ROLE OF RESTING STATE FUNCTIONAL MAGNETIC RESONANCE IMAGING IN PATIENTS WITH DURAL ARTERIO-VENOUS FISTULA

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CERTIFICATE

This is to certify that the work incorporated in this thesis titled **"ROLE OF RESTING STATE FUNCTIONAL MAGNETIC RESONANCE IMAGING IN PATIENTS WITH DURAL ARTERIO-VENOUS FISTULA"** ***for*** *the degree of* ***DM*** **NEUROIMAGING AND INTERVENTIONAL NEURORADIOLOGY** *has been carried out by* ***DR. SABARISH S S*** *under our supervision and guidance. The work done in connection with this thesis has been carried out by the candidate himself and is genuine.*

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DECLARATION

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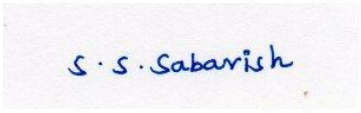

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CONTENTS

INTRODUCTION

Introduction:

Intracranial dural arteriovenous fistula(dAVFs) are acquired lesions from the cerebral arterial vasculature to dural sinuses, represent 10% to 15% of cerebrovascular malformations. The natural history of dAVFs is strongly linked to the absence or presence of drainage into cortical veins, which is termed cortical venous drainage (CVD). Modes of presentation include 1) intracranial hemorrhage (ICH) due to cortical venous hypertension, 2) nonhemorrhagic neurological deficits (NHNDs) due to cortical venous hypertension, 3) symptoms of increased sinus drainage including pulsatile tinnitus and ophthalmological phenomenon, and 4) incidental (1–5)

Dementia as a presenting symptom of high-grade dAVFs is well known. Two types of dAVF-induced dementia have been described, namely cortical dementia, thalamic dementia. Cortical dementia due to dAVF is characterized by rapidly progressive cognitive dysfunction, including impairments in verbal fluency and language comprehension, apraxia, visuospatial discordance, and memory dysfunction that is frequently accompanied by focal cortical deficits including hemiparesis, somatic sensory disturbances, aphasia, alexia, and visual disturbances. Thalamic dementia due to dAVF is characterized by rapidly progressive cognitive dysfunction, including disorientation, executive dysfunction, attention deficits, memory impairment, confabulation, and disinhibition(6–8).

The manner by which this occurs is relatively well established—arterialized venous reflux from the fistula produces regional venous congestion and parenchymal edema, leading to functional compromise of the affected brain regions.

Disruptions of typical organization and interactions within and between functional networks implicate abnormal cognition and behaviour.

Even when a person is at rest, a large number of anatomically separate brain areas show a vast amount of spontaneous low -frequency fluctuations of blood oxygen level-dependent signal and are functionally linked to each other(9,10). Regions that show such synchronized activity during rest are said to form resting-state networks (RSNs). The high level of functional connectivity between RSN regions suggests the existence of direct anatomical pathways between these brain areas to facilitate this high level of ongoing interregional communication

during rest. The interaction among resting-state networks is also critical to normal and aberrant cognitive performance and mental states(11).

Interaction among networks offers valuable insights into the symptom manifestation and pathologic mechanisms of many neurodegenerative diseases(12). More consistent applications are noted in Alzheimer's disease, multiple sclerosis, and amyotrophic lateral sclerosis. The strength of functional connectivity can also be correlated with disease activity.

There are no previous studies on resting-state connectivity changes in dAVF and networks responsible for cognitive changes in DAVF, to the best of our knowledge. Hence this study was undertaken to correlate the neuropsychological assessment, functional connectivity changes using rs-fMRI in a prospective cohort of patients with dural AV fistula before and after embolization.

AIMS AND OBJECTIVES

Hypothesis:

Functional connectivity changes using resting-state fMRI may have a role in predicting cognitive changes in intracranial dural AVF early and may help in further prognostication of the disease process.

Aims and Objectives: -

1. Identification of resting-state fMRI functional connectivity changes in patients with intracranial dural arteriovenous fistula(dAVFs) before and after embolization via functional connectivity analysis in comparison with normal healthy controls
2. Role of functional connectivity changes in the evaluation of cognitive impairment in dAVFs patients in comparison with age-matched cognitively normal healthy controls

REVIEW OF LITERATURE

Dural arteriovenous fistula (DAVF):

Intracranial dural arteriovenous fistula (DAVF)are abnormal arteriovenous shunts located at the layers of the cranial dural mater, supplied through the meningeal branches, constitute about 10-15% of the intracranial vascular malformations(13). Rizzoli in 1881 was the first one to make an anatomic description of dural arteriovenous fistula. Sachs E was the first one to describe the angiographic feature in 1931, and Bergstrand et al. made an angiographic demonstration of dural fistula in 1936(14).

Risk factors for DAVF: 1. Venous sinus thrombosis with intracranial hypertension is the most commonly proposed risk factor. Other risk factors include, 2. Craniotomy 3. Trauma 4. Prior surgery 5. Pro-thrombotic conditions like protein C resistance, antithrombin III deficiency, mutations in factor V Leiden and factor II G20210A 6. Hormonal changes associated with OCP and menopause 7. Ear infections.

Etiopathogenesis and risk factors: Exact pathogenesis of the DAVF is not known. Two different viewpoints on pathogenesis prevailing. (i). Role of angiogenesis (ii). Pathological enlargement of physiological AV shunts. Both of these factors may be additive.

Stages in the development of DAVF:

1. Stage of venous thrombosis and venous hypertension triggers pro-angiogenic state increase in hypoxia-inducible factor-1, which increases vascular endothelial growth factor (VEGF), Stroma cell-derived factor-alpha (SDF-1) and stimulates neutrophilic MMP-9, IL-6

2. Stage of macroscopic fistula/ emergence of initial fistula within the thrombosed venous sinus- enlargement of normal arterio-venous shunts (50-90micomm), break through autoregulation of physiological micro AV shunts, exposure of arterioles to retrograde venous hypertension and loss of sphincter control in arterioles

3. Recanalization of the thrombosed sinus with dural fistula(15,16).Further Development of dural fistula- Persistent AV shunts, further progression dependent on flow volume(17).

The most common locations of DAVF include transverse sigmoid sinus, cavernous sinus, superior sagittal sinus, and the tentorium with slight left-sided dominance noted at transverse and sigmoid sinus(18).

Classification of the dural arteriovenous fistula:

Multiple classifications systems have been proposed for intracranial dural AVFs. In 1978, Djindjian and Marland initially described the classification based on the venous drainage of the fistula into four types. Later Cognard, in 1995, modified previous Djindjian and Marland classification to predict the natural history of the disease and to decide upon the management. Later Borden et al. simplified the Cognard classification based on the direction of the flow and presence or absence of the cortical venous reflux.

Lasjaunia's and Geibprasert et al. proposed the classification based on the embryological craniospinal epidural venous space into three different compartments- ventral epidural, dorsal epidural, and lateral epidural groups. Tanaka et al. proposed classification based on the epidural space and embryological development of the dural layers(19).

Classifications based on hemodynamic patterns of the DAVF:

Djindjian and Merland's classification	**Cognard's classification**	**Borden's classification**
Type 1- Antegrade or retrograde flow into the sinus or meningeal vein	Type 1- Antegrade drainage into the sinus	Type 1- Drainage into the venous sinus or meningeal vein
Type 2- Antegrade or retrograde drainage into the sinus with CVR	Type 2a- Retrograde flow into the sinus Type 2b- Reflux into the cortical veins Type 2a+b- Reflux into the sinus and cortical veins	Type 2- Drainage into dural sinuses or meningeal veins with retrograde drainage
Type 3- Drainage solely into the cortical veins	Type 3- Direct CVR without venous ectasia	Type 3- Drainage into subarachnoid veins (CVR)
Type 4- Drainage into one or more large venous lakes	Type 4- Direct cortical venous drainage with venous ectasia	
	Type 5- Spinal venous drainage	

Classifications based on embryological epidural spaces:

Geibprasert and Lasjaunia's classification	Tanaka's classification
Ventral epidural group- Osteo-cartilaginous group includes basi-occipital group, petrous pyramid, basisphenoid with adjacent sphenoid wings including cavernous sinus **50% of DAVF**	**Ventral endochondral group-** cavernous sinus, sigmoid sinus, anterior condylar confluence at the level of hypoglossal canal
Dorsal epidural group- Osteo-membranous group includes superior sagittal sinus, torcular, transverse sinus, medial occipital sinus, and posterior marginal sinus **22% of DAVF**	**Dorsal membranous group-** Transverse sinus, confluence, superior sagittal sinus
Lateral epidural group- Leptomeningeal group draining into the bridging vein- emissary veins and their homologs includes DAVF involving foramen magnum, superior petrosal vein, basal vein, VOG, veins of anterior cranial fossa and orbit **21%** of DAVF	**Falco-tentorial group-** Olfactory groove, falx cerebri, falx cerebelli, tentorium cerebelli

Baltsavia's et al. proposed novel simplified hemodynamic classification of the dural fistula based on three things, directness, exclusivity, and strain pattern, also known as the DES system. **Directness** refers to the site of dural fistula at bridging vein or dural sinus wall, **Exclusivity** refers to direct or exclusive leptomeningeal drainage without sinus drainage, and **Venous Strain** refers to diffuse or focal venous ectasia, aneurysms, venous congestion, and pseudophelbitic pattern. Based on these three factors, DAVF is classified into the eight different types, which may be better predicting the clinical features and natural course of the disease(20)

Site of fistula	Dural sinus disease		Bridging vein disease	
Non-aggressive (0% aggressive symptoms)	**Non-direct Non-exclusive No strain**	**Non-direct Non-exclusive Strain**	**Direct Non-exclusive No strain**	**Direct Non-exclusive Strain**
Aggressive symptoms (91.5%)	**Non-direct Exclusive No strain**	**Non-direct Exclusive Strain**	**Direct Exclusive No strain**	**Direct Exclusive Strain**

Baltsavia's classification system highlights the falsity of the isolated analysis of the leptomeningeal venous drainage for the natural course of the disease. Additional risk factors like direct exclusive venous reflux and parenchymal venous strain need to be considered to stratify the natural course of the disease(21).

Danis et al. studied the validity of dural fistula classification systems- Cognard and borden systems suggested that incidence of aggressive symptoms at presentation was 2%, 39%, and 79% respectively for borden type I, II and III dural fistula patients. For Cognard classification system incidence of aggressive symptoms at presentation were 0 % - type I, 15%-Type IIA, 38%- Type IIB, 40%-Type II A+B, 69%- Type III, 83%-Type IV and 100% for type V(22).

In all classifications, low-grade DAVFs (Grade I Merland–Djindjian, Grade I–IIa Cognard, Grade I Borden) have an annual risk of hemorrhage of 0%, intermediate lesions (Grade II Merland–Djindjian, Grade IIb, IIa+b Cognard, Grade II Borden) have a 6% annual hemorrhagic risk, and high-grade lesions (Grade III Merland–Djindjian, Grade III–V Cognard, Grade III Borden) have a yearly risk of hemorrhage of 10%(23)

Clinical features of DAVF:

Pathophysiology of the clinical features initially described in detail by Lasjaunias in 1986. He broadly classified symptoms based on them as follows

(i). Arterial symptoms- steal and ischemic dysfunction of the cranial nerves.

(ii)High venous flow- tinnitus

(iii)High venous flow with venous sinus thrombosis- pseudotumor cerebri secondary to chronic dysfunction of CSF absorption. Headache, papilledema and optic atrophy are symptoms related to this.

(iv). Venous ischemia- Focal CNS symptoms secondary to cortical venous drainage resulting in chronic passive congestion and symptoms include aphasia, motor weakness, TIA, ataxia, and seizures.

(V). Venous rupture and combined venous mechanisms responsible for hemorrhagic complications

(vi).Venous mass effect- cranial nerve symptoms and visual symptoms related to mass effect from enlarged draining veins(24–26)

Non-migrainous headache in CCF and migraine-like headache noted in dural fistula other than CCF linked to increased sensitivity of peripheral nerve terminals and neurogenic inflammation secondary to release of neuropeptides(27).

The traditional classification of the dural AV fistula symptoms is benign and aggressive symptoms.

1.**Benign symptoms-** headache, tinnitus, proptosis, chemosis, retro-orbital pain, glaucoma, and visual blurring secondary to raised ICP features.

2. **Aggressive symptoms** include hemorrhage, non-hemorrhagic neurological features, including the focal neurological deficit, TIA, epilepsy, and dementia. Peri medullary venous drainage leads to congestive myelopathy and paraplegia to tetraplegia

Cognitive impairment in dural AV fistula:

Dementia, cognitive decline, and parkinsonism are less common presentations of intracranial DAVF. Hou et al. reported incidence of cognitive impairment is about 21.4%. The most considerable reported incidence in early natural history study, about 12% (Obredor et al.). Ishii et al. reported a cognitive decline in 10 out of 45 patients of transverse sinus-sigmoid sinus dural AV fistula(28).

Risk factors for cognitive decline in DAVF:

(i). Associations like multiple shunts, multiplicity, more common to have dementia (17).
(ii).Dementia associated with DAVF is more common in men, 5^{th} to 7^{th} decade(6).

(iii). The most common locations of fistula associated with cognitive impairment are tentorium, transverse-sigmoid sinus, and superior sagittal sinus. The most common grades of DAVF are type II borden (64%) and type III borden (36%).

(iii).Labeyrie et al. reported the correlation between the anatomical location, venous drainage pattern, and development of dementia in dural fistula(29). Straight sinus and superior sagittal sinus draining DAVFs by virtue of its median nature, can result in bilateral extensive trans ependymal venous involvement and encephalopathy, thus high propensity to develop symptoms of cognitive impairments.

(iv).Similarly, low flow fistula with partial or complete blockage of the draining pathway leads to redistribution into the leptomeningeal veins and results in venous edema as compared to high flow fistula with alternative venous routes(29)

Pathophysiology of cognitive decline in DAVF: Mechanisms for DAVF induced dementia are 1. Cortical dementia 2. Thalamic dementia(6,8,30).

Cortical dementia: (i). Disturbance of CSF resorption secondary to medullary venous congestion due to DAVF → secondary hydrocephalus (similar to dementia in normal pressure hydrocephalus) (ii). Direct reflux into the medullary vein from DAVF → arterialization of medullary veins. Impaired function → venous congestive encephalopathy. (iii). Local alteration in CBF → Low CBF in posterior cingulate gyrus, precuneus, parieto-occipital cortex and bifrontal hypoperfusion(30)

Thalamic dementia: (i). Venous congestion and ischemia of the thalamus → secondary to impairment of the deep venous drainage and venous reflux to straight sinus and vein of Galen (VOG) (ii). Impaired thalamic functions such as learning, attention, executive function. (iii). Dysfunction of the mammillothalamic tract→ Dysfunction of the limbic system.

Presentation of cognitive impairment: Cognitive impairment affecting domains of memory, calculation, orientation, visuospatial function, language has been described. Unlike other dementia syndromes, DAVFs is a rare, reversible cause of dementia and do not have any single constant defining symptom (31). High level of clinical suspicion is needed to diagnose DAVF, as it is one of rapidly progressive dementias(32). Mean duration of symptoms ranges from weeks to months(8). Rapidly advanced dementia associated with intermittent headache, papilledema, urinary disturbances, pyramidal signs should mandate investigation of DAVF(31).

(i) The most common symptoms reported are disorientation in time and place, alexia, short term memory loss, personality changes, executive function disturbances, attention deficits, difficulty in the performance of activities and hypersomnolence (6). (ii).Associated symptoms are abnormal gait, balance, myoclonus, the occurrence of parkinsonism together with progressive cognitive dysfunction secondary to basal ganglia, and brainstem dysfunction(33,34).

(iii). Decreased speech output may result from decreased frontal lobe perfusion

(iv).Seizure may be the result of global venous congestion(31).

Differentials(28,34)**:** Thalamic infarct, viral encephalitis (JE, West Nile), hyponatremia (acute onset), Deep venous infarct (subacute onset) similar to DAVF, Prion disease and tumors → chronic onset are differentials for thalamic dementia secondary to DAVF.

Cortical dementia	Thalamic dementia
1. Rapidly progressive cognitive dysfunction characterized by impairment in verbal fluency, comprehension, apraxia, visuospatial discordance, memory dysfunction	1. Rapidly progressive cognitive dysfunction characterized by disorientation, executive dysfunction, attention deficits, memory impairment, confabulation and disinhibition (Secondary to the involvement of the anteromedial and central thalamic nuclei involvement)
2. Associated neurological symptoms are hemiparesis, somatosensory disturbances, aphasia and alexia	2. Thalamic aphasia, ataxia, signs of internal capsule involvement(hemiparesis), and diplopia secondary to 3rd nerve involvement. Sensory and motor symptoms secondary to posteromedial and inferior thalamic nuclei involvement
3.MR imaging revealed widespread multiple T2 FLAIR hyperintensities	3. Bilateral medial thalamic hyperintensities, patchy enhancement, and vascular abnormalities like dilated deep venous structures.

Imaging features of dementia in DAVF: The severity of dementia depends on diffuse white matter changes and regional cerebral blood flow (rCBF). CT and MRI may show minimal abnormalities. CT imaging features include vascular channels and dural sinus wall calcifications. MR imaging correlates are cortical venous drainage, dilated vascular channels, venous pouch and hyperintensity in the venous territory(28). Most frequently reported imaging correlates are:

(i)Diffuse white matter lesions and subcortical white matter lesions, SPECT hypoperfusion. (35).

(ii)Thalamic and brainstem edema.

(iii)Medullary venous dilatation.

(iv)Hypoperfusion of the basal ganglia, venous ischemia, and hypoperfusion of the frontal & temporal lobes(31). SPECT using ethylcysteinate dimer (ECD) showed a reduction in cerebral blood flow over the left temporal lobe(36)

(v)PET/ SPECT with dopamine transporter agents may be helpful for delineating the site of involvement, especially useful as undiagnosed cases lead on to irreversible neuronal damage and permanent deficits(37)

(vi) Reversibility of the cerebrovascular reactivity with acetazolamide on SPECT suggests the reversibility of the cognitive disorder on treatment(28).

Reversibility of dementia in DAVF:

Cognitive decline ranges from reversible to irreversible changes. Thus early treatment before the induction of irreversible white matter changes is warrented. The outcome depends on time to diagnosis and degree of chronic edema. With rapid diagnosis and treatment, a favourable outcome is possible for these patients(34). Obliteration of the DAVF improves cerebral hemodynamics and reverses venous ischemia(38).

Neuropsychological evaluation in DAVF(39)**:**

Global functioning memory	MMSE, Rey auditory verbal learning
Psychomotor speed	Trial memory test A
Executive function	Trial memory test B
Attention	Symbol digit test
Language	Verbal fluency (Words in 3 min)
Visuospatial memory	Clock drawing test

Natural history of the dural arteriovenous fistula:

When treating a patient with a DAVF, the risks of endovascular treatment has to be carefully considered against the natural outcome based on available natural history studies. Initial studies

suggested that location and angiographic factors are primarily associated with aggressive symptoms. The natural history of DAVFs is a dynamic process, and their angioarchitecture can be altered by venous thrombosis.

Houser et al., in 1972, was the first one to stress upon the association between leptomeningeal venous drainage and aggressive clinical presentation. Mallik et al., in 1984, reported aggressive hemorrhagic presentation in about 7.5%, and all patients with haemorrhage had leptomeningeal venous reflux. Lesions outside the major sinuses like tentorium, basifrontal, clival, and convexity regions had a high propensity for hemorrhage contributing about 51%(40). The number of arterial feeders, contralateral arterial feeder contribution, flow across the shunt did not correlate with aggressive symptoms(41). Long term follow up study by Brown et al. in 1994 reported that the risk of hemorrhage is about 1.6% per year. Lesion involving petrosal sinus and straight sinus high propensity for hemorrhage (42)

Cognard type 1 fistula usually show a benign course. Type 2 has a 20% incidence of intracranial hypertension. Incidence of aggressive symptoms in type 2(2B& 2A+B), type 3, type 4 and type 5 are 11%, 76% ,96% and 100% respectively. The incidence of hemorrhagic symptoms is 40% and 60% for type 3 and type 4, respectively. 50% incidence of congestive myelopathy is noted in type 5 DAVF, and 50% have a haemorrhagic presentation(43).

A long term follow-up study on aggressive DAVF patients (Borden type II and III) with persistent LVR by Davies et al. reported that mortality rate and hemorrhage per year was 19.2% and annual incidence of NHND was 10.2%(44). The natural history of benign DAVF patients by the same author suggested that 98% of patients will have a benign clinical course (45).

Van Dijk et al. reported that persistent leptomeningeal venous reflux results in 10.4% annual mortality rate. The further annual incidence of hemorrhagic and non-hemorrhagic symptoms during follow-up was 8.1% and 6.9%, respectively, and an annual mortality rate of 15%(46).

A study was done by Soderman et al. about the natural history of dural arteriovenous fistula showed that incidence of the hemorrhage in patients with leptomeningeal venous reflux depends on the initial presentation of the disease and those with initial hemorrhagic presentation annual incidence was about 7.4% and those without hemorrhagic presentation was about 1.5%(2). Zipfel et al. studied asymptomatic versus asymptomatic DAVF with cortical venous reflux. They reported that symptomatic cortical venous patients had 5 to 6 times

increased annual risk of intraparenchymal bleed than symptomatic cortical venous reflux(7.4 vs. 2.4 per year(18).

Duffau et al. reported high hemorrhagic risk of about 35% within two weeks of initial hemorrhagic presentation, suggesting the need for early treatment in DAVF patients with LVR(47)

Gross et al., in 2012, done a pooled analysis of the six studies from 395 DAVF patients. Hemorrhagic presentation and annual hemorrhage risk were 18% and 6% in grade 2 and 34% and 10% in grade 3, respectively. Further annual hemorrhage risk in asymptomatic DAVFs was 2%, NHND was 10%, and hemorrhagic presentation was 46%(48)

Short term and long-term study on 227 DAVF patients from Finland population with a mean follow-up of 10 years showed that annual mortality in the first 12 months was 4.4% with excess mortality related to treatment complications. (49)

Change in the grade of the lesion:

Thrombophlebitis, cranial trauma, intracranial tumors and incomplete arterial embolization can modify venous drainage and may result in a change in the type of fistula(43) These lesions could have a dynamic course, so the risk stratification is not rigorous. Satomi et al. (2002) demonstrated angiographic progression to a more aggressive fistula with CVD (about 2 to 3%), resulting from progressive thrombosis of the venous sinus. Thus continued follow-up of patients with Borden type I fistulas is generally recommended (17,25,50).

