often submit to diagnostic genetic testing based on next-generation sequencing."
