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Poster Presentations

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Increase in cerebral blood flow on brain magnetic resonance angiogram following correction of cervical lordosis

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Abstract

Background: Loss of cervical lordosis is associated with decreased vertebral artery hemodynamics. Vertebral arteries merge forming the basilar artery which continues to the circle of Willis and cerebral arteries. A close anatomical relationship exists between the cervical spine, vertebral arteries, and cerebral vasculature.

Aim: Evaluate cerebral blood flow changes on brain MRA in patients with loss of cervical lordosis prior to and following correction of cervical lordosis.

Method: This study is a retrospective consecutive case series. Cervical lordosis of seven patients (five females, two males, 28 to 58 years) was measured on lateral cervical radiographs ranging from −13.1 to 19.0 degrees (ideal is −42.0 degrees). Brain MRAs were analyzed for pixel intensities representing blood flow. Pixel intensity of the cerebral vasculature was quantified, and percent change determined.

A student's t-test established significance of percent change in cerebral blood flow between pre- and post-cervical lordosis adjustment images. Regression analysis was performed. An a priori analysis determined correlation between cervical lordosis and change in MRA pixel intensity. The statistician was blinded to cervical lordosis.

Results/Conclusions: Pixel intensity increased 23.0 to 225.9% and a student's t-test determined the increase was significant ($p < 0.001$). Regression analysis of change in pixel intensity versus cervical lordosis showed that as deviation from a normal cervical lordosis increases, percent change in pixel intensity on MRA decreases.

These results indicate that correction of cervical lordosis may be associated with immediate increase in cerebral blood flow. Further studies are needed to confirm these findings and understand clinical implications.

Table 1. Cervical Lordosis and Cerebral Blood Flow Quantifications of Participants for Pre and Post Cervical Lordosis Adjustment MRA.

Participant	Normal ARA C2–C7 (°)	ARA C2-C7 (°)	Deviation from ideal ARA C2–C7 (°)	Pre-Adjustment MRA area over threshold (in^2)	Post-Adjustment MRA area over threshold (in^2)	Pre-adjustment MRA total pixel intensity	Post-adjustment MRA total pixel intensity	Percent change in total pixel intensity (%)	Pre-adjustment MRA threshold
1	−42.0	19.0	61	0.444	0.525	453094	557461	23.0	76
2	−42.0	6.7	48.7	0.257	0.311	190537	240016	26.0	60
3	−42.0	3.7	45.7	0.104	0.273	84668	249567	194.8	70
4	−42.0	3.0	45	0.304	0.427	300480	444834	48.0	79
5	−42.0	−11.8	30.2	0.190	0.256	170810	256071	49.9	70
6	−42.0	−13.1	28.9	0.333	0.655	386883	841061	117.4	90
7	−42.0	−20.4	21.6	0.235	0.607	176260	574491	225.9	65
Mean	−42.0	−1.8	40.2	1.721	2.815	251819	451929	97.9	73

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Intermittent fasting mediated metabolic reprogramming reshapes T cell immunity and preserves long-term stroke recovery

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Abstract

Background: Ischemic stroke is the top leading cause of death and disability worldwide, while treatments of stroke is limited. $CD4^+$ T cell response is emerging as an intriguing therapeutic target due to its fundamental role in the evolving of post-stroke neuroinflammation. However, the regulatory mechanisms of $CD4^+$ T cell response after stroke remain largely unknown.

Aim: We aim to investigate the metabolic rewiring of $CD4^+$ T cells poststroke and the specific mechanism underlying the role of T cell immunity in stroke neuroinflammation. We sought to explore novel metabolic intervention targeting $CD4^+$ T cells to improve stroke recovery.

Method: We conducted transient middle cerebral artery occlusion (tMCAO) model with wild type, $Foxk1^{fl/fl}$ and $CD4^{cre}Foxk1^{fl/fl}$ mice, followed with an intermittent fasting (IF) model. Metabolic rewiring and its impact on the stroke outcomes were evaluated by combined transcription and metabolomics analyses, flow cytometry, immunofluorescence, and behaviour tests.

Results/Conclusions: In the current study, we found an improvement on the long-term neurobehavioral function in the IF treated mice compared to normal diet (ND) treated mice after stroke. IF also reduced the infarct volume and improve the white matter injury as measured by MBP and SMI32 immunofluorescent staining. Then with flow cytometry, we found the downregulation of Foxk1 in $CD4^+$ T cells and the decrease in Th17/Treg ratio 28 days poststroke both in the peripheral blood and in the brain. In conclusion, IF may induce metabolic reprogramming of peripheral T cells through Foxk1 and reduce Th17/Treg ratio, thus improving the long-term white matter damage and preserving the neurobehavioral function.