In exceedingly rare circumstances, venous hypertension can cause venous stasis within the DAVF and subsequent venous thrombosis, which can result in spontaneous obliteration and "cure" of the fistula(35). Mechanisms described for spontaneous closure are (i) post-traumatic fistula- because of scar tissue progressive thrombosis (ii) small fistula with single feeder and small draining vein (iii) secondary to mass effect from hematoma and vasospasm (iv) Even selective angiogram might lead to a progressive thrombo-embolic phenomenon because of the thrombogenic effects of contrast medium (v) Progressive sinus thrombosis and occlusion of the DAVF(35,51). The disappearance of an old symptom or the onset of a new symptom, must raise the suspicion of a change in drainage pattern and prompt further investigations(14). Gross et al. reported 13% of grade 1 and 3% of grade 2, 3 DAVFs showed spontaneous resolution(48).

Treatment:

The decision of whether to treat DAVFs needs to be based on the patient's clinical presentation, lesion location, and the natural history of the lesion. Specific sites (i.e., anterior cranial fossa) and angiographic findings (i.e., the presentation of leptomeningeal venous drainage) are associated with a higher risk of hemorrhage and indicate treatment.

From a pathophysiological point of view, the condition is a venous disease, and needs to be addressed for permanent cure. The therapeutic strategy is chosen to improve symptoms and to prevent catastrophic consequences of the natural history.

The primary goal of treatment is the complete obliteration of the lesion. The therapeutic armamentarium includes conservative monitoring, arterial embolization, transvenous occlusion, surgical excision and radiation therapy. The primary pathology can be addressed by obliteration of the venous recipient in three fashions: transvenous occlusion of sinus, transvenous occlusion of venous pouch outside the sinus lumen, or transarterial occlusion of venous channel.

Treatment complications:

Potential morbidity associated with the endovascular treatment of DAVFs relates primarily to the method of treatment. Since feeder arteries frequently also provide blood supply to nearby cranial nerves, ischemia in these nerves is possible during transarterial embolization. Another potential source of morbidity from the transarterial approach, in the setting of abnormal cortical venous drainage from a DAVF, is that of cerebral vein thrombosis. Inadvertent passage of liquid embolic agent through the fistula and into the vein may result in venous infarction, hemorrhage, or both. Surgical evacuation of hematoma may then be required.

Traumatic dissection of thin-walled veins occurs quickly, necessitating gentle catheter and guidewire techniques while treating these lesions. One of the drawbacks of venous embolization is the risk of changing the venous drainage of the fistula from benign to one that is more aggressive with subarachnoid vein involvement. There is also a potential risk of venous infarction if the occlusion of a sinus obstructs the outflow of a vein draining normal cerebral tissue (e.g., the vein of Labbe for the transverse sinus)(15).

Resting-state fMRI:

Resting-state functional MRI is the study of the spontaneous fluctuations of the brain activity at the state of rest. Functional connectivity refers to the constellation of temporal functionally organized neural networks, even though they are not in direct anatomical continuity(52). The simultaneous neuronal co-activation of brain region patterns, measured through hemodynamic response at rest. Areas of the brain with similar spontaneous fluctuation of low-frequency blood oxygen level-dependent (BOLD) signals are thought to be functionally connected(9). Functional connectivity aid in keeping functional systems in an alert state.

Biswal et al., in 1995, was the first to describe the resting state network using synchronous time series fluctuations of right and left sensorimotor cortex, suggesting the sensorimotor network. Spontaneous low-frequency fluctuations of neural activity are thought to be involved in memory consolidation. Although structural connectivity is well correlated with functional connectivity, the reverse is not always true. Functional connectivity is determined by a combination of conscious activity, complex cognitive processes and continuous integration of internal neural networks(52).

Resting-state fluctuations are of low frequency 0.01-0.1 Hz and low temporal resolution- two to three per second. Cardiac and respiratory fluctuations (more than 0.3 Hz) can get aliased and resemble low-frequency fluctuations and result in artificial connectivity. Source of resting-state fluctuations to be from neuronal origin is supported through electrophysiological studies on neuronal firing. There is also different frequency bandwidth of resting-state BOLD fluctuations from anatomically separated cortical and sub-cortical regions, reflecting a level of ongoing functional connectivity between brain regions during rest. Frequencies between 0.010 and 0.027 Hz may reflect cortical neuronal activity, 2) frequencies between 0.027 and 0.073 Hz may reflect basal ganglia activity, and 3) frequencies between 0.073 and 0.198 Hz and 0.198 and 0.250 Hz have been associated with physiologic noise and white matter signal, respectively(53).

Advantages of resting-state fMRI over task-based fMRI:

Resting-state spontaneous fluctuations of neural activity, metabolically demanding, consumes almost 80% of brain energy. Energy consumption increases only less than 5% from the base-line on task-based activity. Over all improved signal to noise ratio is seen in rsfMRI since it takes into consideration all spontaneous low-frequency fluctuations. Unlike, task-based fMRI, resting-state fMRI doesn't require the active participation of the patients. No confounding

factors related to the patient's task performance is there. Overall brain function can be assessed in resting functional MRI, as compared to a small fraction of brain function in task-based functional MRI(54). rsfMRI is also highly reproducible within subjects across time intervals ranging from 45 minutes to 16 months providing evidence that functional connectivity reflects stable network measurements(53)

Analysis techniques: Analysis of rs-fMRI data is challenging due to (i). Massive amount of data (ii). Need to separate physiological noise from low-frequency fluctuations of interest.

Software packages available for resting-state fMRI are **Analysis of Functional Neuro Images** (AFNI; http://afni.nimh.nih.gov/afni), the **CONN toolbox** (https:// www.nitrc.org/projects/conn/), **MELODIC** (https://fsl.fmrib.ox. ac.uk/fsl/fslwiki/MELODIC), and **Group ICA of fMRI Toolbox Software** (GIFT; http://mialab.mrn.org/software/gift/), are commonly used to analyze rs-fMRI data. Automatic ''pipelines software'' have also been developed to analyze data almost automatically for a more straightforward data analysis(53).

Analytical techniques can be broadly divided into (i). Pre-processing (ii). Analysis of resting-state functional connectivity.

(i). Pre-processing of resting-state fMRI data: Commonly employed pre-processing steps include as follows, 1. Slice timing correction- correction of differences in image acquisition time between slices, 2. Head motion correction 3. Normalization- into the standardized template -Montreal Neurological Institute space (MNI), normalization consists of three steps – co-registration, segmentation, and writing normalization para-meters 4. Smoothing- increases signal to noise normalizes error distributions and accommodates anatomic and functional variation between subjects 5. Removal of linear tread – long term physiological shifts and residual movement-related noise 6. Filtering using band-pass filters between set bandwidth(53). Additionally, global signal regression (GSR), which refers to the statistical removal of the average signal across all voxels in the brain, is a contentious issue in rsfMRI imaging analysis. GSR can increase the detection of localized neural signals and improve functional connectivity analysis specificity.

(ii). Analysis of resting-state functional connectivity:

Analytic approaches can be broadly divided into two types: functional segregation and functional integration(53,55).

Functional segregation: It suggests the local resting-state activity of function of a specific brain region, mainly employed in brain mapping. Methods used for analysis are the amplitude of low-frequency fluctuations (ALFF), Regional homogeneity (ReHo). Both ALFF and ReHo do not require am a prior definition of the region of interest (ROI), suggests regional resting-state activity. The main disadvantage of functional segregation analysis is the connectivity between different brain regions cannot be studied. Both ALFF, ReHo methods can be used to define ROI for functional integration analysis.

Functional integration: It relies mainly on functional connectivity between different brain regions by analysing the degree of synchrony of the BOLD signal. These are said to be presumably connected, with no direct visualization of connections anatomically. Functional integration methods include 1. available connectivity density analysis,2. ROI based functional connectivity analysis, 3. Independent component analysis, 4. Graph theory analysis. High level of overlap between analytical methods. Other ways of classification of available connectivity analysis include model dependent (ROI based analysis) and model-free /data-driven analysis such as ICA analysis, graph theory analysis. Data-driven approaches are they fit the data better because there are more flexible.

1.Functional Connectivity Density (FCD) analysis: This method is to identify highly connected functional hubs. FCD reveals only how a particular voxel is connected. It doesn't provide information about brain regions that are associated with specific voxel. FCD analysis may be short-range or long-range, with the cut-off being 7.5 cm. Though the straight forward analytical method, not most commonly used, because it does not provide information about the functional connectivity of whole brain regions(53).

2. ROI based/ seed-based analysis: Initially, low-frequency fluctuations extracted from the pre-defined region of interest and finding the part of the brain with significant correlation with selected ROI(9). Selected ROI is called as seed. Mainly dependent on the prior assumption of the ROI. These seed time series may also be due to physiological noise such as breathing and heart rate, hence highly susceptible to signals from the non-neural origin. Challenging to examine functional connectivity patterns in the whole-brain scale. The main advantage is simple, straightforward, and easy to interpret functional connectivity(53,54).

3. ICA-Independent component analysis: It is based on a statistical mathematical algorithm, decomposes the signal into the independent components. Using the BOLD time series, the number of independent spatial maps can be extracted by ICA analysis(9). BOLD signals from

all brain voxels are decomposed into spatially nonoverlapping and temporally coherent networks. After estimating aggregate components from all subjects of the group,

back-reconstruction methods to estimate single subject maps and time courses. Back-reconstruction approaches are (i). regression-based approaches (e.g., spatiotemporal or dual regression) (ii) inversion-based approaches- group information– guided ICA (GIG-ICA).

ICA offers advantages that might reduce the problem of inflated false-positives caused by data pre-processing. ICA represents a data-driven approach for parcellating the brain into different components, depending on the number of ICA components, makes it possible to zoom up and down in the connectivity data through the splitting of spatial maps(56).

3.Graph theory: Graph theory provides a theoretical framework in which the topology of complex networks can be examined, and show important information about both the local and global organization of functional brain networks. It gives the ability to study intermediate and high levels of the organization across the system as a whole- Microscale, mesoscale and macroscale network analysis

Graph G= (V, E), with V, the collection of nodes reflecting the brain regions. A graph G is composed of N nodes (or vertices) and E edges (region-region relationships). The graph G is encoded in an adjacency matrix, A, whose (i,j) th element represents the weight of the edge between node i and node j. The edges of a graph are binary (including only 0s and 1s) or weighted (including a range of other values)(57).

Different aspects of connectivity graph parameters are (i) average path length- the level of global connectivity of the network information can be integrated between other systems (ii) clustering coefficient- information about the status of local neighbourhood clustering within a graph- Local connectedness of a graph; (iii) degree of node-number of connections of a node (iv) centrality measures; and (v) the level of modularity - extent groups of nodes in the graph are connected to the members of their own group, indicating the formation of sub-networks within the full network.

The main advantage of graph analysis is (i) highly efficient origination of brain network both at local and global efficiency (ii). Automatically performed using software without any prior assumptions and minimal bias. The disadvantage is difficult to interpret the results.

Resting-state networks (RSN):

Spatially distributed functionally connected region of the brain, share common time series BOLD signal fluctuation. These are strongly linked sub-regions during rest. These networks show a high correlation of BOLD signal time series fluctuations, although the difference in data acquisition and analytical methods(9). Brain activity at rest is organized into multiple resting-state functional networks, which are defined by spatio-temporal configuration and functional roles. Different resting-state networks are characterized based on their internal cohesion and integration(58). Many resting-state networks have been described, which include default mode network, salience network, executive control network or frontoparietal network, attention network, visual network, language network, sensorimotor network, cerebellar network, auditory network. There are also multiple sub-networks also been described(53,54,59,60). Here, we can briefly discuss resting-state networks used in our analysis with their functions and affections, images taken from current thesis control groups.

1. Default mode network (DMN): This network active preferentially when individuals are not focused on the external environment, one of the significant task-negative networks. Comprised of posterior cingulate, lateral parietal or inferior parietal lobule, medial prefrontal cortex, and medial temporal lobe subsystem(61). A recent study also showed that anterior and mediodorsal thalamic nuclei belong to the DMN, structural connectivity underlying functional connectivity(62). Among the nodes of DMN, the pre-cuneus-posterior cingulate acts as a central mediator, strongly connected with other nodes of DMN and the rest of regions of the brain. This network is negatively correlated with task demanding areas.

Functions of DMN: 1. Most active network during rest and deactivated during visuospatial, working memory tasks(9). 2. Tasks that encourage subjects toward internal mentation, including autobiographical memory, thinking about one's future, theory of mind, self-referential and affective decision making, tend to activate regions within the default network 3. Medial pre-frontal area -is associated with personal significance, introspection about one's own mental states, perceived similarity, and self-referential processing(62,63). This subsystem was considered to have a broader role in metacognition, social cognition, and mental state inference (62). 4. The medial temporal lobe subsystem comprised of the hippocampus, parahippocampal gyrus provides information from past memories, have a role in the consolidation of episodic memory(63). MTL subsystem increased its activity preferentially when participants made episodic decisions about their future. (64)

Affection: Specific changes have been described in normal aging, Alzheimer's disease (AD), multiple sclerosis (MS), and temporal lobe epilepsy.

2. Salience network (SN): Salience network is a large scale limbic-paralimbic network, consists of the bilateral anterior insula (AI), dorsal anterior cingulate region(dACC), the bilateral rostral pre-frontal cortex (RPFC), bilateral supra-marginal gyrus as seed points. SN also consists of limbic areas such as the amygdala, ventral striatum, dorsomedial thalamus, hypothalamus, and substantia nigra. SN is often interchangeably called a cingulo-opercular network in studies, as the anterior insula and anterior cingulate form the core of the salience network(65). The anterior insula and anterior cingulate region of SN have distinct neurons called von economo neurons (VENs), which have wider axons adds unique functional connectivity within it(66).

Functions: 1. Anterior insula of SN receives significant inputs from external signals through multiple sensory modalities and internal signals through autonomic processes. 2. Dorsal ACC of SN involved in response selection (strong motor output) and monitoring 3. Sub-cortical nodes of SN, such as the amygdala, ventral tegmental area, provide affective and reward cues 4. SN also acts as a dynamic switch, controlling interactions between default mode network and frontoparietal executive control network(67)

Affection: Salience network dysfunction has been described in autism, schizophrenia, attention deficit hyperkinetic disorder, frontotemporal dementia, mood and anxiety disorders, drug addiction, and pain disorders(66,67).

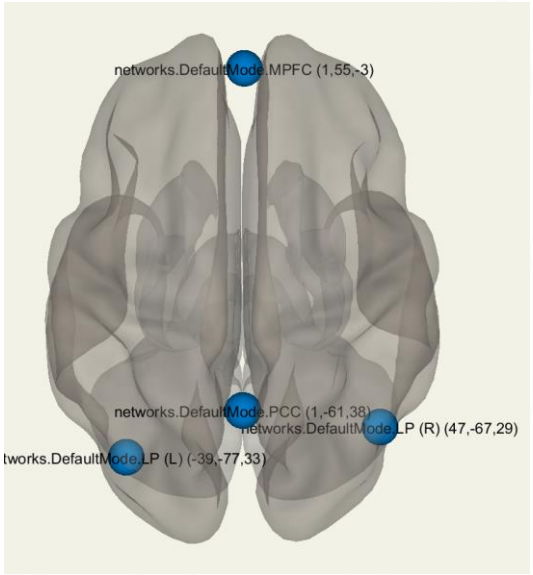
3. Fronto-parietal or executive control network (FPCN): Fronto-parietal control network consists of the bilateral lateral pre-frontal cortex (LPFC), posterior parietal cortices (PPC) as seed points. FPCN plays a central role in executive control. Tasks are involved in executive functions such as working memory and control processes. Correlated with trail making test in neuropsychology(9). Recent studies suggest that FPCN consists of two subsystems, FPCNa and FPCNb(68).

Functions: 1. FPCNa is centered around the lateral prefrontal cortex (LPFC), shows more vital connectivity with default mode network, and is involved in the regulation of internal thoughts and mento-cognitive awareness of emotional states. 2. FPCNb is centered around posterior parietal sulcus, shows more vital connectivity with dorsal attention network and involved in the regulation of visuospatial perceptual attention(68)

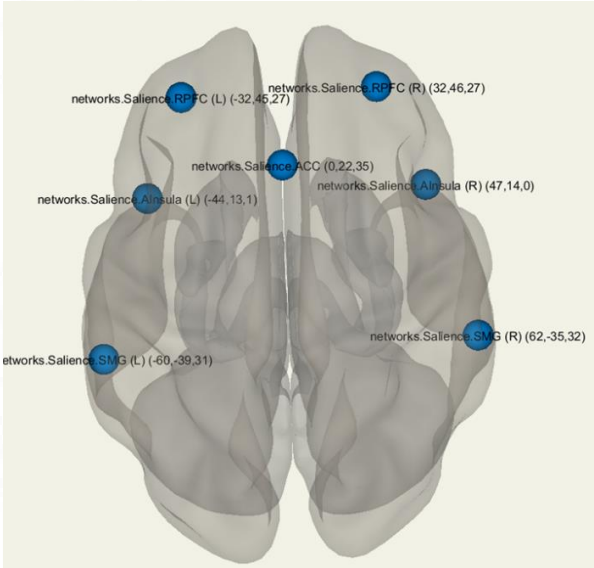
Affection: Connectivity of the frontoparietal network is known to be essential for working memory performance. Dysfunction of the frontoparietal network described in neurocognitive and neuropsychiatric disorders(69).

4. **Dorsal attention network (DAN):** Dorsal attention network, the task-positive network consists of bilateral frontal eye field and intra-parietal sulcus as seed points. Engaged during externally directed attentional tasks and comprised functionally connected brain regions

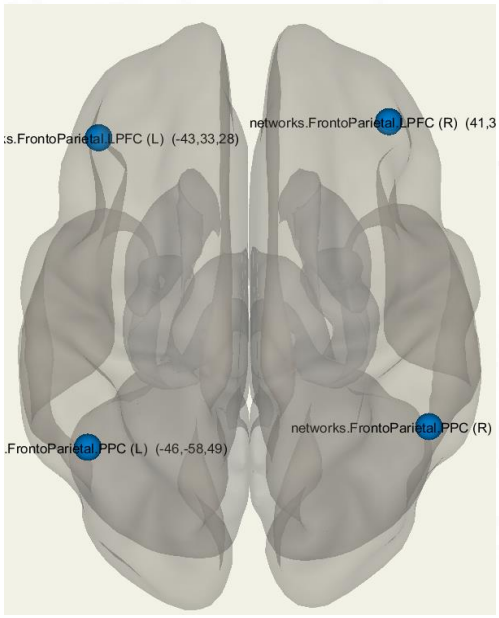
Default mode network



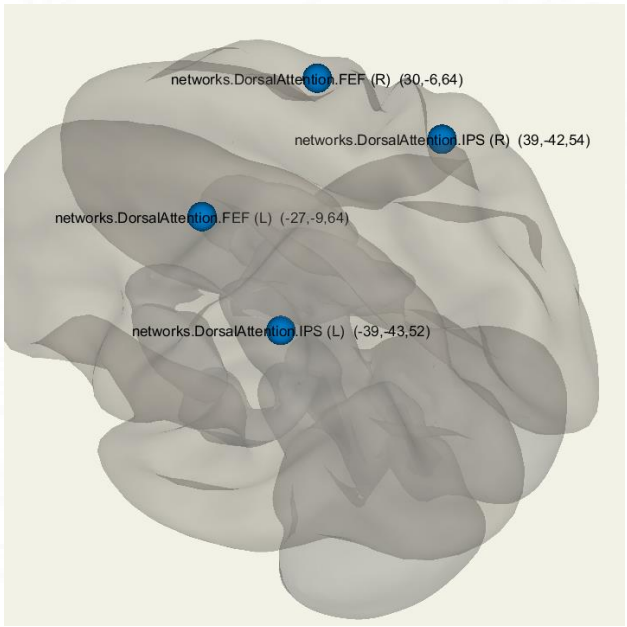
Salience network



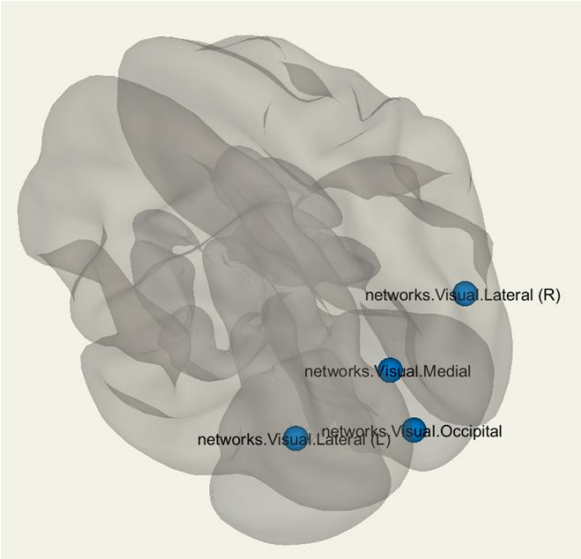
Fronto-parietal network



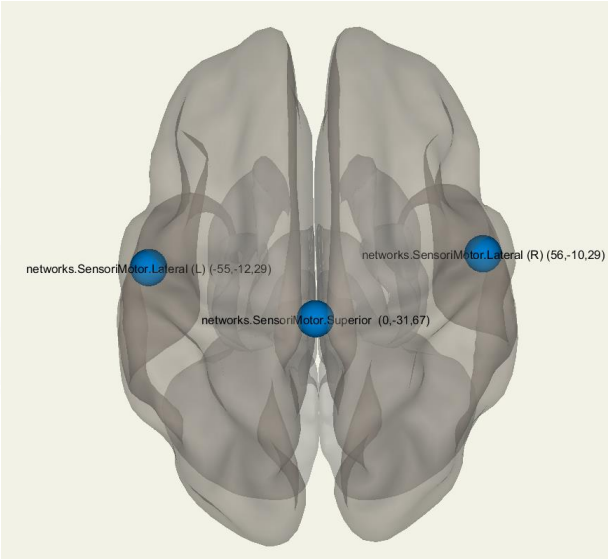
Dorsal attention network



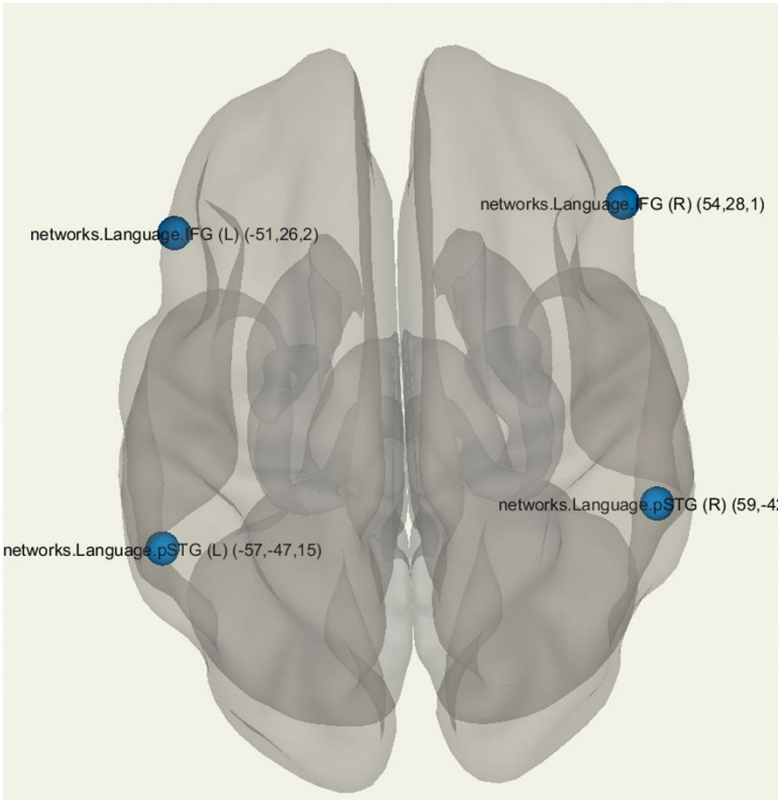
Visual network



Sensori-motor network



Language network



including visual motion area, frontal eye fields, superior parietal lobule, intraparietal sulcus, and ventral premotor cortex.

