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Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "Stroke Newsletter" which contains latest and interesting news in the field of Neuropsychiatry.

This issue contains:

1. **Association between patterns of brain infarction and increased incidence of late onset movement disorders after acute ischemic stroke**
2. **Association of transient ischemic attack and acute ischemic stroke progression with gut microbiota**
3. **Association of Gadolinium Leakage into Ocular Structures with Stroke Outcomes: Insights from the WAKE-UP Trial**
4. **A Rare Case of Multi-Territory Ischemic Stroke in Fahr's Disease**

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Looking forward to your valuable feedback
Best Regards,
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Association between patterns of brain infarction and increased incidence of late onset movement disorders after acute ischemic stroke

Introduction –

AIS patients treated with IVT/MT have more late-onset movement disorders and worse 90-day outcomes, especially with basal ganglia involvement.

Movement disorders following acute ischemic stroke (AIS) in the basal ganglia (BG) are common, presenting with both hyperkinetic and hypokinetic symptoms.[1] With a prevalence of 1-4%, these disorders typically emerge at varying latencies, such as hemichorea around 4.3 days post-stroke and hemi parkinsonism about 118 days later. Due to their delayed onset and variability in post-acute care follow-up, late-onset movement disorders are often under-recognized. Although treatable, the impact of these conditions on functional recovery and quality of life remains poorly understood, underscoring the need for standardized screening and long-term neurological follow-up.[2] So, this study evaluated the incidence and characteristics of these conditions in AIS patients treated with intravenous thrombolysis (IVT), mechanical thrombectomy (MT), or both, focusing on infarction patterns in the basal ganglia.

Ischemic stroke

Methods –

This retrospective cohort study included patients aged 18 and older with acute ischemic stroke (AIS) treated with IVT, MT, or both of at least one post-acute care follow-up in the Neurology Clinic within the first year after stroke. Follow-up done at 1-3 months, 6 months, and 12 months. Data were extracted from electronic health records (EHR), including demographics, comorbidities, stroke severity, treatments, neuroimaging, movement disorders, and functional outcomes. Neuroimages were reviewed by trained team members to identify BG infarcts, extensive MCA cortical infarcts, and primary motor cortex infarcts. Discharge summaries and

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outpatient notes were assessed for movement disorders. Statistical analysis involved descriptive statistics, using Fisher's exact test.

Results–

This study included 364 patients with AIS treated with revascularization therapies. Of these, 24 survivors (6.6%) developed late-onset movement disorders by one year. The average onset of movement disorders was 115 days post-stroke (SD = 102). Among those with movement disorders, 71% had hemi-parkinsonism, 25% had tremor, and 4% had dystonia. Survivors with BG infarcts without extensive middle cerebral artery (MCA) cortical infarcts or motor cortex involvement had an 18% incidence of movement disorders. Figure 1 shows the relationship between infarct patterns and movement disorder incidence. The incidence of movement disorders was significantly higher in patients with BG infarcts compared to those without (15.6% vs 1.3%, p <0.001). Patients with BG infarcts without substantial MCA cortical infarctions had a higher risk of developing Movement disorders (17.9% vs 6.9%, p = 0.25). Patients with BG infarcts but no motor cortex infarcts were more likely to have movement abnormalities than those with motor cortex infarcts (17.5% vs 4.8%, p = 0.20). Patients with BG infarcts without substantial MCA cortical infarcts or primary motor cortex infarcts had a higher risk of developing movement disorders (18% vs 0%, p = 0.07). There were no significant differences between MT and IVT alone in the likelihood of developing movement disorders (p = 0.14).

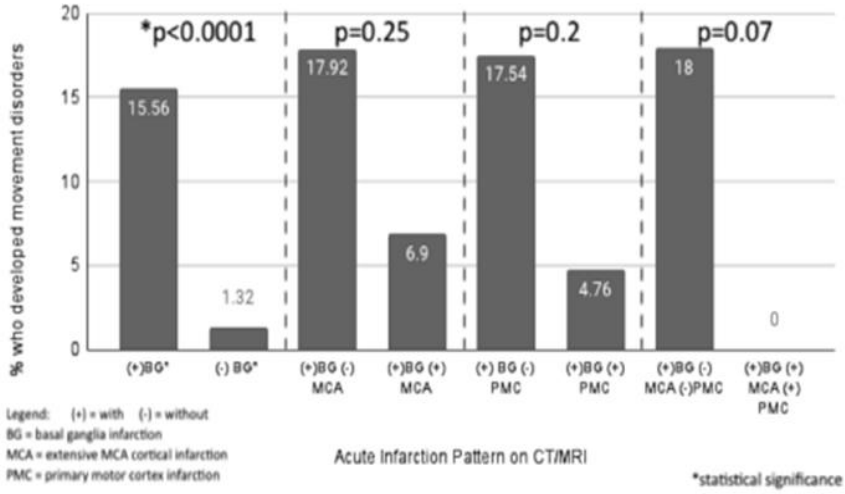

Figure 1. Association between infarction patterns and late-onset movement disorder rates.