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Advanced theranostic nanocarrier-mediated delivery of NGF in a combination therapy trigger enhanced recovery after stroke

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Abstract

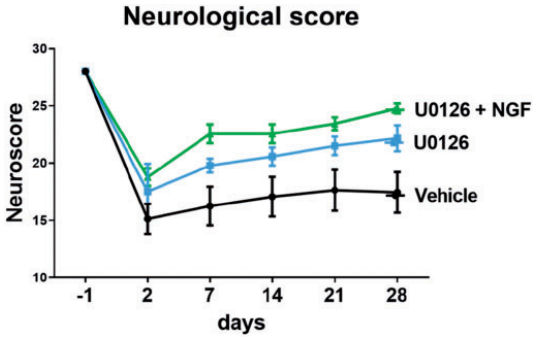
Background: The majority of people who survive the acute phase of stroke remain permanently disabled. So far, no treatment to improve function exist, nerve growth factor (NGF) has emerged as excellent candidate to boost recovery processes. However, the approach to effective deliver NGF has not been possible since it does not pass the blood brain barrier.

Aim: To evaluate if use of an advanced theranostic nanocarrier-mediated delivery of NGF to after stroke enhance recovery of the brain by inducing endogenous repair mechanisms such as neurogenesis and angiogenesis.

Method: Transient middle cerebral artery occlusion was induced in male rats for two hours followed by reperfusion. The specific MEK1/2 inhibitor U0126 was administered i.p at 6 and 24 hours and the NGF was given i.v at day 3 post-reperfusion. Neurological functions were assessed up to 4 weeks after stroke and 9.4 T magnetic resonance imaging was used to monitor perfusion and morphological changes. Recovery processes such as neurogenesis and angiogenesis were evaluated at 4 weeks post stroke by Western Blot.

Results: The combination therapy with NGF and U0126 significantly improved neurological function, perfusion and recovery processes compared to vehicle and U0126 treatment alone. An enhanced NGF protein levels and activation of the TRKa/b signaling pathway in addition to enhanced neurogenesis were observed.

Conclusion: NGF delivered by advanced theranostic nanocarrier promotes recovery processes after stroke and most importantly our delivery approach has demonstrated to be successful. This will be the first step that will lead to novel treatment strategies for neurological disorders.



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Zero-Dose FDG-PET imaging for patients with brain neoplasms using deep learning with multi-contrast MRI inputs

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Abstract

Background: FDG-PET is shown to be of diagnostic value in differentiating the type of brain tumors. However, PET's shortcoming of radiation exposure, high cost and the lack of availability in the world makes the great value to achieve zero-dose PET, i.e., synthesize PET from MRIs.

Aim: To synthesize realistic and diagnostic FDG-PET images by multi-contrast MRI using Transformer-based U-Net with attention modules.

Method: Data: 59 patients with brain neoplasms with paired FDG PET and MRI (T1, T1 with contrast, T2-FLAIR, and ASL) were acquired. Images were co-registered to T1, placed in standard template space. The volumes were normalized by the mean of the non-zero regions. Flipping along X axis was used for data augmentation. Case-wise 5-fold validation was adopted.

Model: A 2.5D U-Net worked as the backbone with adversarial training for better synthesis quality. A CNN-Transformer encoder was employed to leverage detailed high-resolution spatial information by CNN and global context by Transformer. Symmetry-aware spatial-wise attention module and channel-wise attention module are added on short-cuts to emphasize the abnormalities and the useful channels respectively.

Results/Conclusions: Quantitatively, we achieved 27.832 in PSNR and 0.878 in SSIM, improving 7.47% in PSNR and 6.55% in SSIM from U-Net. On neoplasm region, we achieved 22.856 in PSNR and 0.724 in SSIM, increasing 11.19% in PSNR and 6.13% in SSIM from U-Net. Qualitatively, we generated images with accurate pathological features on the neoplasm region. In conclusion, multi-contrast MRIs can be used to synthesize FDG-PET images by deep learning.

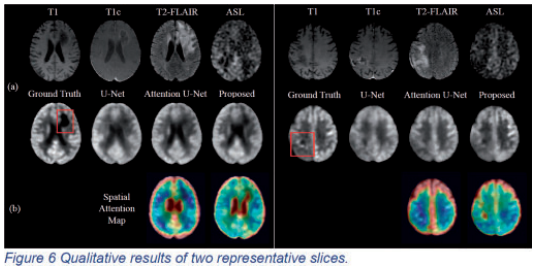

Figure 6 Qualitative results of two representative slices.

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LRRC8A is dispensable for the microglial response to acute stroke

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Abstract

Background: Microglia are brain-resident macrophages, critical for coordinating proinflammatory and regenerative processes following central nervous system (CNS) injury. After cerebral ischaemia, microglia transition to a reactive, amoeboid morphology characterised by increased cell volume at process retraction. However, the regulation of dynamic microglial morphology is unclear. Chloride channels, including the volume-regulated ion channel (VRAC), have been implicated in microglial functions involving cell shape changes, such as motility, phagocytosis, and chemotaxis. VRAC has been proposed as a therapeutic target for acute stroke, but previous studies are limited due to their reliance on non-selective VRAC inhibitors.

Aim: This study aimed to definitively examine the contribution of VRAC to microglial morphology and response to ischaemic damage, using conditional LRRC8A-knockout mice which lack the essential VRAC subunit LRRC8A in microglia.

Methods: Following middle cerebral artery occlusion (MCAo) in mice, immunohistochemistry and confocal imaging were used to visualise microglia for automated morphological analysis. Parameters included volumetric