Functions: 1. Goal-oriented and attention-oriented control exhibits increased activity during cognitive tasks that focus on external visuospatial attention. 2. Anticorrelations between DAN and DMN networks are considered to be a core neural mechanism supporting executive functioning(70). 3. FC maturation in the DAN supports the development of attention skills during early childhood(71).

Affection: Dysfunction of dorsal attention network have been described in neurodevelopmental disorders such as autism spectrum disorder (ASD), attention deficit hyperactivity disorder (ADHD), fetal alcohol spectrum disorder, fragile X syndrome, Williams syndrome, and Turner syndrome

5. Sensorimotor network (SMN): Consists of pre and postcentral gyrus (sensorimotor lateral), the supplementary motor cortex (Sensorimotor superior) as seed points. It is the task-positive network. In resting state, degree of lateralization, the same region that active during activity. Somatotropic sub-networks within the primary motor cortex.

Functions: 1.Co-ordinated ongoing information processing between these regions before the active task(9).

Affection: Dysfunction or plasticity of the sensorimotor network have been evaluated in amyotrophic lateral sclerosis, post-stroke, and perinatal insult.

6. Visual network (VN): Mesial visual cortex- Lingual gyrus, inferior division of precuneus, the lateral geniculate nucleus of the thalamus, Lateral visual cortex- Occipital and temporo-occipital regions together constitutes a visual network**.** Totally consist of 4 seed regions- visual medial, visual occipital, and bilateral lateral visual regions**.** Spontaneous fluctuations can be altered by the visual task performed before the activity(9,55). Within the ventral visual stream, the human fusiform gyrus (FG), topographically the striate cortex to the inferior temporal lobe, plays a pivotal role in high-level visual/cognitive functions. Resting-state functional network connectivity pattern suggests three sub-divisions of FG. The medial part of the posterior FG (FGm) is involved in low-level visual processing, correlated with the primary visual network. The lateral part of the posterior FG(FGl) is involved in visual cognition, such as face and object recognition. Studies suggest that Left lateral fusiform gyrus(FGl) shows high functional

connectivity with the language network(72). The anterior part of the fusiform gyrus (FGa) shows functional connectivity with DMN, suggests its role in semantic memory(72).

7.Language network (LN): Language network consists of frontal component- bilateral inferior frontal gyrus and temporal component- bilateral posterior part of superior temporal gyrus. **Functions:** 1. The network is involved in functions such as speech, comprehension, reading, interpreting, mimicking, etc. 2. Mirror neurons within Broca's area have a role in goal-directed activities and imitate motor activities(55). Differential dysfunction pattern of language network has been described in Alzheimer's disease and a semantic variant of a primary progressive aphasia(73).

8.Cerebellar network: Cerebellar network consists of anterior and posterior cerebellar seed regions. **Functions:** 1. Anterior portions of the cerebellum are part of motor networks. In contrast, the majority of the posterior regions of the cerebellum are part of networks, including prefrontal and parietal cortices, associated most typically with cognitive functions. 2. The FC clusters of cerebellum belonging to different RSNs, which including the DMN, SN, FECN, DAN, LN, and VN(74). The dysfunction of the cerebellar network has been described in autistic spectrum disorders.

Functional applications of the resting-state fMRI: Interaction among networks is also critical to normal and aberrant cognitive performance, and mental states offered valuable insights about the symptom manifestation and pathologic mechanisms of many neurodegenerative diseases(12). More consistent applications noted in Alzheimer's disease, multiple sclerosis, and amyotrophic lateral sclerosis. The strength of functional connectivity can correlate with disease activity.

Functional connectivity and cognition: Although it has long been assumed that cognitive functions are attributable to the remote operations of single brain areas, cognition results from the dynamic interactions of distributed brain areas operating in large-scale networks. (75) The main applications of functional connectivity changes are (1). To find out syndrome specific network changes in neurodegenerative diseases, (2) To uncover disease mechanism and the underlying neuropathology, and (3) To detect early changes and track disease severity

MATERIALS AND METHODS

Materials and Methods:

The present study was prospective exploratory study. Patients who were diagnosed to have an intracranial dural arteriovenous fistula (DAVF) at interventional neuroradiology outpatient/ ward of Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST) were screened for eligibility and willingness to participate in the study.

Inclusion criteria: 1. Patients with dural arteriovenous fistula proven by angiography **2**. Controls- healthy subjects matched for age, gender and education

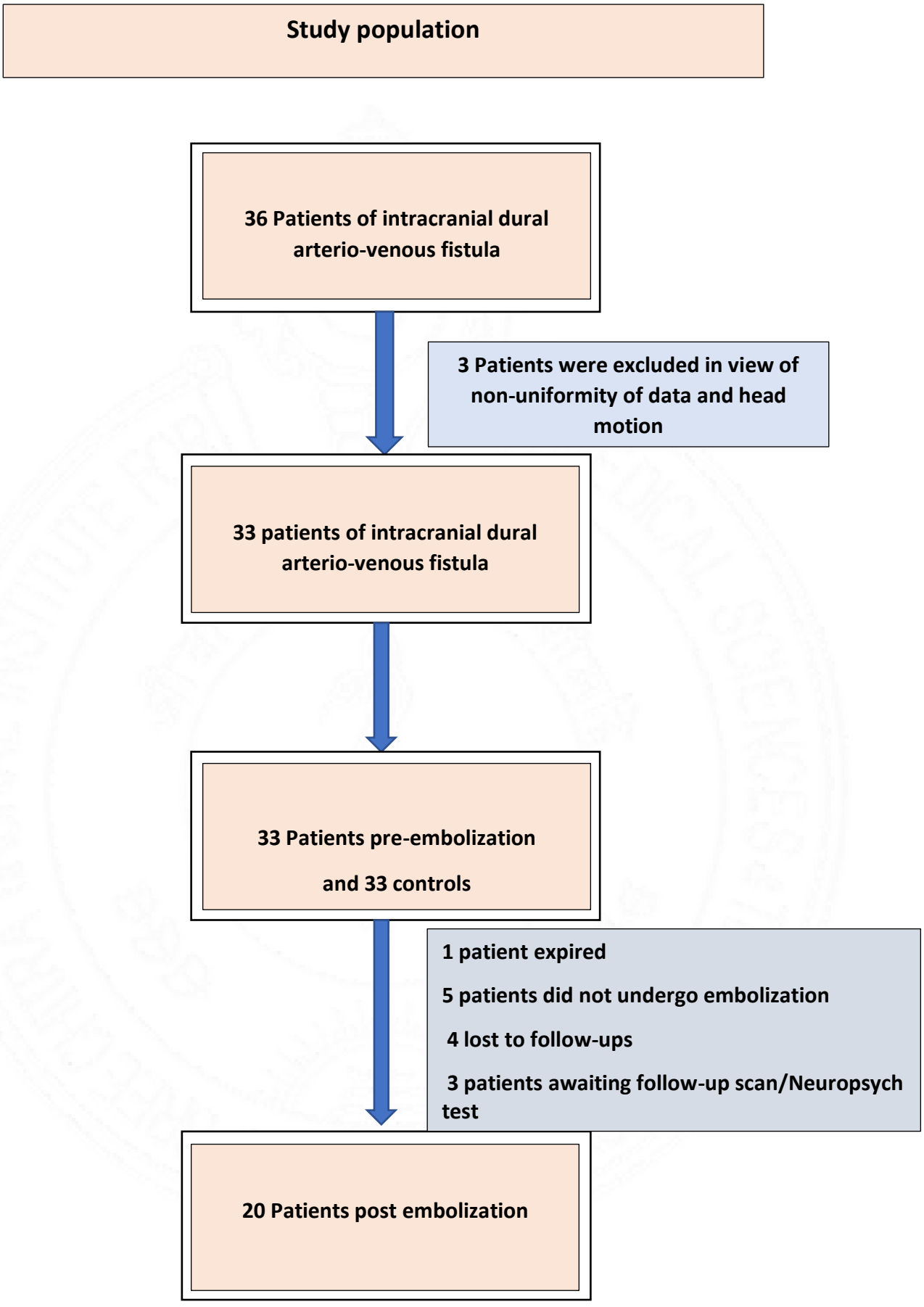
Exclusion criteria:

1. Patients who already underwent embolization/ recurrent DAVF patients
2. Requiring sedation for imaging
3. Current medical conditions or treatments possibly compromising cognitive functions (i.e., psychosis, chemotherapy or corticosteroid treatment within one month)
4.Gross visual or motor impairment compromising neuropsychological performances
5. Patients not co-operative for MRI, patient clinical condition contraindicating MR imaging.

Consecutive 36 DAVF patients fulfilling the inclusion criteria between October 2018 to July 2020 were included in the study who underwent initial pre-procedure fMRI. Out of which three were excluded because of the non-uniformity of MRI data and patient motion. So, 33 patients were included in the final analysis. An equal number of age, gender, and education matched healthy controls were recruited for the study from the local community of Trivandrum.

The study was conducted with approval from the Institute Ethics committee all the patients and healthy controls gave their informed consent before their inclusion in the study (SCT/IEC/1240/August 2018 and on-project SCT/IEC/1467/November 2019). Few of the controls taken from the previous project of our institute (SCT/ IEC/976-october 2016 & IEC/1030-april 2017). Such controls will be included only, if both rs fMRI, neuropsychology data available.

All subjects also underwent a neuropsychological evaluation within one week of the pre-procedural fMRI study. Out of 33 DAVF patients, 20 patients underwent endovascular embolization. These 20 post embolized patients, after a month of this treatment underwent post treatment resting state fMRI and neuropsychological examination.


Study population
36 Patients of intracranial dural arterio-venous fistula
3 Patients were excluded in view of non-uniformity of data and head motion
33 patients of intracranial dural arterio-venous fistula
33 Patients pre-embolization
and 33 controls
1 patient expired
5 patients did not undergo embolization
4 lost to follow-ups
3 patients awaiting follow-up scan/Neuropsych test
20 Patients post embolization

Neuropsychological evaluation:

After a thorough neurological examination, all DAVF patients (baseline pre-embolization and post embolization at 1-month follow-up) & all controls subjects underwent neuropsychological evaluation for cognitive assessment. The participants were cognitively screened using following neuropsychological tests – Mini-Mental State Examination, Vernacular (Malayalam) adaptation of Addenbrooke's Cognitive Examination battery (ACE-M), Semantic battery-confrontation naming, Weschler Memory scale for digit span, Trail making test A and B, Rey Auditory verbal learning test (RAVLT), Weschler memory scale – verbal immediate and delayed, Weschler memory scale – verbal immediate and delayed, Warrington face recognition test, hospital anxiety and depression scale

MRI acquisitions:

A Discovery MR750W 3.0 T MRI scanner (GE Health care, Milwaukee) with 32 channel phased array head coil was used to acquire structural and rs-fMRI images from each subject. These were acquired using following parameters: TR/ TE= 2500/ 30 ms, voxel size =3.31 x 3.31 x 4 mm3, FOV= 21.2 cm, slice thickness = 3.2 mm, matrix 64 x 64. A high-resolution reference axial 3D brain volume imaging sequence (BRAVO) with TR/TE = 7/2.98 ms, slice thickness = 1mm, flip angle = 12o, matrix size = 256 x 256, voxel size = 1 mm x 1mm x 1mm was collected for anatomical reference. All the participants were instructed to close their eyes and relax while inside the scanner while conducting the task-free resting-state fMRI acquisition.

Data pre-processing:

Initially, all the structural images were oriented in the AC-PC line, and their respective fMRI images were re-oriented to it using SPM 12. Following this, the pre-processing of the images was performed using the CONN 18.b toolbox. The involved steps include functional realignment (subject motion estimation and correction), functional outlier detection(ART-based identification of outlier scans for scrubbing), functional direct co-registration to structural (rigid body transformation), structural segmentation (Grey/ white/ CSF tissue estimation), functional direct segmentation & normalization (simultaneous grey/ white/ CSF segmentation and MNI normalization), functional smoothing (spatial convolution with Gaussian kernel). Images were smoothed using a Gaussian kernel of 8mm FMWH.

Linear de-spiking was performed on the fMRI data to regress the confounding effects. Potential confounding effects used in CONN's default de-noising pipeline, such as noise components from cerebral white matter and cerebrospinal fluid areas, estimated subject-motion parameters, identified outlier scans, or scrubbing were used in this study. Component base noise reduction method (CompCor) in CONN was used to remove principal components from noise regions of interest. The motion parameters were used as first level co-variates for the analysis. The bandpass filter of 0.008 to 0.09 was applied to data to reduce noise effects and low-frequency drift.

Analysis of resting-state data:

Resting-state connectivity analysis was performed using the CONN toolbox. Group ICA analysis, ROI to ROI analysis, seed to voxel analysis methods were used for the analysis of functional connectivity difference between DAVF patients (pre and post embolization), and healthy controls. Further, patients were divided into two groups based on the neuropsychology scores and the presence or absence of cognitive decline at presentation and compared with controls to delineate the connectivity changes related to the clinical presentation as cognitive decline in DAVF.

1.Resting-state networks using group ICA analysis:

Group ICA was performed using Calhoun's group-level ICA approach in the CONN toolbox with group-level dimensionality reduction, fast ICA for estimation of independent spatial components, and GICA1 back-projection for individual subject level spatial map estimation. The number of independent components estimated was set to 20, and dimensionality reduction was set to 64. By selecting a spatial match to explore the estimated ICA networks, the correlation between each group-level spatial map and to identify networks of interest. In the second-level analysis, ICA maps of all subjects were entered into GLM, which was used for measuring the group differences of ICA for each resting-state network. Statistical significance for all comparisons were thresholded at $p < 0.05$, FDR corrected for cluster threshold, and $p < 0.001$, uncorrected for voxel-level height threshold.

2.ROI to ROI analysis:

All seed regions from each resting-state networks-default mode network(DMN), salience network(SN), dorsal attention network(DAN), frontoparietal network(FPN), sensorimotor network(SMN), language network(LN), visual network(VN), cerebellar network (CBN) as

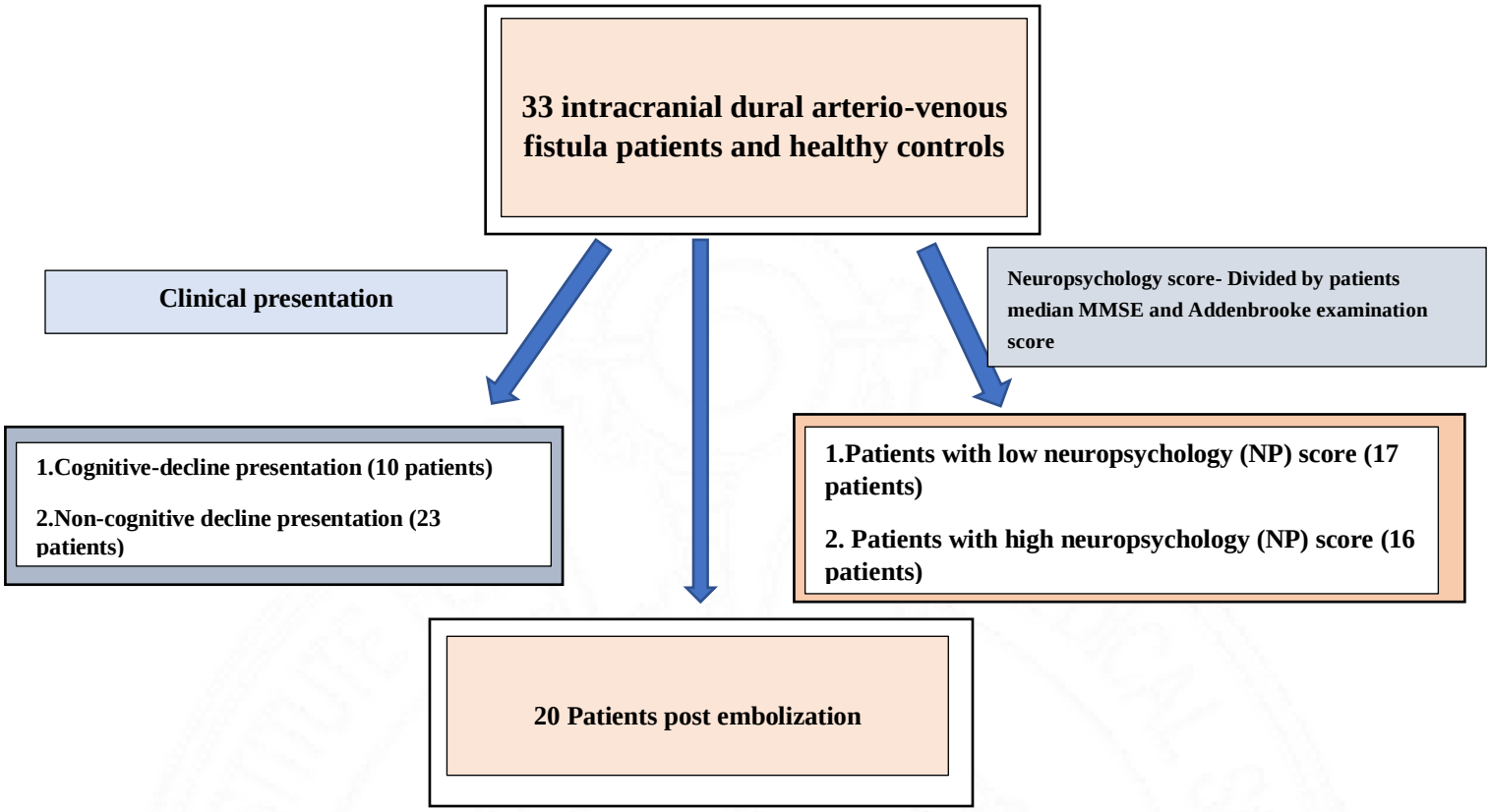
provided by the CONN toolbox were used as seed area and estimated the ROI-to-ROI functional connectivity (bivariate correlation measure) between seed and a set of 164 ROIs defining the Brodmann areas. Then, individual correlation maps were generated for each of these eight networks. Correlations were obtained by applying the general linear model (GLM) and bivariate correlation analysis weighted for hemodynamic response function (HRF). Statistical were obtained and used as rs FC measures. Statistical significance for all ROI to ROI (by intensity) comparisons were thresholded at $p < 0.05$, FDR corrected for seed level correction.

3.Seed to voxel analysis:

Seed to voxel analysis method was used to know the effect of functional connectivity of different ICNs reported change in connectivity on group ICA comparison between DAVF patients and healthy controls. The regions with the highest connectivity value on group ICA or ROI to ROI analysis within each network were used as seeds for the next level of analysis.

Fisher's r to z transformation of correlation co-efficient was implemented. In the second-level analysis, to compute group differences in FC for each network, all subject's connectivity maps were entered into GLM with neuropsychology score and clinical presentation as co-variates. Statistical significance for all comparisons were thresholded at $p<0.05$, FDR corrected for cluster level threshold and < 0.001, uncorrected for voxel level height threshold. Corrections for multiple comparisons were done in voxel and cluster levels.

Groups in the resting state fMRI data analysis:



By median neuropsychological scores, (i) Mini-mental state examination (MMSE) -cut off score as 24 (ii)Addenbrooke cognitive examination (ACE) score cut off score as 76, we have stratified patient group into high and low neuropsychology score group. Either one to be satisfied, to stratify as low neuropsychology score

We have assessed functional connectivity changes as follows

(i). Patients compared to controls

(ii). Post embolization patients at 1-month follow-up compared to controls

(iii). Pre and post embolization patients at 1-month follow-up

(iv). Patients with cognitive decline presentation compared to controls

(v). Patients with non-cognitive decline presentation compared to controls

(vi). Patients with low neuropsychological performance compared to controls

(vii). Patients with high neuropsychological performance compared to controls.

For the stratified patient group, i.e., cognitive and non-cognitive decline presentation, low and high neuropsychological performance group comparison made with the whole control group (33 controls vs. stratified groups).

Statistical analysis:

The statistical analysis of the study was performed using IBM SPSS Statistics for Windows Version 25(Armonk, NY, USA). Categorical variables were expressed as frequencies and percentages, and continuous variables as means (SD) or medians (IQR) for non-normal distribution. The normality of distributions was assessed graphically and using Shapiro-wilk test. Categorical variables compared with chi-square test and continuous variables compared using student's t, Wilcoxon signed ranked test or Mann–Whitney *U tests* as appropriate. Neuropsychological scores between the patients and controls, post-embolization patients and controls were compared using Mann–Whitney *U* test. Neuropsychological scores between the patients pre and post embolization was compared using Wilcoxon signed ranked test. In all the analysis, the significant threshold was set at $p<0.05$.