Discussion–

This was the first study to report the one-year incidence of late-onset movement disorders after AIS treated with revascularization therapies. It was found that survivors with isolated BG infarcts or BG-dominant infarcts were more likely to develop movement disorders, aligning with prior research linking BG involvement to such disorders.[3,4] This study shows that certain

brain infarct patterns are linked to a higher risk of late-onset movement disorders and poorer outcomes at 90 days, contrasting with broader AIS studies that include a wider range of infarct patterns not directly related to movement disorders.[2]

Conclusion –

Patients with AIS treated with IVT, MT, or both have an increased incidence of late-onset movement disorders, particularly those with BG involvement, which correlates with poorer functional outcomes at 90 days.

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Association of transient ischemic attack and acute ischemic stroke progression with gut microbiota

Introduction-

Gut microbiome changes may serve as early biomarkers for predicting the progression from TIA to AIS, enabling potential early detection of stroke.

Acute ischemic stroke (AIS) remains a significant global health concern, ranking as a leading cause of mortality and long-term disability.[1] The pathogenesis of AIS is influenced by multiple factors, including metabolic disorders, systemic inflammation, and disruptions in gut microbiota composition. Approximately 30% of AIS cases are preceded by transient ischemic attack (TIA), but reliable biomarkers for predicting the progression from TIA to AIS are scarce. Existing diagnostic approaches primarily rely on medical history and imaging and have limited sensitivity. Despite these findings, previous studies have mainly focused on the relationship between microbiota and AIS or TIA individually, leaving the potential of microbiome signatures in predicting the

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progression from TIA to AIS unexplored.[2] So, this study investigated gut microbiome signatures as predictive biomarkers for the progression from TIA to AIS.

Methods – This cohort study recruited 235 AIS patients, 28 TIA patients, and 75 healthy controls including participants with large-artery atherosclerosis and excluding those with recent antibiotic use, severe comorbidities, or non-atherosclerotic stroke causes. Demographic, clinical, and lifestyle data were collected, along with laboratory measurements of fasting glucose, HbA1c, homocysteine, triglycerides, HDL, and D-dimer. Fecal samples were obtained, DNA extracted, and the 16S rRNA gene sequenced. Microbial diversity was assessed using alpha (Ace, Shannon) and beta (PCoA) diversity indices, and the microbiota dysbiosis index (MDI) was calculated. Significant species were identified using LEfSe, and correlations between genera and clinical variables were visualized using heatmaps.

Results- Eighteen participants were excluded, and nine dropped out, leaving 28 TIA and 235 AIS patients. TIA patients had a median age of 65 years and were 50% female. α-diversity indices showed no significant differences between HC and TIA or HC and AIS ($p>0.05$), but significant differences were observed between TIA and AIS ($p<0.05$). The MDI showed microbial dysbiosis increasing from TIA, AIS to HC. At the phylum level, Firmicutes, Proteobacteria, Bacteroidota, and Actinobacteriota predominated, with higher Proteobacteria in TIA. At the genus level, Escherichia-Shigella was more abundant in TIA. Key bacterial families, including Lachnospiraceae and Enterobacteriaceae, differed across groups. Correlation analysis revealed Lactobacillus was positively correlated with homocysteine ($\rho = 0.2235$, $p < 0.05$) and negatively with HDL ($\rho = -0.2395$, $p < 0.05$). Lactobacillus and Streptococcus were identified as microbial biomarkers distinguishing TIA from AIS, with AUC values of 0.626 ($p < 0.05$) and 0.699 ($p < 0.05$), respectively (Figure 1).