For resting-state functional MRI data analysis, comparisons were thresholded at $p <0.05$, FDR corrected for cluster threshold, and $p< 0.001$, uncorrected for voxel-level height threshold in group ICA analysis. In seed to voxel analysis, all comparisons were thresholded at $p<0.05$, FDR corrected for cluster-level threshold and < 0.001, uncorrected for voxel-level height threshold. Corrections for multiple comparisons (posthoc-Bonferroni) were done in voxel and cluster levels. In ROI to ROI analysis, comparisons were thresholded at $p <0.05$, FDR corrected for seed level correction.

OBSERVATIONS AND RESULTS

Table 1: Demographic and Clinical Characteristics

Variable	Number (%)		
A. Demographic characteristics	**Patients**	**Controls**	**p-Value**
Mean	45.9(±13.644)	45.09(± 17.837)	0.822
Sex –no (%)			
(i). Male	29(87.9%)	27(81.8%)	0.246
(ii). Female	4(12.1%)	6(18.2%)	
B. Clinical presentation			
1. Headache, tinnitus, blurring of vision	15(45.5 %)		
2. Cognitive decline	10(30.3 %)		
3. Seizures	3(9.1%)		
4. Haemorrhagic presentation	5(15.2%)		
C. Risk factors			
Nil	12(36.4%)		
CVT	9(27.3%)		
Trauma	3(9.1%)		
Others (HTN and Diabetes)	9(27.3%)		
D. Clinical characteristics			
1.Benign symptoms	15(45.5%)		
2.Aggressive symptoms	18(54.4%)		
E. Location of fistula			
Superior sagittal sinus	7(21.2%)		
Tentorial	2(6.1%)		
TS-SS	9(27.3%)		
Torcular	8(24.2%)		
Convexity	7(21.2%)		
F. MRI haemorrhage			
No bleed	26(78.8%)		
Haemorrhage	7(21.2%)		

Base line demographic analysis revealed, no statistically significant difference of baseline characteristics between patients and controls. Incidence of cognitive decline presentation is about 30.3%. Incidence of benign and aggressive symptoms are 45.5 % and 54.4% respectively. Most common location of the fistula is transverse sinus-sigmoid sinus followed by torcular (24.2%) and superior sagittal sinus (21.2%)

Table 2: Angiographic Characteristics

Variable	Number (%)	
A. Cognard grades of fistula		
Grade 1 Grade 2A 2B 2A+B Grade 3 Grade 4	3(9.1%) 1(3%) 8(24.2%) 12(36.4%) 8(24.2%) 1(3%)	
B. Borden grade of fistula		
Grade 1 Grade 2 Grade 3	4(12.1%) 20(60.6%) 9(27.3%)	
C. Single/ Multi-site fistula		
Single Multiple	26(78.8%) 7(21.2%)	
D. Circulation time (Mean circulation time)		
Right anterior Left anterior Posterior	6(5-7) 6(5.5-7.5) 6(5.5-7)	
E. Management -In whole patient (33 patients) group		1-Month post embolization follow-up (20 patients)
Not done Complete embolization Significant reduction	5(15.2%) 20(60.6%) 8(24.2%)	0 18(90%) 2(10%)

Incidence of benign fistula (Cognard 1, 2A or Borden grade 1) corresponds to 12.1%. Aggressive fistula contributes to 87.9% in our study population. Incidence of multi-site dural fistula is about 21.2%. In patients to multi-site dural fistula, highest grade of fistula taken into consideration. Mean right anterior, left anterior and posterior circulation time is 6 sec in DAVF patients. Out of 20 patients followed by at 1-month post embolization, 18 underwent complete embolization and 2 underwent significant reduction.

Table3: Neuropsychology profile: Patients versus controls

Variable	Patient (n=33) Median (IQR)	Control(n=33) Median (IQR)	p-value
MMSE	24(23-26.5)	30(30-30)	0.000
Addenbrooke cognitive examination (ACE)	76(63-80)	94(92.5-96.5)	0.000
Rey auditory verbal learning test			
Immediate recall	3(2-4)	7(6-8)	0.000
Delayed recall	5(3-6.6)	12(11-13.5)	0.000
Recognition	11(7-12.5)	14(13-15)	0.000
Weschler memory scale- Verbal			
Immediate recall	14(4-18)	38(35-41.5)	0.000
Delayed	5(2-10.5)	38(34.5-40)	0.000
Weschler memory scale- Visual			
Immediate recall	14(6-24)	38(36-41)	0.000
Delayed	11(0-21)	36(35-40)	0.000
Weschler memory scale- Digit span			
Total	7(6-10)	16(15-17)	0.000
Forward	4(3.5-5.5)	9(8-9)	0.000
Reverse	3(2.5-4)	8(7-8)	0.000
TRAIL-A (In seconds)	143(95-143)	53(52-54)	0.000
TRAIL-B (In seconds)	309(245-347)	63(58-72)	0.000
Semantic picture -Naming	32(23-39)	112(81-134)	0.000
Faces	15(12-19)	22(21-23)	0.000

IQR- Interquartile Range

Pre embolization neuropsychology evaluation showed median scores of neuropsychological variables were low in patients' group as compared to controls (median comparison using Mann-Whitney U test, $p<0.000$ for all neuropsychological variables). Median MMSE and Addenbrooke cognitive examination score in patients' group are 24(23-26.5) and 76(63-80).

Table4: Neuropsychology profile: Patients pre embolization versus post embolization

Variable	Pre embolization (n=20)	Post embolization (n=20)	p-value
MMSE	25.5(23-26.75)	29(28-30)	0.000
Addenbrooke cognitive examination (ACE)	77.5(70-80)	87(84-91.5)	0.000
Rey auditory verbal learning test			
Immediate recall	3(2.25-4)	4(3-4)	0.340
Delayed recall	5(2.25-6.75)	7.5(6-9)	0.011
Recognition	11(7-12.75)	13(9-14)	0.114
Weschler memory scale- Verbal			
Immediate recall	15(4.75-17.75)	28.5(23-31.75)	0.000
Delayed	5(2-9)	29(27-32.5)	0.000
Weschler memory scale- Visual			
Immediate recall	16(7-23)	29.5(25.5-32.5)	0.000
Delayed	11(0-21)	27.5(25-29)	0.001
Weschler memory scale- Digit span			
Total	7.5(6-10)	10(8-11)	0.014
Forward	4(3.25-6)	5(5-6)	0.035
Reverse	3.5(2.25-4)	5(3.25-5)	0.018
TRAIL-A	129.5(96.75-175.5)	107.5(92.5-140.5)	0.214
TRAIL-B	325(250.75-352)	210(183-255)	0.002
Semantic picture -Naming	33(23.75-39.25)	39(31.75-43)	0.044
Faces	15.5(12.5-19.25)	18(15-20.5)	0.00

Post embolization neuropsychology evaluation at one-month follow-up showed statistically significant improvement in neuro-psychological variables as compared to pre-embolization base-line neuropsychological scores, suggestive of cognitive improvement at one-month follow-up.

Table 5: Neuropsychology profile: Patients post embolization versus controls

Variable	Post embolization (n=20)	Control(n=33)	p-value
MMSE	29(28-30)	30(30-30)	0.000
Addenbrooke cognitive examination (ACE)	87(84-91.5)	94(92.5-96.5)	0.000
Rey auditory verbal learning test			
Immediate recall	4(3-4)	7(6-8)	0.000
Delayed recall	7.5(6-9)	12(11-13.5)	0.000
Recognition	13(9-14)	14(13-15)	0.000
Weschler memory scale- Verbal			
Immediate recall	28.5(23-31.75)	38(35-41.5)	0.000
Delayed	29(27-32.5)	38(34.5-40)	0.000
Weschler memory scale- Visual			
Immediate recall	29.5(25.5-32.5)	38(36-41)	0.003
Delayed	27.5(25-29)	36(35-40)	0.000
Weschler memory scale- Digit span			
Total	10(8-11)	16(15-17)	0.000
Forward	5(5-6)	9(8-9)	0.000
Reverse	5(3.25-5)	8(7-8)	0.000
TRAIL-A (In seconds)	39(31.75-43)	53(52-54)	0.000
TRAIL-B (In seconds)	107.5 (92.5-140.5)	63(58-72)	0.000
Semantic picture -Naming	210(183-255)	112(81-134)	0.000
Faces	18(15-20.5)	22(21-23)	0.000

Post embolization neuropsychology evaluation at one-month follow-up showed improvement in neuropsychological scores. In comparison with healthy controls, median scores of neuropsychological variables statistically significant ($p < 0.001$). This suggests that improvement in cognitive performance is less, as compared to healthy controls at 1-month follow-up

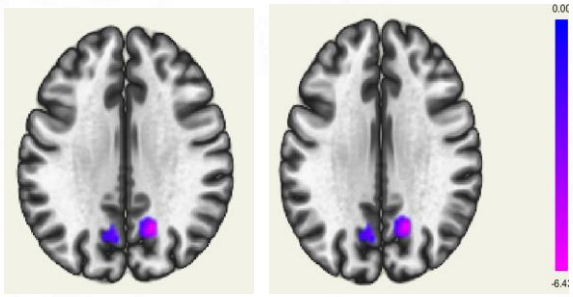
1.Connectivity analysis Results: Group-ICA analysis

(i). Default mode network: Group- ICA analysis: (Red-Positive connectivity, Blue-Negative connectivity)

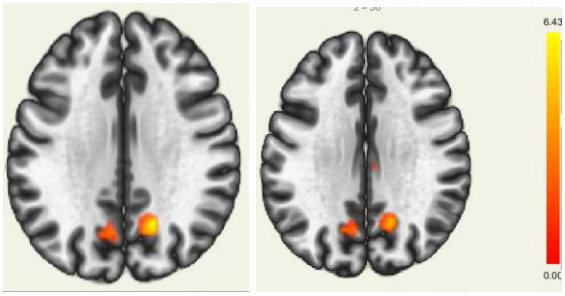
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	+00 -74 +50(Pre) +04 -26 +24(PCC)	1408 324	0.0000 0.0000	0.000000 0.001913	0.002077 0.276344
Post embolization >HC	+00 -72 +56(Pre) -02 -38 +18(PCC) +24 -66 -09(Rt FG)	203 178 167	0.013857 0.025281 0.033183	0.014504 0.014504 0.014504	0.581396 0.529803 0.888900
Low NP> HC	+02 -74 +52(Pre-PCC)	895	0.000000	0.000000	0.067497
High NP >HC	+2 -76 +50(PCC)	544	0.000010	0.000009	0.168349
Cognitive decline present > HC	-06 -70 +36(Pre-PCC) +38 -62 -32(Rt CBM) +4 -26 +24(PCC)	750 283 116	0.000000 0.001725 0.109202	0.000000 0.000591 0.026373	0.221020 0.854034 0.839712
Non-cognitive decline >HC	+00 -76 +52(Pre-PCC) +10 +12 +42(ACC)	632 169	0.000004 0.032264	0.000007 0.029790	0.013677 0.054337

(Abbreviations: PCC- Posterior cingulate, Pre-Precuneus, CBM- Cerebellum, ACC-Anterior cingulate)

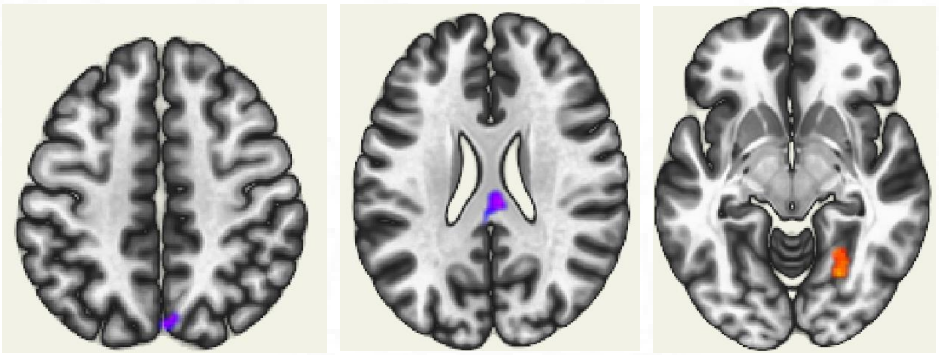
Patient >Healthy controls-DMN-gICA



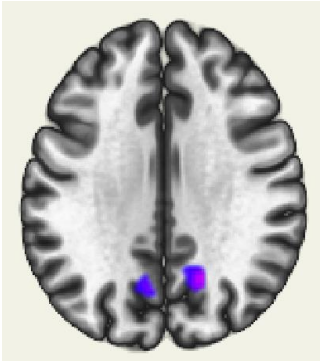
Healthy controls> Patients -DMN-gICA



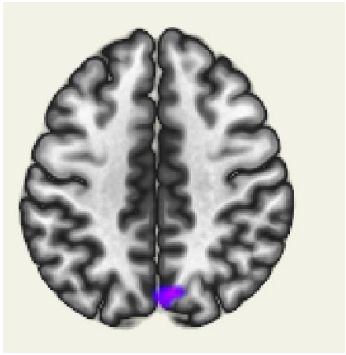
Post Embolization>HC- DMN gICA



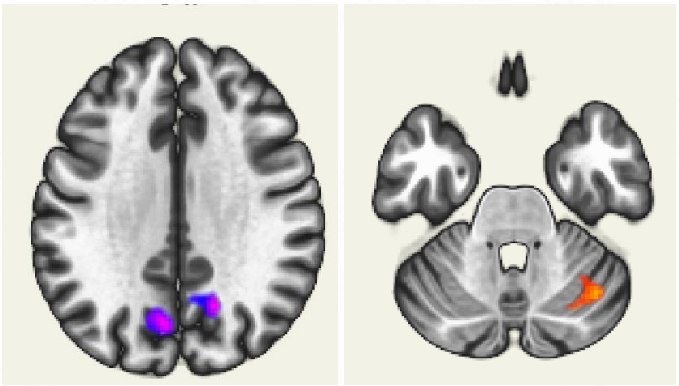
Low NP Pts> HC



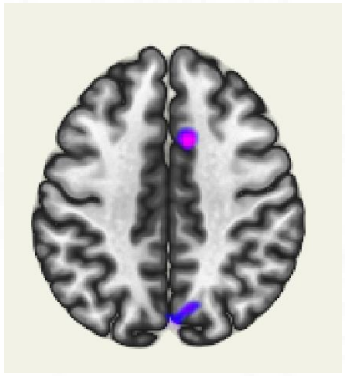
High NP Pts> HC



Cognitive decline presentation > HC



Non-cognitive decline presentation > HC



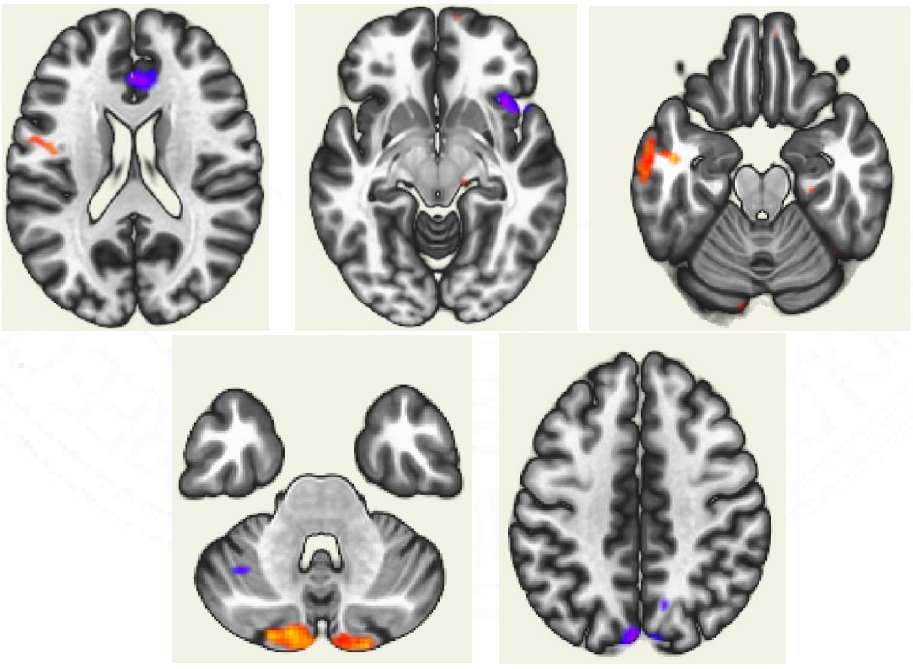
Group ICA analysis- DMN: gICA analysis shows significantly reduced connectivity noted at the precuneus and posterior cingulate (PC-PCC) in DAVF patients, patients presented with cognitive decline, and patients with low neuropsychology scores. Besides, patient with low NP score shows increased connectivity with the right cerebellum. Post embolization patients group showed increased connectivity within right fusiform gyrus and mild reduction in reduced connectivity cluster at PC-PCC. The patient group with non-cognitive decline presentation shows reduced connectivity cluster at anterior cingulate cortex (ACC) in addition to PC-PCC (Orange-red→ Positive, Blue-purple → Negative correlation)

(ii). Salience network: Group ICA analysis: (Red-Positive connectivity, Blue-Negative connectivity)

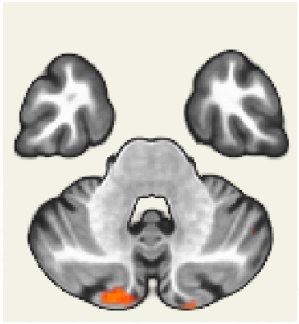
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	-04 -90 -38 (CBM) +04 +28+30(ACC) +06 -78 +54(PC) -48 -08 -22(Lt MTG) +38 +20 12(Rt insula) -46 -04 +20(Lt PCG)	644 621 379 279 259 230	0.000004 0.000006 0.000377 0.002785 0.004266 0.008070	0.000009 0.000009 0.000417 0.002309 0.002831 0.004472	0.002077 0.276344 0.510815 0.492349 0.244736 0.955274
Post embolization >HC	-06 -86 -28(Rt CBM)	333	0.000590	0.001212	0.568598
Low NP> HC	-02 +32 +16(ACC) -16 -84 -34(Lt CBM) +24 -26 -18(Rt PHG) -28 -04 -24(Lt Amyg)	774 204 160 138	0.000000 0.011587 0.034904 0.062402	0.000001 0.012739 0.025889 0.035215	0.307928 0.711377 0.717713 0.634003
Cognitive decline present > HC	+14 +30 +16 (ACC)	294	0.001108	0.001361	0.048089
Non-cognitive decline >HC	-14 -86 -38 (CBM) +04 -78 +50(ACC) +04 +28 +32(PCC) +38 +20 -10(Rt Insula)	544 311 305 182	0.000013 0.001116 0.001267 0.020898	0.000043 0.001339 0.001339 0.016737	0.318002 0.808101 0.253705 0.615432

(Abbreviations: CBM- Cerebellum, ACC-Anterior cingulate, Pre-Precuneus, MTG- Middle temporal gyrus, PHG-Para-hippocampal gyrus, PCG- Pre-central gyrus, Amyg-Amygdala)

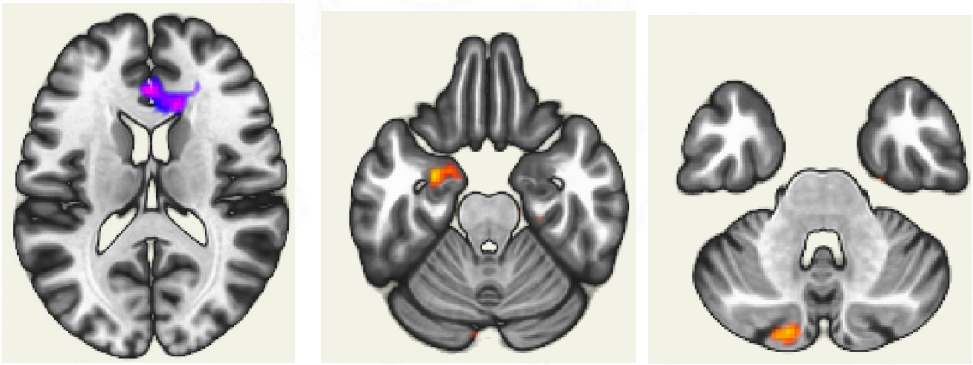
Patients > Healthy controls: Salience network: group ICA



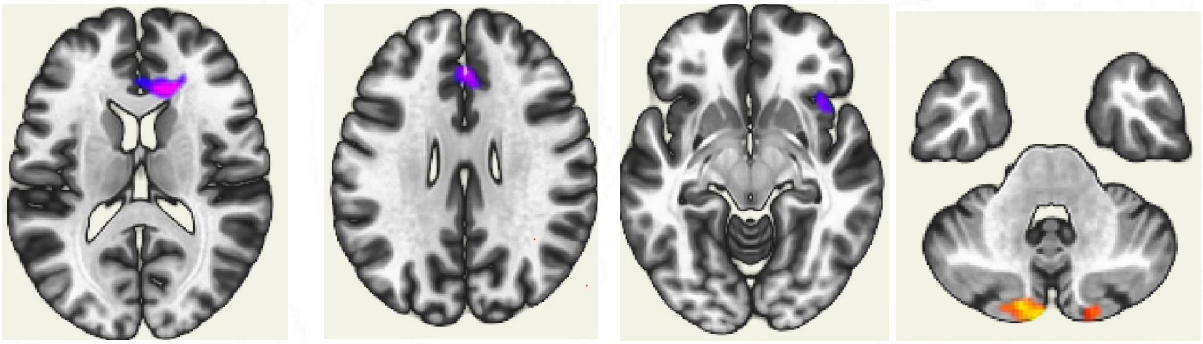
Post embolization > HC: Salience network-group ICA



Low NP > HC: Salience network-group ICA



Cognitive decline> HC **Non-cognitive decline > HC: Salience network-group ICA**



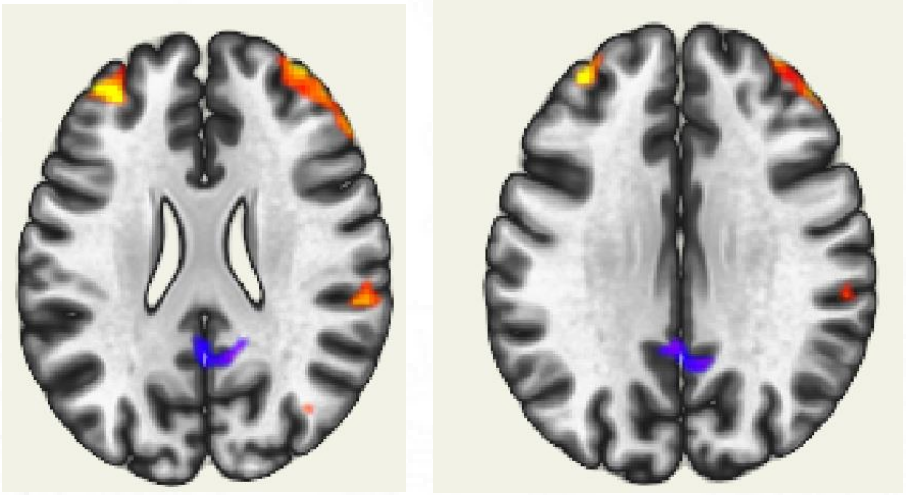
Salience network-group ICA: Patients irrespective of clinical presentation and NP score show reduced connectivity at the anterior cingulate region (ACC). Also, they have increased connectivity at the cerebellum and decreased connectivity at the pre-cuneus -posterior cingulate region. Patients with non-cognitive presentations show increased cerebellar connectivity and decreased connectivity at the right insula. (Orange-red→ Positive, Blue-purple → Negative correlation).