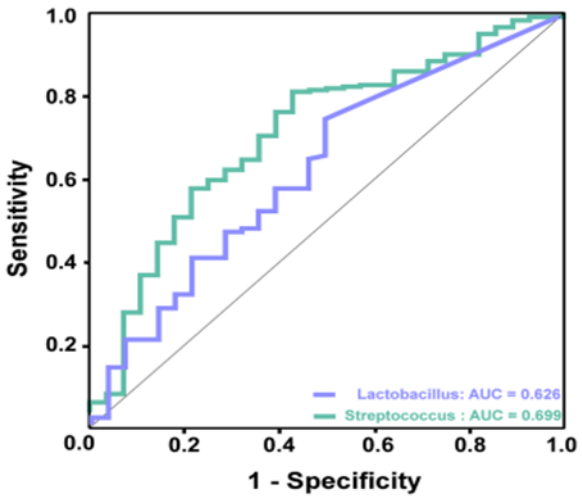

Figure 1: ROC analysis of microbial biomarkers for AIS prediction.

Discussion – This study highlighted significant differences in gut microbiota between TIA, AIS, and HC groups, with an increased abundance of Streptococcus and Lactobacillus and a decreased presence of SCFA-producing bacteria like Lachnospiraceae_UCG-004 in AIS patients. These findings align with previous studies linking microbial dysbiosis to stroke, where Streptococcus is associated with inflammation and Lactobacillus may have modulating

effects.[3] Also, this study found gut microbiota dysbiosis in TIA and AIS groups, with increased Streptococcus and Lactobacillus and decreased SCFA-producing bacteria like Butyricicoccaceae and Lachnospiraceae_UCG-004 compared to HC. The progressive increase of Streptococcus and Lactobacillus and decrease of SCFAs across groups aligns with previous studies, supporting the role of microbial imbalance in stroke pathogenesis.[4]

Conclusion – Distinct changes in the gut microbiome were identified and associated with the progression from TIA to AIS, with specific bacteria highlighted as potential predictive biomarkers. These findings support the development of microbiome-based diagnostic methods for early AIS detection.

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Association of Gadolinium Leakage into Ocular Structures with Stroke Outcomes: Insights from the WAKE-UP Trial

Introduction – The blood-brain barrier (BBB) is a critical structure that maintains homeostasis and protects the central nervous system (CNS) by limiting the passage of harmful substances.[1] BBB disruption is common in acute ischemic stroke and is linked to hemorrhagic complications. Imaging biomarkers such as dynamic contrast-enhanced imaging and the hyperintense acute reperfusion marker (HARM) detect BBB disruption, with HARM indicating gadolinium leakage into cerebrospinal fluid (CSF) and serving as a predictor of hemorrhage after reperfusion therapy. Gadolinium leakage into ocular structures (GLOS), observed in ischemic stroke, results from disruption of the blood-ocular barrier (BOB) and is visualized on post-contrast fluid-attenuated

GLOS in acute ischemic stroke is associated with age, renal dysfunction, white matter hyperintensity, and HARM.

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inversion recovery (FLAIR) imaging. GLOS prevalence in ischemic stroke patients ranges from 46% to 76%, and it has also been observed in patients with vascular risk factors but without clear brain or ocular abnormalities.[2] So, this study aimed to investigate the association of GLOS with clinical characteristics, HARM, hemorrhagic transformation at 24 hours, and functional outcomes at 90 days in acute stroke patients from the WAKE-UP trial (MRI-Based Thrombolysis in Wake-Up Stroke).

Methods – Data from the WAKE-UP trial, a multicentre, randomized, double-blind, placebo-controlled study, were analysed. This trial included acute stroke patients with a DWI-FLAIR mismatch and unknown stroke onset time, randomized to receive alteplase (IV tPA) or placebo. Baseline imaging included MRI (DWI, FLAIR, and GE/SWI) with optional PWI, and follow-up imaging was performed 22–36 hours later. Only patients who received gadolinium contrast for dynamic susceptibility contrast PWI and had sufficient quality baseline and follow-up FLAIR images were included. The primary outcomes assessed were hemorrhagic transformation (HT) using the Heidelberg criteria and functional outcome based on the modified Rankin Scale (mRS) at 90 days, with poor functional outcomes defined as mRS 3–6.

Results – In the WAKE-UP trial, 192 patients with baseline PWI and FLAIR imaging were analyzed, of which 56 (29%) developed GLOS, which was significantly associated with older age (73 vs. 65 years). GLOS primarily affected both the aqueous and vitreous chambers, with most cases being bilateral. HARM was more frequent in patients with GLOS (16%) compared to those without (3%). However, the rates of hemorrhagic transformation (HT) (21% vs. 24%) and parenchymal hematoma (PH) (7% vs. 5%) were similar between the groups. Multivariable analysis showed no independent association of GLOS with poor functional outcome at 90 days (25% vs. 26%) (Table 1). These findings suggest that while GLOS is more common in older patients and

Follow-up Characteristics	GLOS+ (n=56)	GLOS- (n=136)	p-Value
HARM	9 (16%)	4 (3%)	<0.01
Any HT	12 (21%)	32 (24%)	0.90
Any PH	4 (7%)	7 (5%)	0.74
Poor outcome	14 (25%)	35 (26%)	1.00

Table 1. HARM and outcome characteristics in patients with vs. without GLOS

associated with higher HARM rates, it does not independently predict hemorrhagic complications or functional recovery.

Discussion – GLOS was significantly associated with older age, worse renal function, and higher WMH volume suggesting that it reflects general vascular health and endothelial integrity, which was consistent with previous findings linking GLOS to aging and small vessel disease.[3,4] In the current study, GLOS and HARM both identify changes linked to age, renal function, and gadolinium dosage, but HARM is more specific to acute ischemic brain injury and less frequent. While HARM has been associated with hemorrhagic transformation (HT) in some studies, this association was not consistent and was not observed for GLOS, suggesting that these markers reflect distinct pathophysiological mechanisms.[5]

Conclusion – GLOS is a prevalent finding in acute ischemic stroke and is associated with advanced age, impaired renal function, increased white matter hyperintensity burden, and HARM.

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A Rare Case of Multi-Territory Ischemic Stroke in Fahr's Disease

Introduction –

Substantial calcium deposits in afflicted arteries may lead to small-artery blockage and, ultimately, ischemic stroke.

Fahr's disease, also known as bilateral striopallidodentate calcinosis, is a rare neurodegenerative condition characterized by bilateral calcifications in the basal ganglia and other brain regions. The disease

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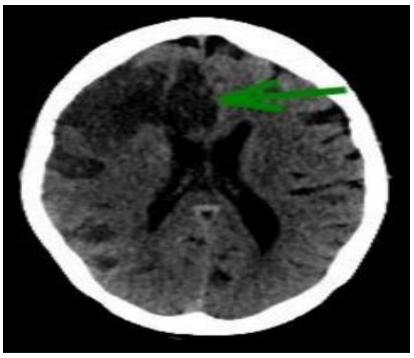
typically manifests with neuropsychiatric symptoms such as dementia, schizophrenia-like psychosis, mood disturbances, and extrapyramidal movement disorders. It was first described by Fahr in 1930 and the condition is characterized by T2 hyperintensity on MRI, which may indicate a progressive inflammatory or metabolic process contributing to calcification in the vascular structures. While movement disorders and cognitive impairments are prevalent, ischemic stroke as an initial symptom is uncommon.[2] Here, this case presents Fahr's disease with stroke as the presenting symptom.



Case presentation –

A 75-year-old female presented to the emergency department with elevated blood pressure and slurred speech. The emergency non-contrast CT imaging of the brain revealed extensive bilateral symmetrical calcifications in the dentate nuclei and basal ganglia, consistent with Fahr's disease. In addition, hypodensities in the right frontoparietal lobe and basal ganglia suggested acute infarcts in the right MCA and ACA territories, accompanied by mild effacement of the right frontal horn and a subtle midline shift of 3.5 mm (Figure 1). Internal hyperdensities with a CT attenuation of 60 HU suggest hemorrhagic conversion of the infarcts. Additionally, subcortical and periventricular white matter changes are present, indicating chronic microvascular ischemic alterations. Carotid ultrasound showed a 50% stenosis at the right carotid bifurcation with elevated peak systolic velocity (180 cm/s), while the left carotid bifurcation demonstrated no significant stenosis. ECG showed normal sinus rhythm with premature ventricular contractions (PVCs). The echocardiogram and lab markers were unremarkable. This case represents a rare co-occurrence of Fahr's disease, multi-territory ischemic stroke, and a small falx lipoma.

Figure 1. CT non-contrast axial image showing right ACA and MCA infarcts.

Discussion– Fahr's disease is a rare neurodegenerative disorder marked by basal ganglia calcifications, often due to calcium-phosphorus metabolism disruptions or blood-brain barrier dysfunction, with SLC20A2 mutations identified as a key cause. This aligns with previous studies on genetic and calcium dysregulation.[3] Although ischemic stroke is not typically linked to Fahr's disease, some reports suggest calcifications impair vascular reactivity, contrasting with the common view of the disease.[2]

Conclusion– There were only a few case studies reported acute ischemic stroke or transient ischemic attack-like events in FD. Therefore, the findings in this case may provide valuable insights for predicting and managing stroke in FD patients in the future.

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