(iii). Dorsal attention network: Group ICA analysis

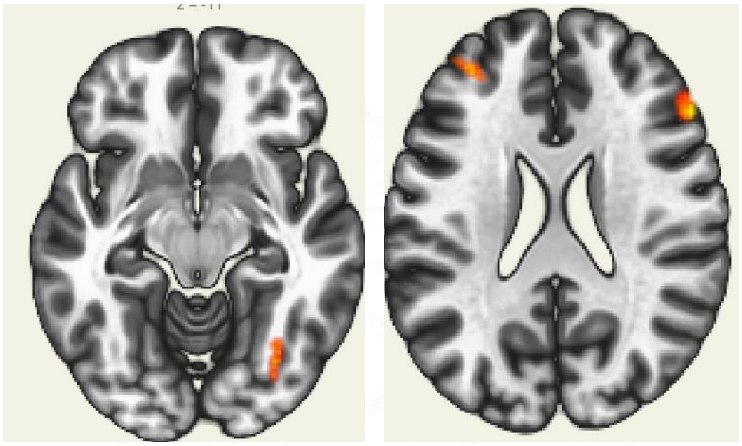
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	+40 +54 +20 (Rt FP) -36 +46 +28 (Lt FP) +10 -52 +26 (PCC) -36 +14 -02(Lt insula) +58 -32 +24 (Rt FO) +38 -26 +04 (Rt SMG) -38 -70 +22 (Rt Occ) -12 +00 +06(Rt caud)	713 292 245 231 194 148 145 137	0.000003 0.003026 0.007868 0.010574 0.023739 0.069014 0.074171 0.090008	0.000009 0.004940 0.008586 0.008666 0.015668 0.035899 0.035899 0.038445	0.030563 0.022839 0.940836 0.501340 0.375167 0.658039 0.082858 0.005303
Post embolization >HC	+34 -54 -16 (Rt FG) +54 +28 +22 (Rt MFG) -36 +46 +28 (Lt FP)	302 234 163	0.001958 0.008176 0.042043	0.004954 0.010374 0.036184	0.585301 0.297225 0.376965
Low NP> HC	+50 +38 +12 (Rt FP)	192	0.020498	0.024312	0.751736
Non-cognitive decline >HC	+18 -42 +20(PCC) +44 +52 +20(Rt Fron) -26 +16 -04(Lt Fron) +58 -30 +24 (Rt SMG)	381 377 321 151	0.000404 0.000436 0.001288 0.055293	0.000512 0.000512 0.001010 0.026734	0.640188 0.091554 0.146984 0.685905

(Abbreviations: FP- Frontal pole, PCC- Posterior cingulate, FO-Fronto-opercular, SMG-Supra-marginal gyrus, Caud-Caudate nucleus, MFG-Middle frontal gyrus, Fron-Superior Frontal)

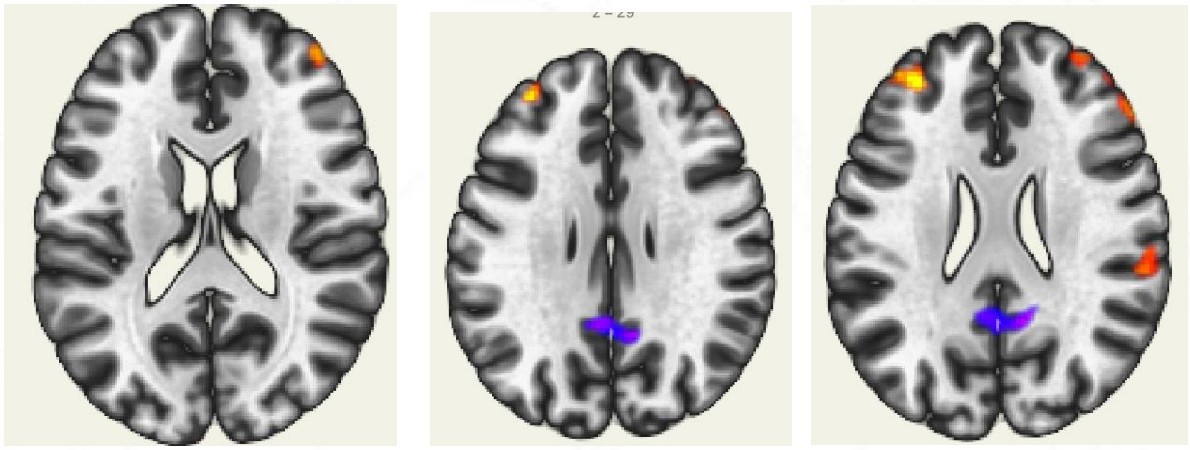
Patient >HC: Dorsal attention network: group ICA analysis



Post patients > HC: Dorsal attention network- group ICA analysis



Low NP patients > HC **Non-cognitive presentation > HC: group ICA analysis**



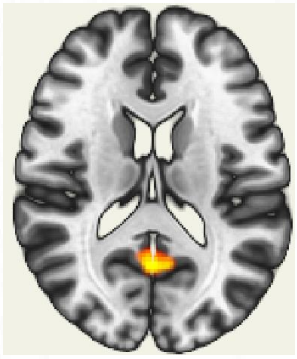
Dorsal attention network-group ICA: Patients show reduced connectivity with the posterior cingulate cortex (PCC). Also, they have increased connectivity at B/L frontal pole, right supra-marginal gyrus, suggesting an over-all anterior-posterior increase in connectivity. In low NP scores, patients increased frontal connectivity is less. Post- embolization patient group shows normalization of decreased connectivity at PCC. (Orange-red→ Positive, Blue-purple → Negative correlation).

(iv). Fronto-parietal network: Group ICA analysis

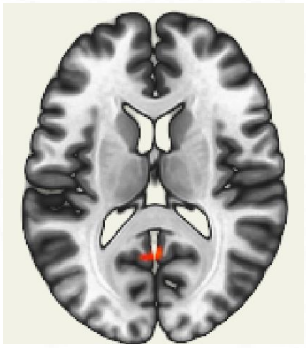
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	+00 -60 +18(PCC)	620	0.000003	0.000007	0.162922
Post embolization >HC	-	-	-	-	-
Low NP> HC	+02 -58 +18(PCC)	191	0.013783	0.015972	0.956158
High NP >HC	-	-	-	-	-
Cognitive decline present > HC	+06 -24 +78(B/L PCS, PtCG)	194	0.010427	0.007667	0.214417
Non-cognitive decline >HC	-2 -60 +20(PCC)	399	0.000119	0.000235	0.443467

(Abbreviations: PCC- Posterior cingulate, PCS- Pre-central gyrus, PtCG- Post central gyrus)

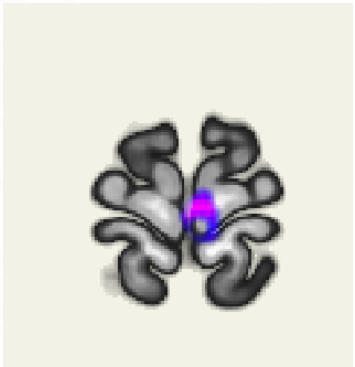
Patients > control



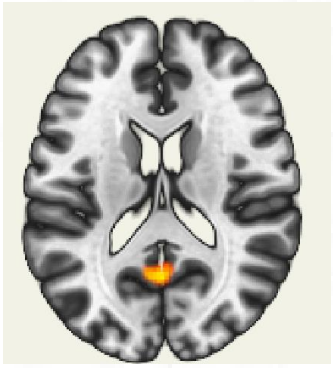
Low NP> HC



Cognitive decline > HC



Non-cognitive decline > HC



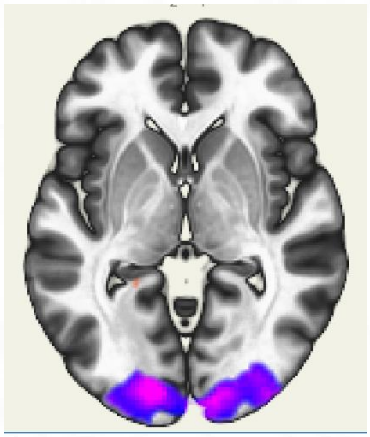
Fronto-parietal network- group ICA analysis: Patients show increased group ICA connectivity at the precuneus-posterior cingulate region. In low NP score, this increased connectivity is less prominent. In patients with cognitive decline presentation, decreased connectivity was noted in B/L Pre-central and post-central gyrus. No significant difference was noted in post embolization patients and patients with high NP scores. (Orange-red→ Positive, Blue-purple → Negative correlation).

(v). Visual network: Group ICA analysis:

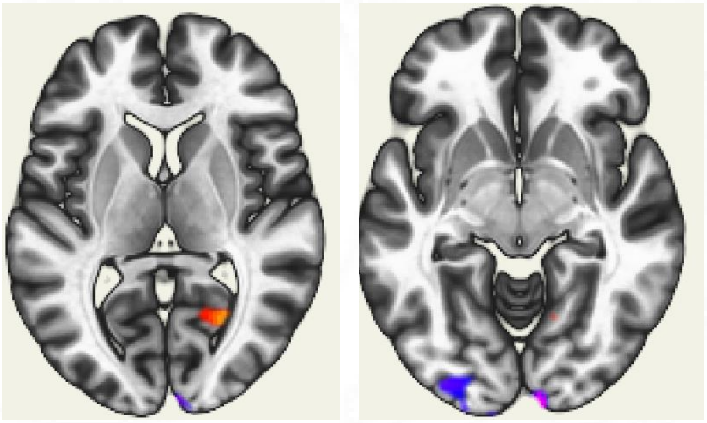
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	+08 -90 -08 (B/L Occ) -20 -30 -28(Lt PHG) +20 -76 -34(Rt CBM)	8670 271 175	0.000000 0.004888 0.038084	0.000000 0.006137 0.032417	0.003792 0.279073 0.443877
Post embolization >HC	+24 -62 +08(PCC) +08 -100 -06(Rt Occ) -12 -106 -08(Lt Occ)	253 241 210	0.005828 0.007526 0.014852	0.003507 0.003507 0.004631	0.931708 0.116678 0.982180
Low NP> HC	-16 -92 -04(B/L Occ + FG)	4285	0.000000	0.000000	0.070730
High NP >HC	-22 -102 +08(B/L occ) -44 -58 -26(Lt FG)	1090 189	0.000000 0.019280	0.000000 0.010533	0.136091 0.847544
Cognitive decline present > HC	-16 -92 -06(Lt FG) +40 -72 -16(Rt FG)	920 303	0.000000 0.001714	0.000000 0.000633	0.350633 0.465917
Non-cognitive decline >HC	+06 -100 -06 (B/L Occ +FG)	4701	0.000000	0.000000	0.028354

(Abbreviations: Occ- Occipital, PHG- Para-hippocampal gyrus, FG-Fusiform gyrus)

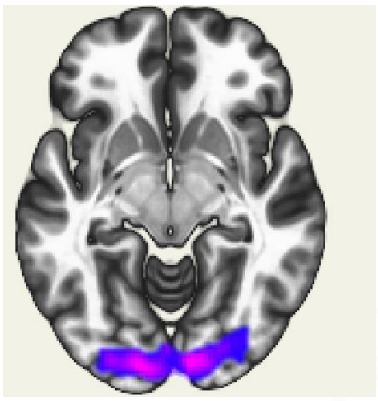
Patients > HC: Visual network



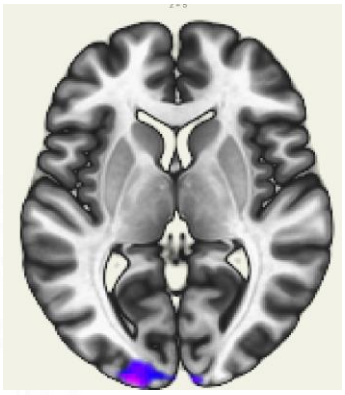
Post patients >HC-Visual network- group ICA



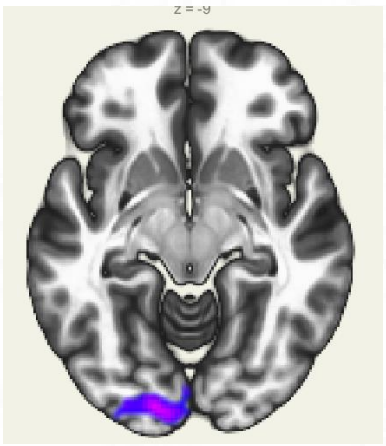
Low NP patients > HC: Visual network

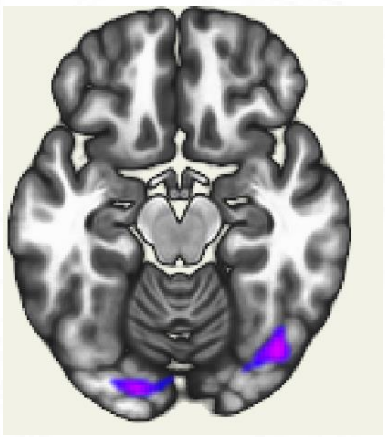


High NP > HC: Visual network

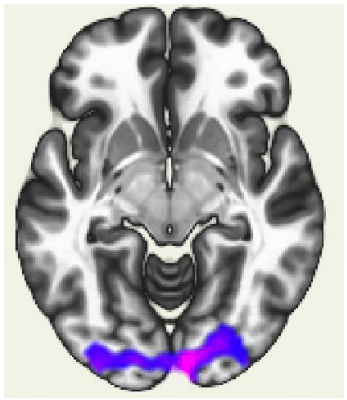


Cognitive decline > HC: Visual network





Non-cognitive decline> HC: Visual network



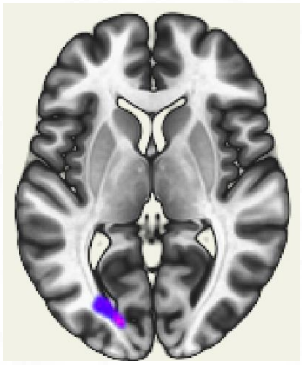
Visual network- group ICA analysis: Patients irrespective of their presentation and NP score show decreased group ICA connectivity at B/L occipital region and fusiform gyrus. In low NP score and cognitive decline presentation, a decrease in connectivity is more prominent at fusiform gyrus as compared to the bilateral lateral occipital cortex. Post embolization patient's decrease in visual network connectivity is less prominent, and an increase in connectivity is noted at the posterior cingulate region. (Orange-red→ Positive, Blue-purple → Negative correlation).

(vi). Cerebellar network: Group ICA analysis:

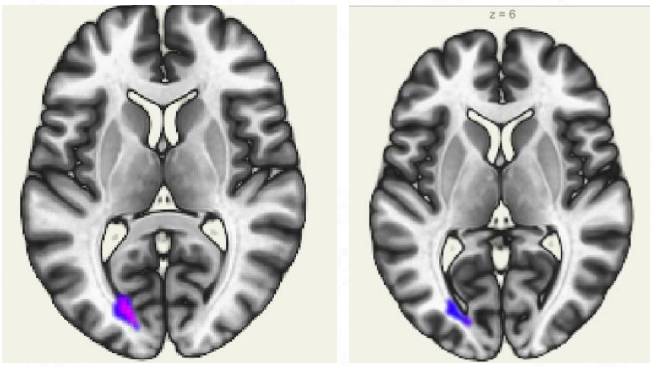
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	**-16 -86 +08 (Lt Occ)**	**311**	**0.003682**	**0.006485**	**0.279912**
Post embolization >HC	-	-	-	-	-
Low NP> HC	**-20 -80 +12 (Lt Occ)**	**274**	**0.006409**	**0.014144**	**0.446548**
High NP >HC	-	-	-	-	-
Cognitive decline present > HC	**-26 -76 +20 (Lt Occ)** **-10 +50 +40 (B/L SFG)**	**468** **435**	**0.000161** **0.000280**	**0.000270** **0.000270**	**0.700881** **0.265530**
Non-cognitive decline >HC	-	-	-	-	-

(Abbreviations: Occ-Occipital, SFG-Superior Frontal Gyrus)

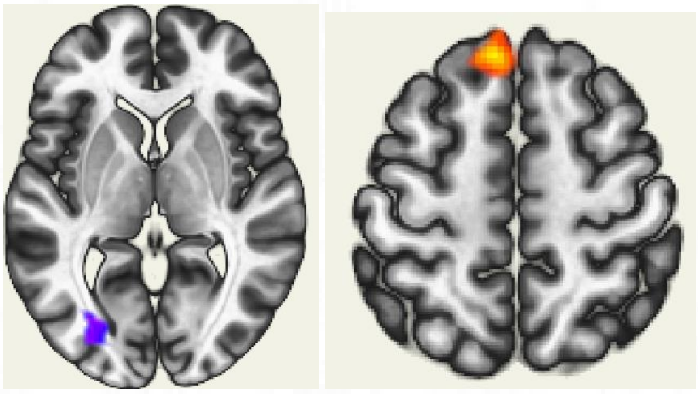
Patient > HC



Low NP > HC: Cerebellar network



Cognitive decline > Healthy controls



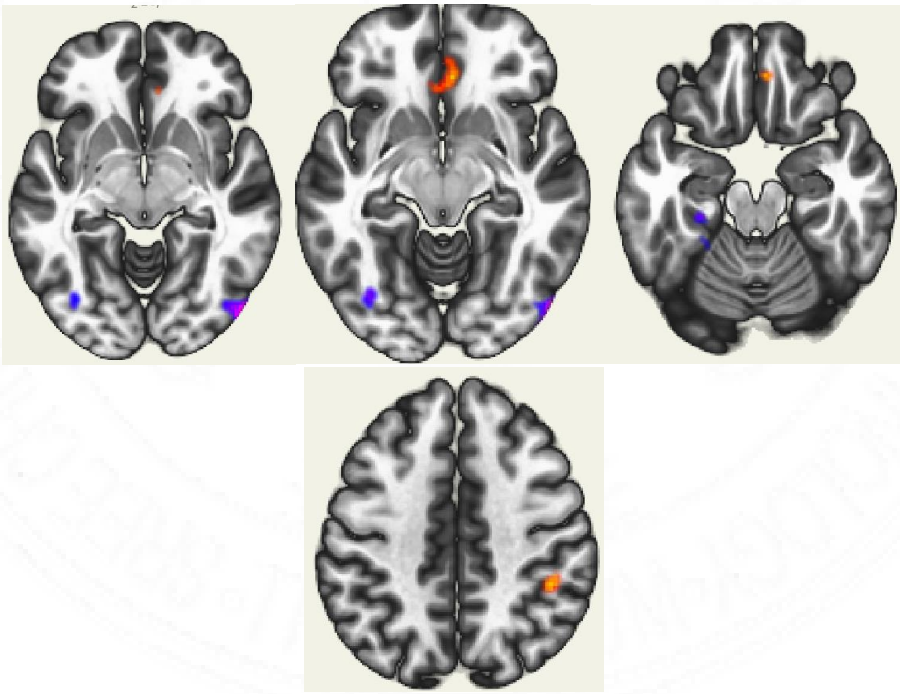
Cerebellar network- group ICA analysis: Patients with low NP score and cognitive decline show decreased connectivity at the left lateral occipital cortex and left fusiform gyrus. Patients with cognitive decline additionally show increased connectivity at the frontal pole. (Orange-red→ Positive, Blue-purple → Negative correlation).

7.Language network- group ICA analysis

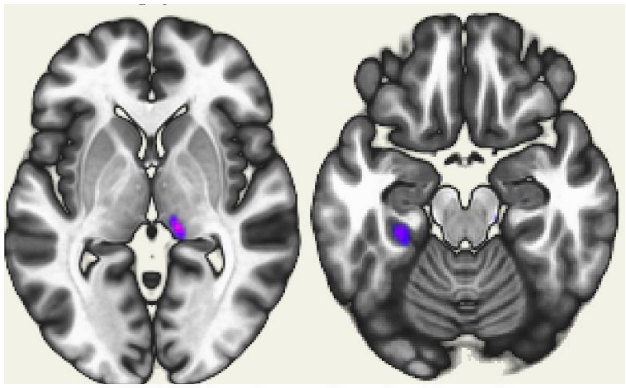
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	+52 -78 -10 (Rt Occ) +04 +34 -10(ACC) -26 -42 -26(Lt FG) -36 -72 -12(Lt Occ) +44 -40 +48(Rt SMG)	332 193 167 147 134	0.002253 0.032881 0.057357 0.089167 0.119450	0.002768 0.020520 0.024169 0.028661 0.031230	0.011398 0.668709 0.266876 0.804892 0.601548
Post embolization >HC	-32 -30 -14(Rt thal) +12 -28 +00(Lt FG)	193 191	0.030797 0.032142	0.020646 0.020646	0.794693 0.196510
Low NP> HC	-26 -42 -26 (Lt FG) +50 -80 -04(Lt Occ) -50 -80 -04(Rt occ) +44 -42 +48(Rt SMG)	427 335 256 166	0.000386 0.001898 0.008395 0.054994	0.000463 0.001140 0.003374 0.016980	0.031739 0.263329 0.493397 0.702293
High NP >HC	-	-	-	-	-
Cognitive decline present > HC	-26 -42 -26 (Lt FG)	191	0.026146	0.024027	0.332203
Non-cognitive decline >HC	+04 +40 -18(ACC) +52 -78 -10(Rt Occ)	214 162	0.019386 0.059562	0.024603 0.038588	0.958948 0.236837

(Occ-Occipital, SMG-Supra-marginal gyrus, FG-Fusi-form gyrus, ACC-Anterior cingulate, Thal-Thalamus)

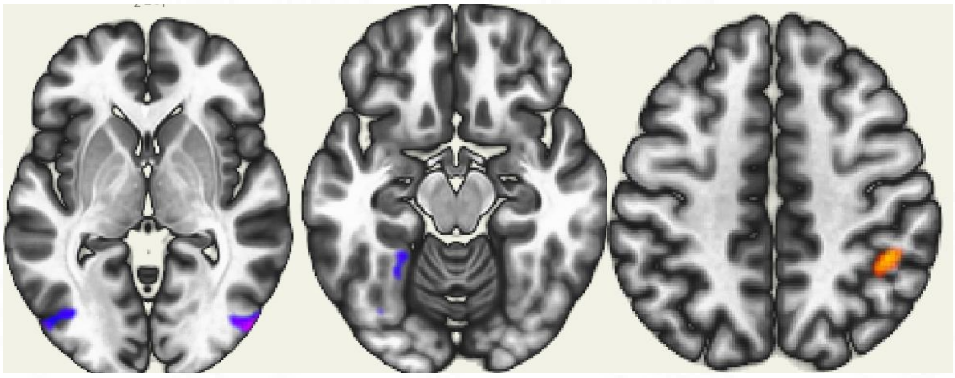
Patients > HC: Language network- group ICA analysis



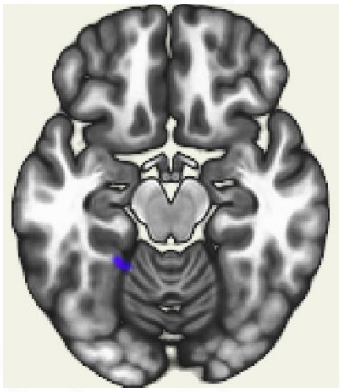
Post > HC: Language network- group ICA analysis



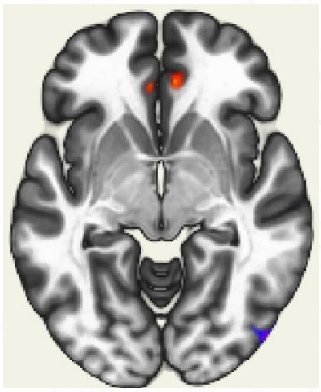
Low NP > HC: Language network- group ICA analysis



Cognitive decline> HC



Noncognitive decline> HC



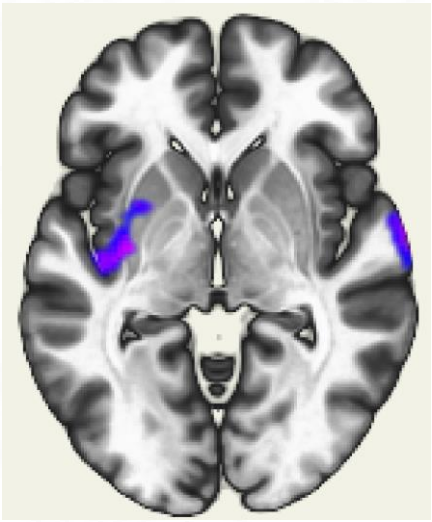
Language network- group ICA analysis: Patients show increased group ICA connectivity at anterior cingulate region (ACC) and right supra-marginal gyrus (SMG) suggests increased salience network connectivity and decreased connectivity clusters at left occipital and fusiform gyrus (anti-correlation with DMN's compensation). In low NP score and cognitive decline presentation, a decrease in connectivity is more prominent at left fusiform gyrus, occipital lobes (suggests more prominent anti-correlation with DMN). And Post embolization patient's increase in connectivity at ACC and SMG is less prominent. (Orange-red→ Positive, Blue-purple → Negative correlation)

8.Sensori-motor network: group ICA analysis

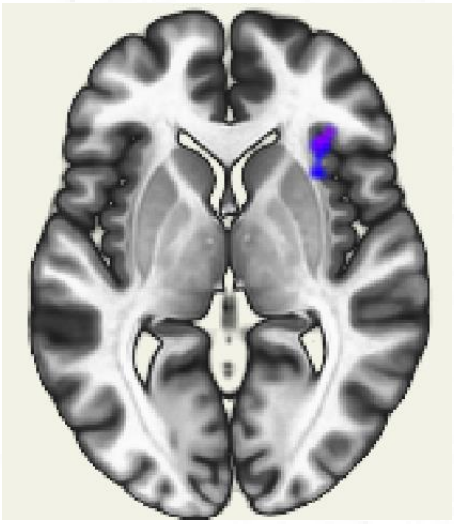
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	-34 -10 +02(Lt Insula) +70 -10 +00 (Rt opercula) -64 -26 +14(Lt opercula)	886 275 224	0.000001 0.007588 0.019997	0.000002 0.006554 0.011587	0.008879 0.149453 0.042592
Post embolization >HC	+32 +16 +10(Rt Insula)	287	0.004857	0.005615	0.772038
Low NP> HC	--32 -08 +02(Lt insula) +70 -10 +02(Rt insula) -64 -26 +12(Lt SMG)	261 160 142	0.008134 0.065590 0.098075	0.011449 0.047551 0.048235	0.293091 0.290203 0.579796
High NP >HC	-62 -26 +14(Lt insula)	312	0.002566	0.003015	0.643172
Cognitive decline present > HC					
Non-cognitive decline >HC	-34 -10 +02(Left insula)	597	0.000034	0.000046	0.134552

(Abbreviations- SMG: Supra Marginal gyrus)

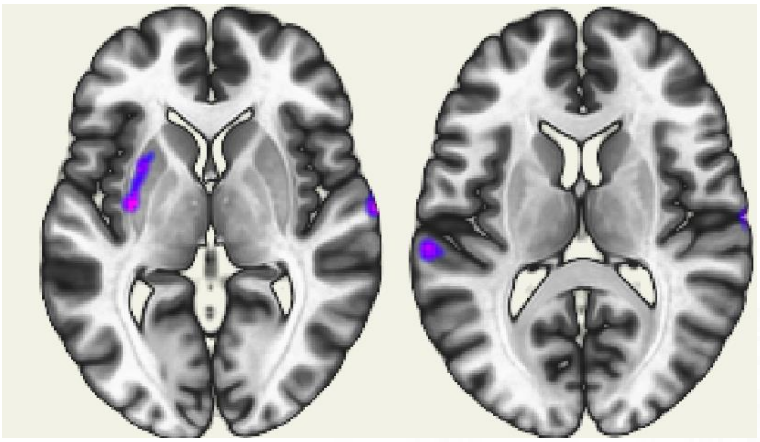
Patient > HC



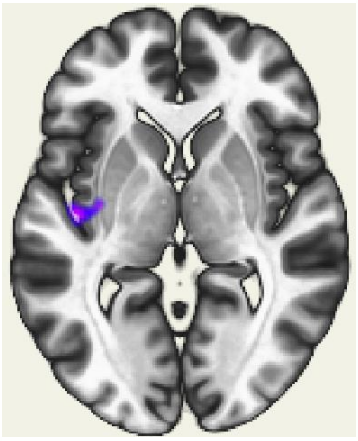
Post > HC



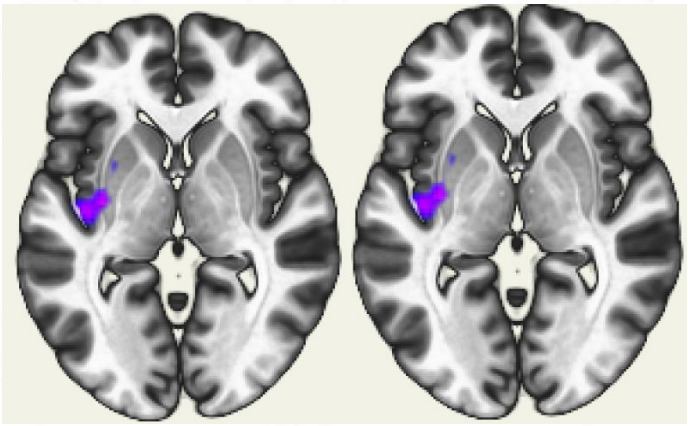
Low NP>HC: Language network



High NP> HC



Non cognitive decline > control: Sensori-motor network



Sensori-motor network- group ICA analysis: Patients show decreased group ICA connectivity at bilateral insular and opercular regions. In low NP score a decrease in connectivity is noted on both sides as compared to left side in high NP score group. In Cognitive decline group decreased in connectivity is absent as compared to prominent decrease in connectivity in non-cognitive decline group, suggests that language network act as compensatory network for salience network. (Orange-red→ Positive, Blue-purple → Negative correlation)

1.Summary of group ICA analysis:

By selecting a spatial match to explore the estimated ICA networks, the correlation between each group-level spatial map and networks of interest made. Based on visual inspection, eight components were identified, which include default mode network, salience network, dorsal attention network, frontoparietal network, visual network, cerebellar network, sensorimotor network, and language network. On analysing group differences between patient and control groups, significant difference noted all 8resting state networks, which include default mode network, salience network, dorsal attention network, frontoparietal network, visual network, cerebellar network.

RSN	Pt> HC	Pt post >HC	L NP >HC	H NP >HC	Cog >NC	Non.Cog>HC
DMN	⬇ PC-PCC	⬇ PC ⬆ Rt FG	⬇ PC-PCC	⬇ PC-PCC	⬇ PC-PCC ⬆ Rt-CBM	⬇ PC-PCC ⬇ ACC
Salience network (SN)	⬇ ACC ⬇ Rt-Insula ⬇ Precuneus ⬆ CBM	⬆ CBM	⬇ ACC ⬆ CBM ⬆ Rt PHG ⬆ Lt Amyg	-	⬇ ACC	⬇ ACC ⬇ PC-PCC ⬇ Rt insula ⬆ CBM
Dorsal attention	⬇ PCC ⬆ B/L Fron ⬆ (AP conn)	⬆ Rt FG, B/L Frontal	⬆ Rt Front	-	-	⬇ PCC ⬆ B/L FP ⬆ Rt SMG
Fronto-parietal	⬆ PCC	-	⬆ PCC	-	⬇ B/L PCG, PtCG	⬆ PCC
Visual	⬆ Lt PHG ⬇ B/L Occ ⬇ Rt CBM	⬆ PCC ⬇ B/L occ	⬇ B/L Occ	⬇ B/L Occ ⬇ Lt FG	⬇ B/L FG	⬇ B/L Occ +FG
Cerebellar	⬇ Lt Occ		⬇ Lt Occ		⬇ Lt occ ⬆ B/L SFG	-
Language	⬆ ACC, SMG ⬇ Lt Occ,FG	⬇ Rt Thalamus and Lt FG	⬆ SMG ⬇ Lt FG, B/L occipital	-	⬇ Lt FG	⬆ ACC
Sensori-motor	⬇ B/L insular	⬇ Rt insula	⬇ B/L insula, Lt SMG	⬇ Lt insula	-	⬇ Lt Insula

(Abbreviations: PC-PCC-Precuneus-Posterior cingulate, FG-Fusiform gyrus, CBM-Cerebellum, ACC-Anterior cingulate, PHG-Para-hippocampal gyrus, Fron- superior frontal, SMG-Supra-marginal gyrus, Occ-Occipital, FP-Frontal pole)

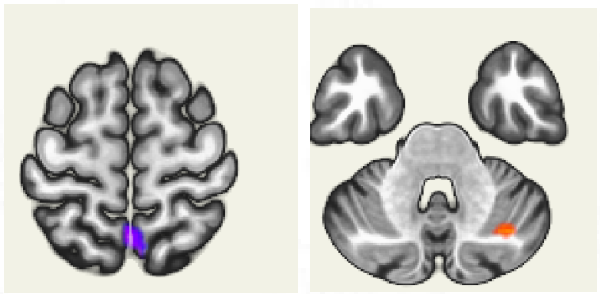
2.Connectivity analysis- Seed to voxel analysis:

(i). DMN (PCC used as seed)- Seed to voxel analysis

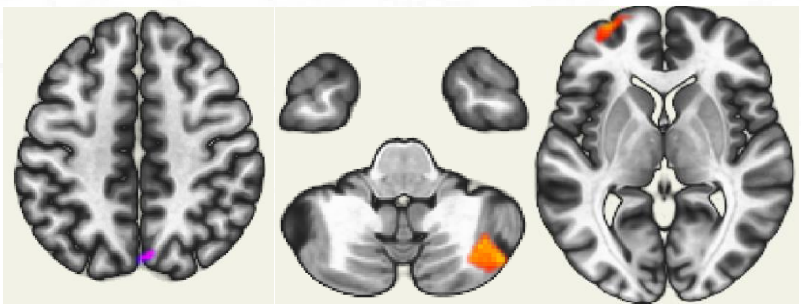
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	-36 +52 +00(Lt FP) +36 -76 -40(CBM) +02 -66 +62(Pre) -20 +30 +50(Lt SFG) +26 -72 -18(Rt FG) +34 +46 -06(Rt FP)	752 548 515 398 330 150	0.000001 0.000021 0.000037 0.000292 0.001072 0.056528	0.000002 0.000021 0.000037 0.000292 0.001072 0.056528	0.138821 0.101681 0.020928 0.305833 0.556509 0.491700
Post embolization >HC	+40 -64 -50(CBM) -32 +64 +04(Lt FP) +06 -72 +50(Pre)	403 264 188	0.000312 0.002618 0.010072	0.000010 0.000175 0.001007	0.054139 0.592238 0.195351
Low NP> HC	+04 -60 +66(Pre) +44 -58 -50(Rt CBM) -18 +32 +50(Lt FP) +14 +28 +46(Rt FP)	561 303 292 146	0.000016 0.001768 0.002215 0.061164	0.000030 0.001370 0.001370 0.029255	0.003667 0.489860 0.350608 0.865957
High NP >HC	-32 +50 +02(Lt FP) +40 -62 -50(Rt CBM)	314 181	0.000010 0.017101	0.001817 0.021286	0.857325 0.873880
Cognitive decline present > HC	+40 -62 -48(Pre) +04 -60 +66(Rt CBM)	360 277	0.000393 0.002230	0.000707 0.002009	0.146072 0.364070
Non-cognitive decline >HC	-34 +62 +02(SFG L) -20 +28 +50(FP L) +38 -78 -42(CBM RT) +02 -74 +54(Pre) +64 -26 +34(SMG R) +28 -70 -16(FG)	420 366 320 278 209 174	0.000133 0.000379 0.000961 0.002335 0.011132 0.026102	0.000007 0.000019 0.000049 0.000118 0.000567 0.001339	0.482580 0.801360 0.649405 0.098944 0.055641 0.801174

(FP-Frontal pole, CBM-Cerebellum, SFG-Superior frontal gyrus, Pre-precuneus, FG-Fusiform gyrus)

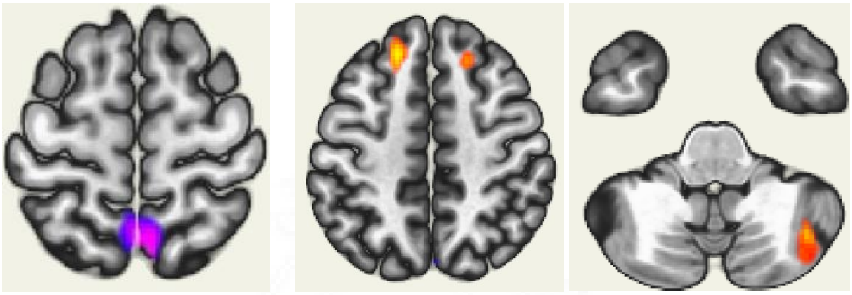
Patient > HC (DMN): Seed to voxel analysis



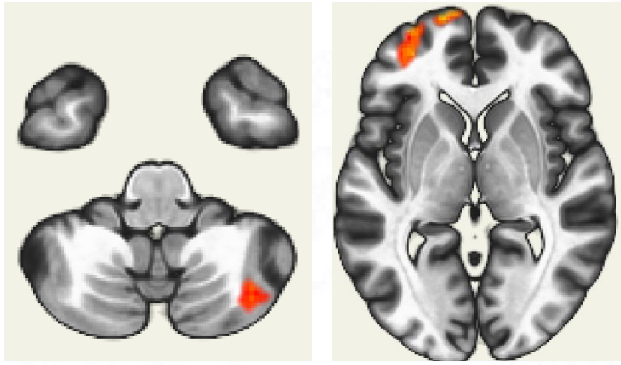
Post embolization> HC(DMN): Seed to voxel analysis



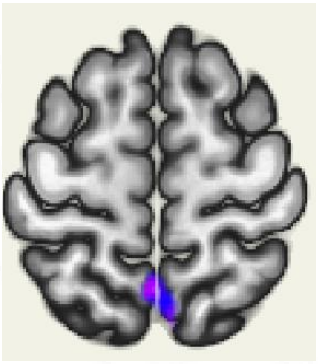
Low NP > HC(DMN): Seed to voxel analysis



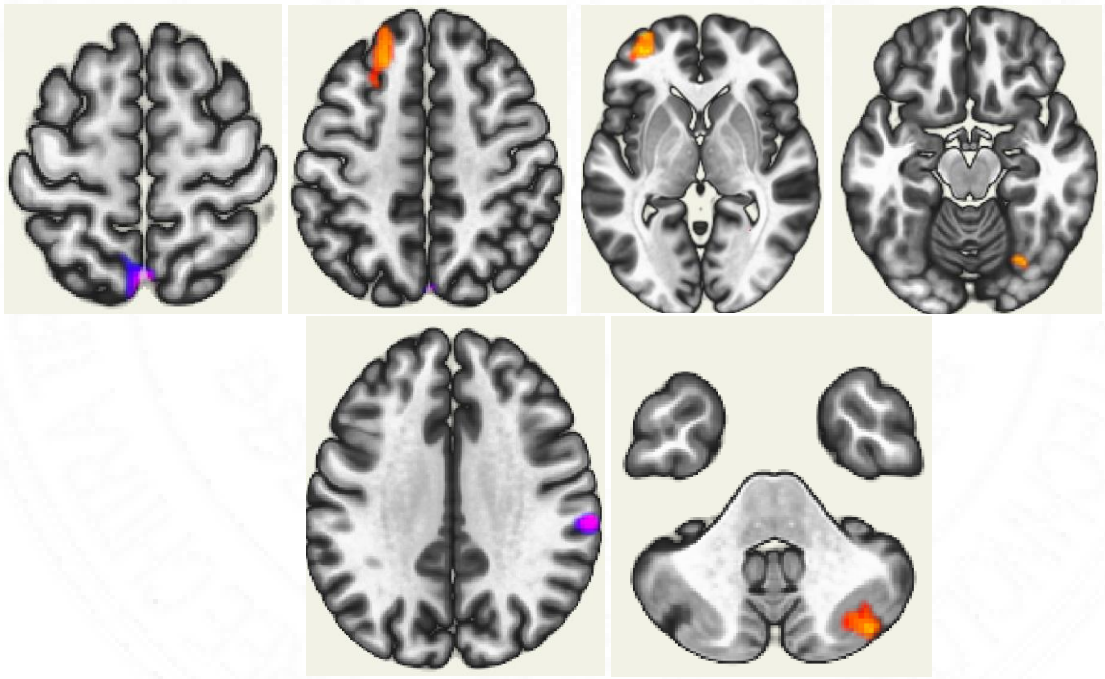
High NP> HC (DMN)



Cognitive decline > HC(DMN)



Non-cognitive decline presentation > HC(DMN)



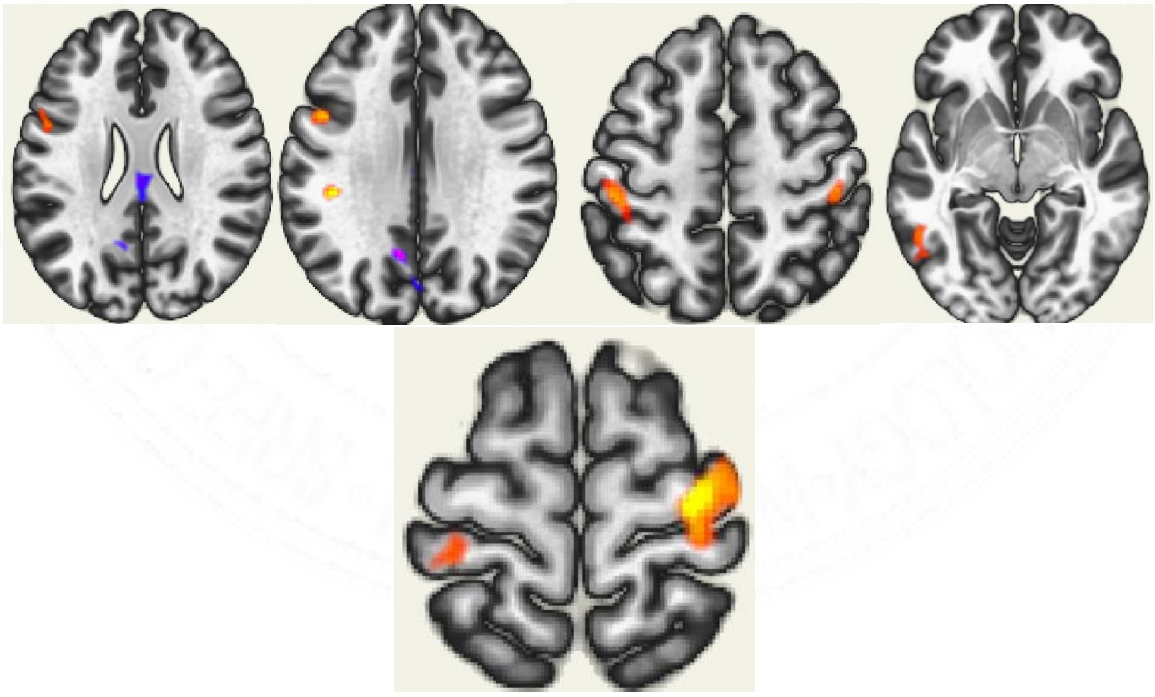
DMN- seed to voxel analysis (PCC): PCC of DMN shows decreased connectivity in patients, which is less prominent in post embolization patient groups and patients with the non-cognitive presentation. There is increased right frontal connectivity cluster. Low NP score and cognitive decline presentation group shows increased right cerebellar connectivity cluster. (Orange-red→ Positive, Blue-purple → Negative correlation).

(ii). Salience network (ACC used as seed)- Seed to voxel analysis

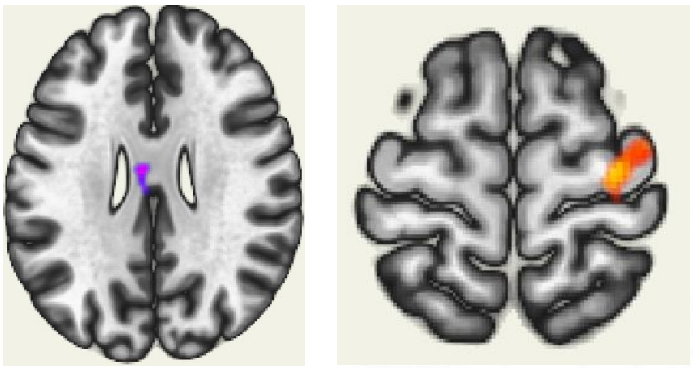
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	+32 -16 +68 (P&PtCG Lt) -44 -30 +32(Pt CG Rt) -06 -28 +16(PCC) -52 -60 -02(Lt TO) -50 +08 +34(Lt PCG) -10 -60 +32(Pre)	687 658 468 244 237 163	0.000004 0.000006 0.000377 0.002785 0.004266 0.008070	0.000009 0.000009 0.000417 0.002309 0.002831 0.004472	0.002077 0.276344 0.510815 0.492349 0.244736 0.955274
Post embolization >HC	-	-	-	-	-
Low NP> HC	-06 -10 +30(PCC) +32 -18 +70 (Rt PCG & PtCG)	210 203	0.013167 0.015469	0.017767 0.017767	0.197601 0.639860
High NP >HC	-54 -22 +56(Lt PCG & PtCG) +28 -18 +70(Rt PCG & PtCG)	740 232	0.000000 0.008013	0.000001 0.008013	0.276217 0.691988
Cognitive decline present > HC	+26 -20 +76(Rt PCG & PtCG) -62 +00 +26(Lt PCG & PtCG)	251 180	0.004353 0.022964	0.005997 0.015969	0.631591 0.558484
Non-cognitive decline >HC	+42 -28 +36(Lt Pre &PtCG) -10 -62 +32(Precuneus) +32 -16 +68 (Rt Pre &PCG) +40 +28 +22(Rt FP) -06 -28 +16(Thalamus)	714 546 229 193 159	0.000001 0.000018 0.007896 0.018192 0.041746	0.000003 0.000024 0.007150 0.012420 0.023078	0.076357 0.284818 0.746898 0.420907 0.212104

(ACC-Anterior cingulate, PCG-Pre central gyrus, PtCG-Post central gyrus, FP-Frontal pole, TO-Temporo-occipital)

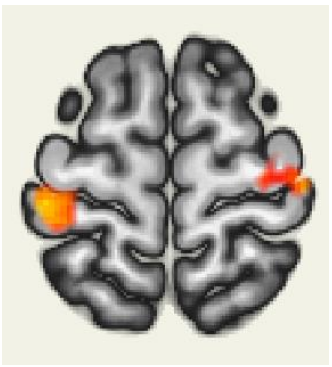
Pt > HC: Salience network



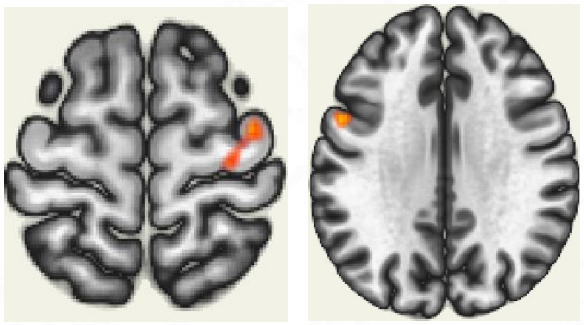
Low NP> HC



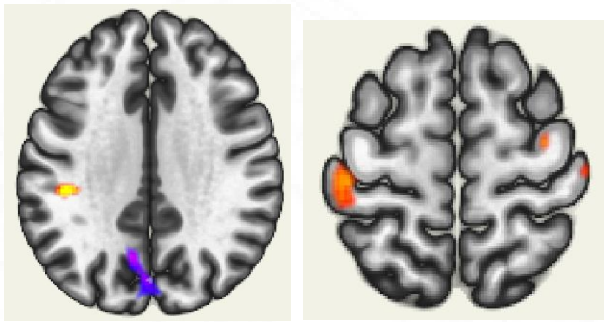
High NP>HC



Cognitive decline present> HC



Non-cognitive decline present> HC



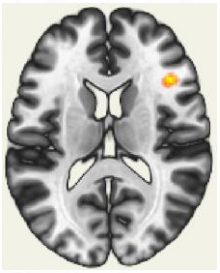
Salience network- seed to voxel analysis (ACC as seed point): Anterior cingulate shows decreased connectivity cluster with precuneus- posterior cingulate region and increased connectivity with bilateral pre and postcentral gyrus. Low NP patient group and patient with cognitive decline presentation show prominent right pre and postcentral gyrus connectivity as compared to left pre and postcentral gyrus. No significant difference was noted between the post patient and a healthy control group. (Orange-red→ Positive, Blue-purple → Negative correlation).

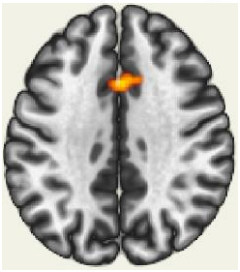
(iii). Dorsal attention network (IPS Left used as seed)- Seed to voxel analysis:

Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	**+40 +28 +04(Rt IFG)**	**498**	**0.000064**	**0.000147**	**0.172887**
Post embolization >HC	**+44 +30 +02(Rt IFG)** **+02 +16 +40(ACC)** **+36 +54 +18(Rt FP)** **+10 -16 +06(Rt Thal)** **+22 +10 -16(Rt puta)**	**331(I)** **248(I)** **174(I)** **159(I)** **158(I)**	**0.001235** **0.006613** **0.034502** **0.049306** **0.050508**	**0.002576** **0.006915** **0.021607** **0.021607** **0.021607**	**0.510811** **0.087931** **0.574137** **0.526475** **0.055938**
Low NP> HC	-	-	-	-	-
High NP >HC	-	-	-	-	-
Cognitive decline present > HC	-	-	-	-	-
Non-cognitive decline >HC	**+42 +24 +14(Rt IFG)** **+08 +18 +34(ACC)** **+28 +06 +06(Rt put)**	**339** **199** **198**	**0.000869** **0.017040** **0.017441**	**0.001890** **0.012759** **0.012759**	**0.188562** **0.662062** **0.382547**

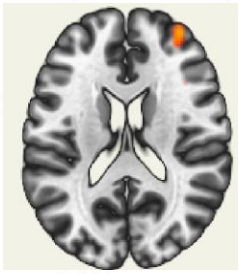
(IFG-Inferior frontal gyrus, ACC-Anterior cingulate, FP-Frontal pole, Thal-Thalamus, Put-Putamen)

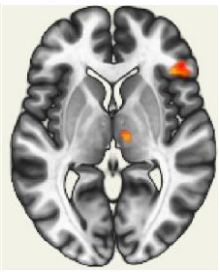
Patient> HC

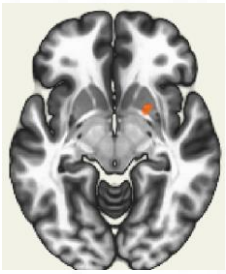




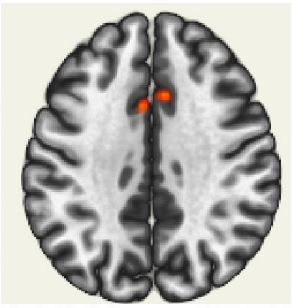
Post embolization> HC

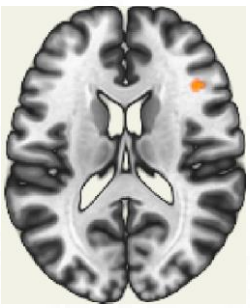


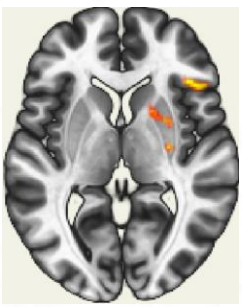




Non-cognitive decline patients > HC







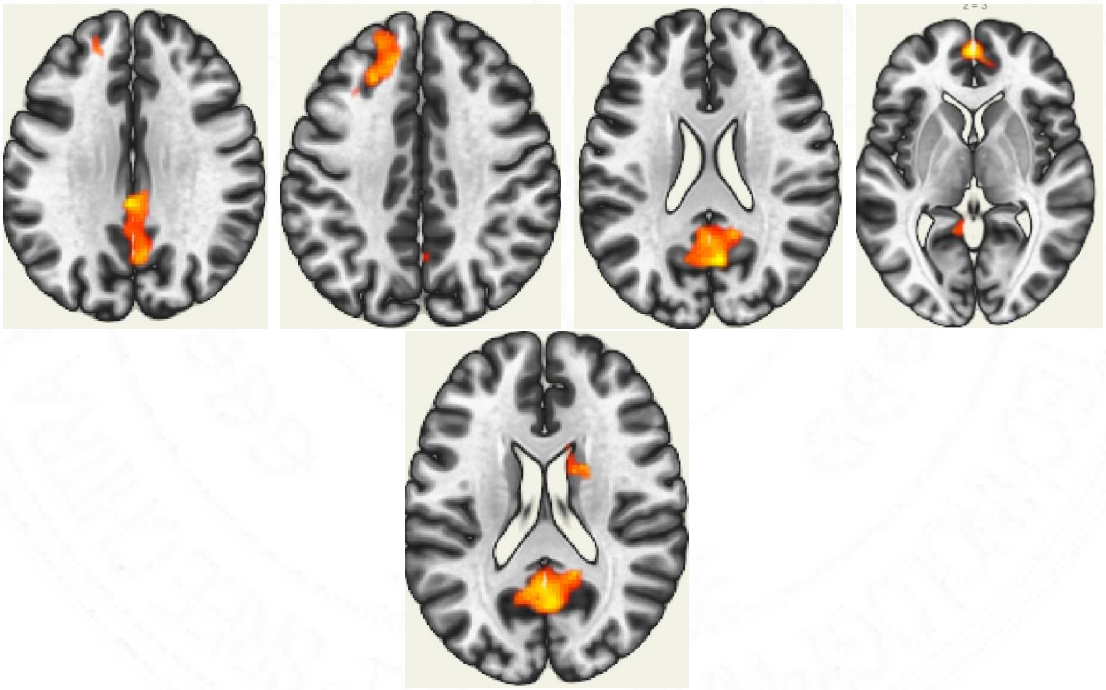
Dorsal attention network- Seed to voxel analysis (Left IPS as seed): In the patient group, left IPS show increased right frontal connectivity cluster. In the post embolization patient group and patient with non-cognitive decline presentation, left IPS show increased functional connectivity with the anterior cingulate cortex. (Orange-red→ Positive, Blue-purple → Negative correlation).

(iv). Frontoparietal network (LPFC- Right as seed)- Seed to voxel analysis

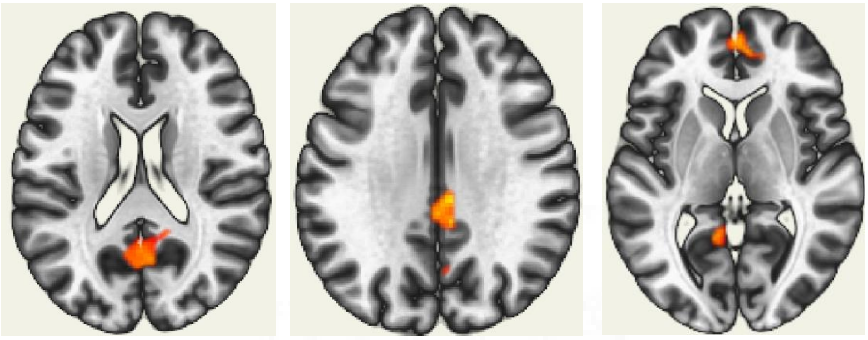
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	+00 -36 +32(Pre-PCC) -20 +46 +36(Lt SFG) +16 +46 +08 (Rt FP) +22 +04 +18 (Rt Caud)	1978 562 436 137	0.000000 0.000015 0.000131 0.075309	0.000000 0.000001 0.000007 0.004117	0.174988 0.132980 0.142038 0.768301
Post embolization >HC	-	-	-	-	-
Low NP> HC	-10 -52 +04(Precuneus) +16 +48 +08(Rt PC) +06 -30 +32(PCC)	712 290 270	0.000001 0.001776 0.002738	0.000001 0.001301 0.001338	0.888153 0.743476 0.525367
High NP >HC	+02 -70 +40(Pre-PCC)	254	0.008570	0.014371	0.000513
Cognitive decline present > HC	-	-	-	-	-
Non-cognitive decline >HC	-02 -34 +34(Pre-PCC) -20 +46 +36(Lt FP) +16 +46 +08(Rt PCG) +12 +14 +16(Caud) -36 -78 +38(Lat Occ)	2474 647 549 201 167	0.000000 0.000016 0.000068 0.028327 0.058254	0.000000 0.000018 0.000050 0.015917 0.026595	0.222575 0.227474 0.134031 0.114723 0.898919

(Pre-PCC: Precuneus-Posterior cingulate, PC-Para cingulate, Caud-Caudate, Occ-Occipital)

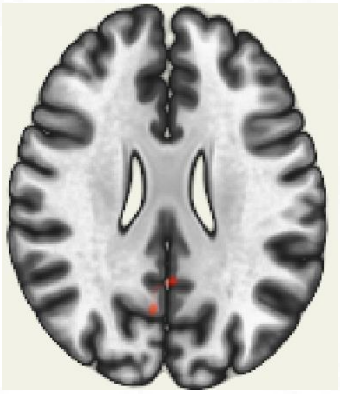
Patients > HC: Fronto-parietal network



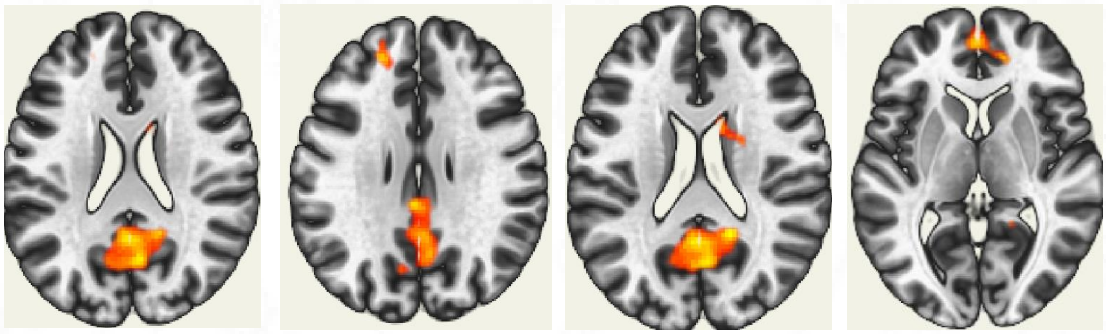
Low NP > HC: Fronto-parietal network



High NP > HC: Fronto-parietal network



Non-cognitive decline> HC: Fronto-parietal network



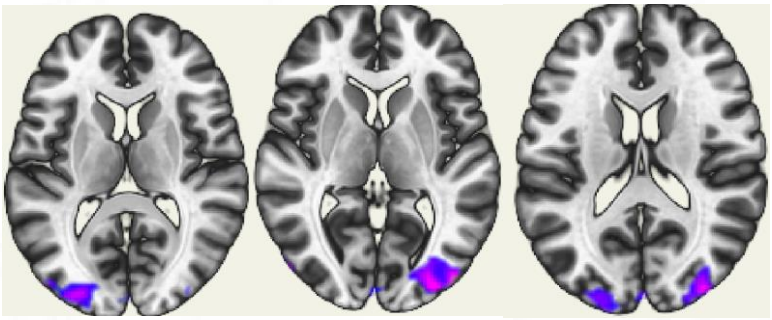
Fronto-parietal network-seed to voxel analysis (Right LPFC as seed): Right LPFC show increased functional connectivity with pre-cuneus and posterior cingulate region & left the frontal region in the patient group. Inpatient with non-cognitive decline shows an additional increase in functional connectivity with the right caudate nucleus. (Orange-red→ Positive, Blue-purple → Negative correlation).

(v). Visual network (Right lateral occipital as seed region): Seed to voxel analysis

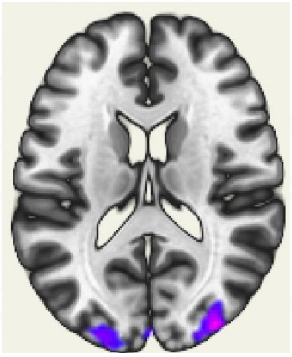
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	-44 -88 +06(Lt FG) +36 -56 -24(Rt FG) +32 -90 +22(Rt OP) +52 -80 -04(Rt LO)	3346 843 531 140	0.000000 0.000000 0.000047 0.086069	0.000000 0.000000 0.000022 0.031967	0.049059 0.016105 0.006360 0.052642
Post embolization >HC	+08 -54 +10(Pre)	279	0.003342	0.005832	0.994073
Low NP> HC	-42 -80 -08(LO+FG) +30 -90 +20(RO) +34 -56 -26(R FG)	3631 654 636	0.000000 0.000005 0.000007	0.000000 0.000002 0.000002	0.009508 0.033242 0.648670
High NP >HC	+36 -54 -26(Rt Lat occ)	174	0.026726	0.023469	0.014394
Cognitive decline present > HC	-34 -68 -22(B/L FG)	2157	0.000000	0.000000	0.049577
Non-cognitive decline >HC	-46 -86 +06(LO+FG) +36 -54 -26(Rt FG) +34 -88 +24(RO) +00 -90 +20(OP)	636 454 341 139	0.000006 0.000116 0.000928 0.076999	0.000011 0.000116 0.000618 0.040023	0.722532 0.005042 0.049416 0.963396

(FG-Fusiform gyrus, OP-Occipital pole, LO-Lateral occipital, Occ-Occipital, Pre-Precuneus)

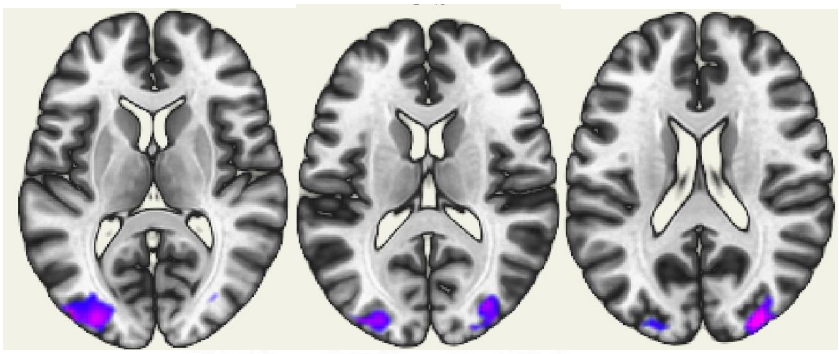
Patients > HC: Visual network



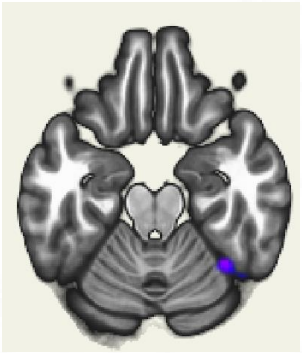
Post > HC: Visual network



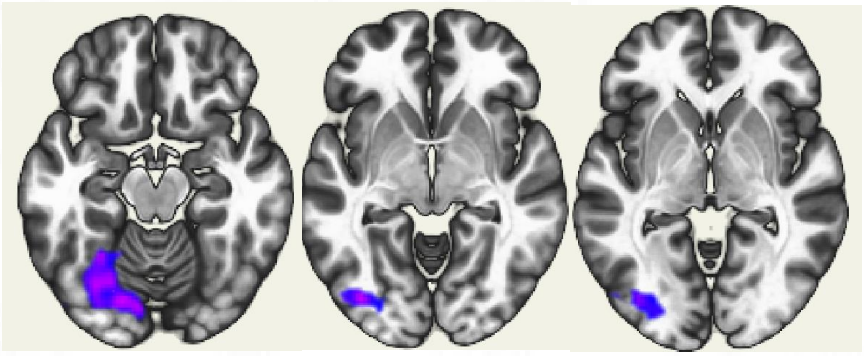
Low NP > HC: Visual network



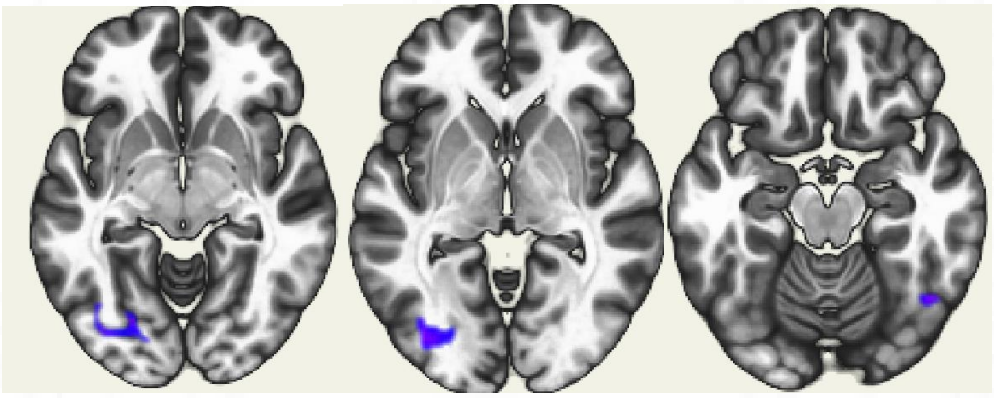
High NP> HC: Visual network



Cognitive decline presentation > HC



Non-cognitive presentation > HC



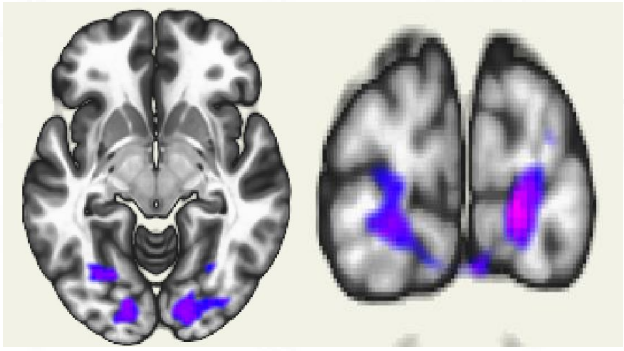
Visual network- Seed to voxel analysis (Right lateral occipital as seed): Right occipital cortex shows a global reduction in functional connectivity with bilateral occipital, fusiform gyrus in the patient group. Patients with low NP group, cognitive decline presentation group, show a significant reduction in functional connectivity at fusiform gyrus. The post embolization patient group shows complete resolution of occipital connectivity and an increase in functional connectivity with the posterior cingulate cortex. (Orange-red→ Positive, Blue-purple → Negative correlation).

(vi). Cerebellar network: (Posterior cerebellum as seed): Seed to voxel analysis

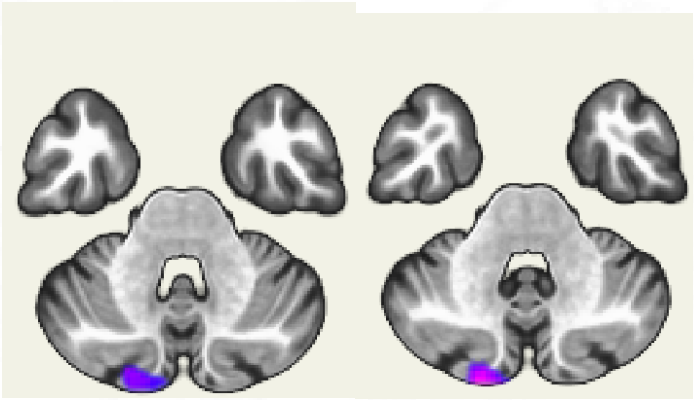
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	-16 -84 +00(B/L OP and FG)	4461	0.000000	0.000000	0.005853
Post embolization >HC	-18 -92 -40(Lt CBM)	226	0.010001	0.016310	0.006150
Low NP> HC	-16 -84 +00(Lt OP) +16 -94 +00(Rt OP) +30 -76 -20(Rt FG)	1025 196 166	0.000000 0.020908 0.042005	0.000000 0.015103 0.020448	0.042831 0.576701 0.759935
High NP >HC	+20 -88 -18(Rt FG) -10 -88 -34(Lt FG)	545 393	0.000013 0.000207	0.000022 0.000181	0.195093 0.252279
Non-cognitive decline present > HC	-16 -84 +00(B/L Occ) -34 -66 -04(Lt FG)	3302 166	0.000000 0.036110	0.00000 0.031857	0.064343 0.140907
Cognitive decline >HC	-	-	-	-	-

(OP-Occipital pole, CBM-Cerebellum, FG-Fusiform gyrus, Occ-Occipital)

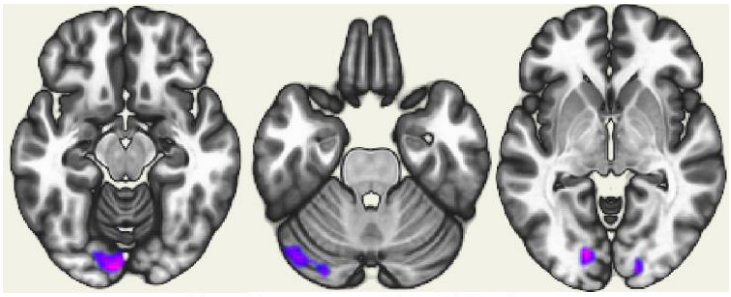
Patients > HC: Cerebellar network



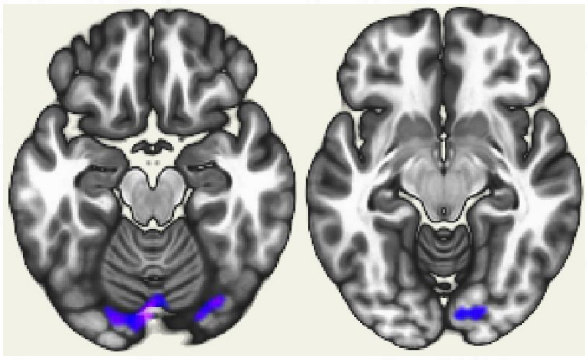
Post > HC: Cerebellar network



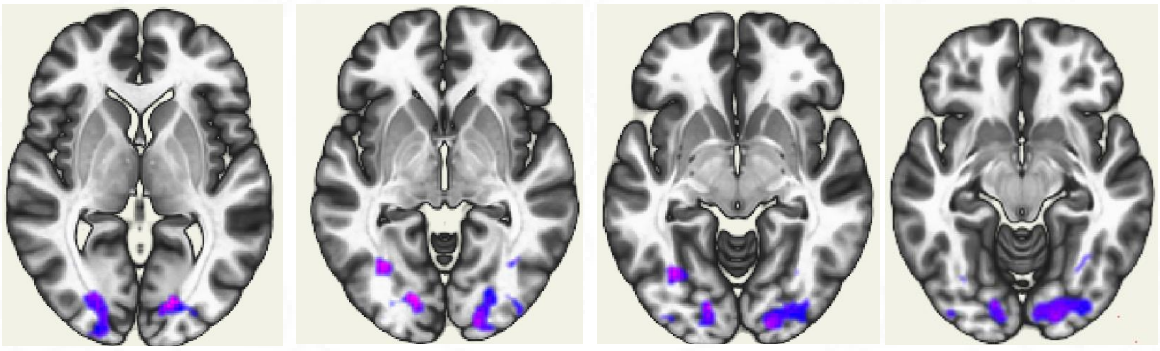
Low NP patients > Controls



High NP patients > controls



Non-cognitive decline > HC



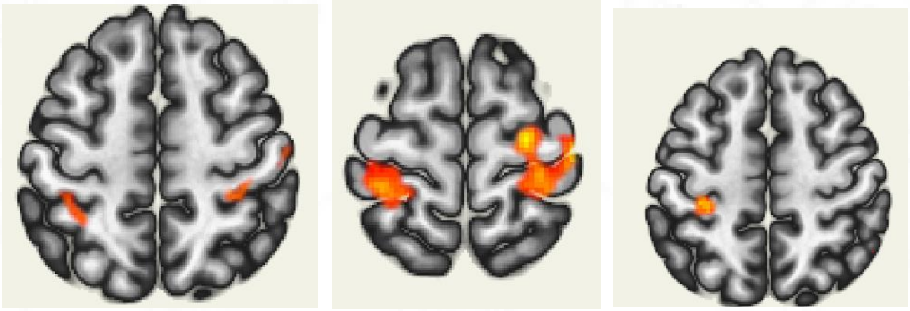
Cerebellar network (Posterior cerebellar as seed): Posterior cerebellum show decreased functional connectivity with bilateral occipital and fusiform region in patient group. Post embolization patient group show complete resolution of decrease in functional connectivity with bilateral occipital region. (Orange-red→ Positive, Blue-purple → Negative correlation).

7.Language network: Seed to voxel analysis- Right IFG analysis

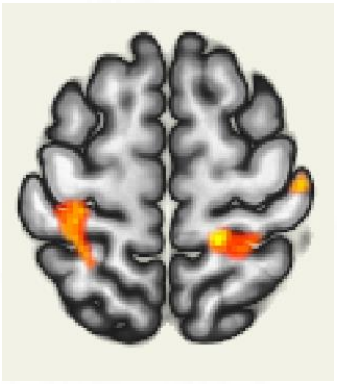
Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	**-16 -84 +00(Lt pre, Pt CG)**	**671**	**0.000003**	**0.000006**	**0.054149**
Post embolization >HC	**-28 -38 +42(Lt Pt CG and SPL)** **+20 -36 +74(Rt PtCG and SPL)**	**647** **459**	**0.000003** **0.000069**	**0.000004** **0.000049**	**0.360726** **0.711362**
Low NP> HC	-	-	-	-	-
High NP >HC	**+48 -18 +46(Lt Pre and Pt CG)** **-34 -34 +70(Rt pre and Pt CG)**	**1982** **684**	**0.000000** **0.000001**	**0.000000** **0.000000**	**0.001932** **0.327616**
Non-cognitive decline present > HC	**-34 -34 +70(Lt Pre and Pt CG)** **+48 -26 +64(Rt pre and Pt CG)** **+18 -38 +62(Rt SPL)**	**993** **392** **294**	**0.000000** **0.000241** **0.001734**	**0.000000** **0.000185** **0.000886**	**0.134282** **0.370904** **0.132695**
Cognitive decline >HC	-	-	-	-	-

(PCG-Pre-central gyrus, PtCG-post central gyrus, SPL-Superior parietal)

Patient > controls **Post >HC** **High NP >HC**



Non-Cognitive >HC

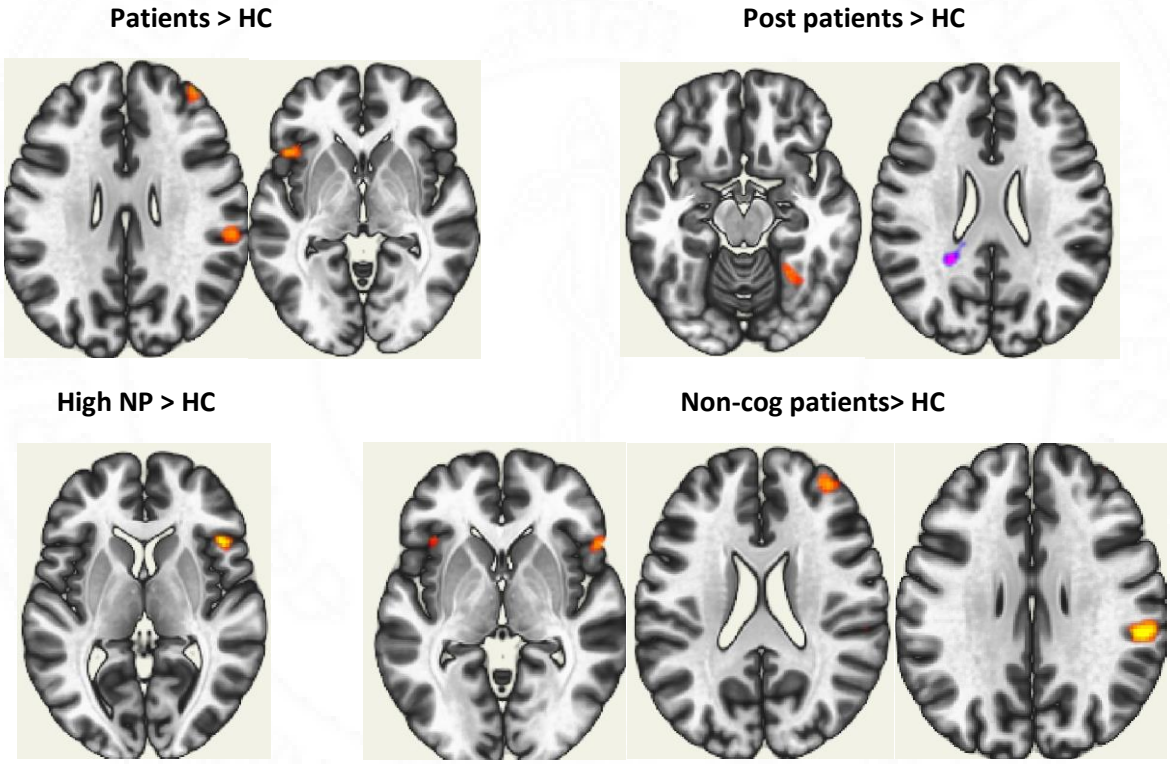


Language network- seed to voxel analysis (Right IFG as seed point): Right IFG shows increased connectivity with bilateral pre and postcentral gyrus. Low NP patient group and patient with cognitive decline presentation group, increased connectivity at pre and postcentral gyrus is absent. In non-cognitive decline group and High NP score group, increased connectivity with bilateral pre and post central gyrus is very prominent, suggestive of compensatory activity. (Orange-red→ Positive, Blue-purple → Negative correlation).

8.Sensorimotor network: Seed to voxel analysis (Superior sensorimotor area used as seed)

Group	Cluster (X, Y, Z)	Size	Size p-FWE	Size-p-FDR	Peak p-FWE
Pt > HC	**+56 -30 +32(Rt SMG)** **-46 +20 -06(Lt FO)** **+38 +54 +28(Rt FP)**	**224** **205** **156**	**0.017416** **0.025666** **0.073149**	**0.024754** **0.024754** **0.048213**	**0.332812** **0.224461** **0.683332**
Post embolization >HC	+24 -44 +24(Lt cingulate) +32 -58 -12(Rt FG)	234 169	0.009305 0.040063	0.018642 0.040765	0.141630 0.909212
Low NP> HC	-	-	-	-	-
High NP >HC	**+44 +22 +06(Rt IFG)**	**189**	**0.036966**	**0.379880**	**0.000009**
Non-cognitive decline present > HC	**+56 -30 +32(Rt SMG)** **+54 +22 +00(Rt IFG & FO)** **+36 +50 +20(Rt FP)** **-48 +18 -06(Lt FO)**	**297** **220** **199** **147**	**0.002878** **0.013908** **0.021979** **0.072552**	**0.006216** **0.015102** **0.015977** **0.040609**	**0.064294** **0.787192** **0.505936** **0.461467**
Cognitive decline >HC	-	-	-	-	-

(SMG-Supra-marginal gyrus, FO-Frontal pole, FO-Fronto-opercular, IFG-Inferior frontal gyrus)



Sensori-motor network- seed to voxel analysis (Sensori-motor superior as seed point): Sensory motor superior seed region shows increased connectivity with right superior frontal (RPFC) and right SMG, left fronto-opercular region which is more prominent in High NP group and non-cognitive decline group. Low NP patient group and patient with cognitive decline presentation group, this increased connectivity is absent. (Orange-red→ Positive, Blue-purple → Negative correlation).

2.Summary of seed to Voxel analysis:

For the seed to voxel analysis, regions with the highest connectivity value on group ICA or ROI to ROI analysis within each network were used as seeds for the next level of analysis. Seed regions selected for each resting-state networks are as follows, (i). Posterior cingulate region (PCC)- DMN, (ii). Anterior cingulate cortex (ACC)-Salience network (iii). Dorsal attention network- Left IPS, (iv). Fronto-parietal network- right LPFC, (v). Visual cortex- right occipital region, (vi). Cerebellar network- posterior cerebellar region, vii). Language network- right inferior frontal gyrus (IFG), viii). Sensorimotor network- Sensorimotor superior

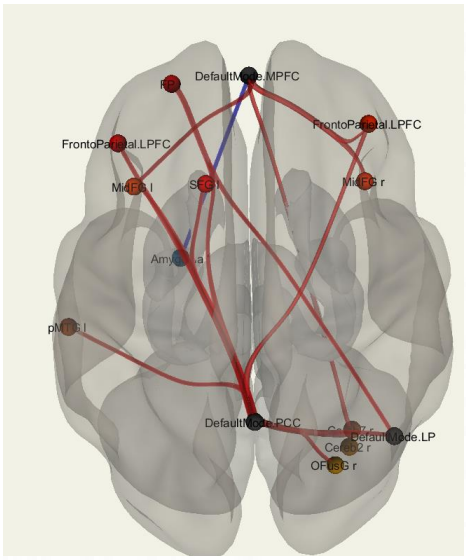
RSN (Seed region used)	Pt> HC	Pt post >HC	L NP >HC	H NP >HC	Cog >NC	Non.cog>HC
DMN (PCC)	↓PC-PCC ↑Rt-Frontal ↑Rt CBM	↓PC(less prominent) ↑ CBM ↑ Lt FT	↓PC-PCC ↑ CBM ↑ Frontal	↑ CBM ↑ Frontal (No PC-PCC changes)	↓PC-PCC ↑ Rt-CBM	↑ Frontal ↑CBM ↑ FG
Salience network (ACC)	↓ PC-PCC ↑ B/L pre and Pt CG	-	↓PCC ↑ Rt Pre and Pt CG	↑ Both Pre and Pt CG	↑-Rt pre and Pt CG	↓ PC-PCC ↑ B/L Pre and post CG ↑Thalamus
Dorsal attention (Left IPS)	↑ Rt Fron	↑ ACC ↑ Fron, Thal, putamen	-	-	-	↑ ACC ↑ Rt Fron ↑ Putamen
Fronto-parietal (Rt LPFC)	↑ PC-PCC ↑ Frontal ↑ Rt Caud	-	↑ PC-PCC	-		↑ PC-PCC ↑ Rt card ↑ B/L Fron
Visual (Rt Lat Occ)	↓ B/L Occ +FG	↑ PCC	↓ B/L Occ ↓ Lt >Rt FG	↓ B/L Occ	↓ B/L FG (Lt>Rt)	↓ B/L Occ +FG(Rt>Lt)
Cerebellar (Post cerebellar)	↓ B/L Occ And FG	↓ Lt CBM	↓ B/L Occ and FG	↓B/L FG	-	↓ B/L Occ and FG
Language network (Right IFG)	↑Pre and PtCG	↑ B/L Pre and ptCG	-	↑B/L Pre &PtCG	-	↑ B/L Pre and PtCG
Sensori-motor network (Sensori-motor superior)	↑-Rt SMG, Lt FO, Rt FP	↑ Rt FG	-	↑ Rt IFG	-	↑ Rt SMG, B/L FO and FP

(PC-PCC-Precuneus posterior cingulate, CBM-Cerebellum, FG-Fusiform gyrus, Caud-Caudate, Occ-Occipital, PCG-Pre-central gyrus, PtCG-Post central gyrus, SMG-Supra-marginal gyrus)

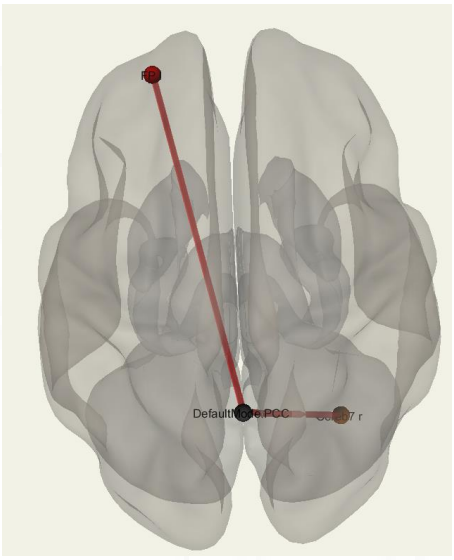
3.ROI to ROI analysis:

1.Default mode network- ROI to ROI analysis: (p-FDR corrected < 0.05)

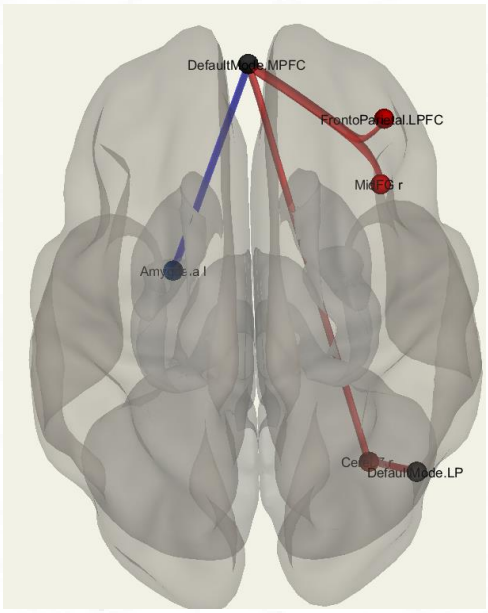
Patient > HC



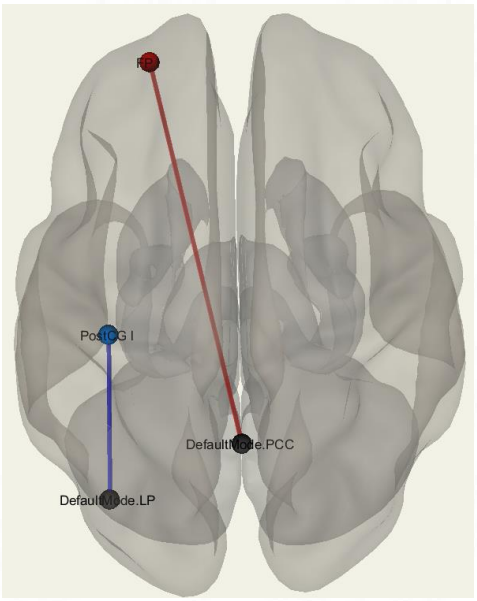
Post embolization >HC



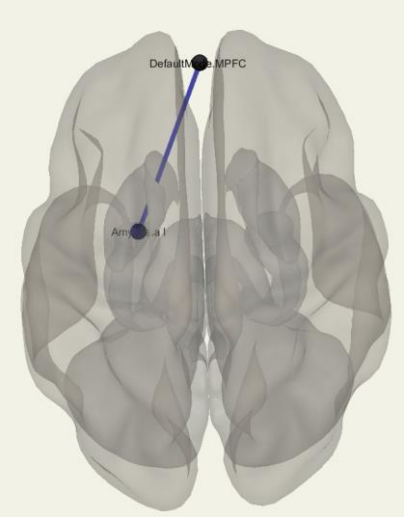
Low NP > HC



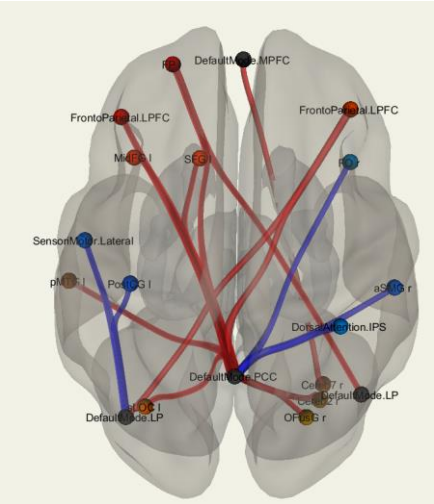
High NP > HC



Cognitive decline presentation> HC



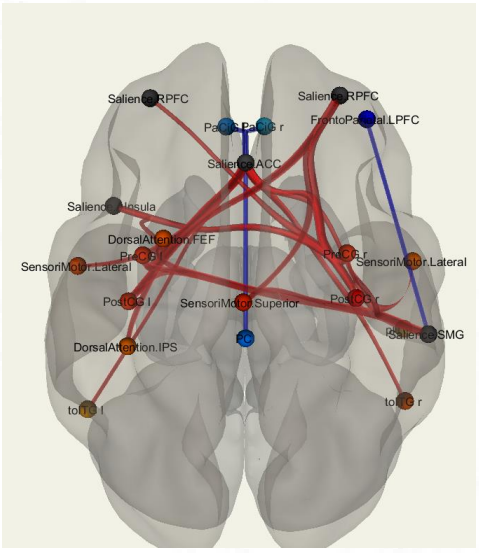
Non-cognitive presentation > HC



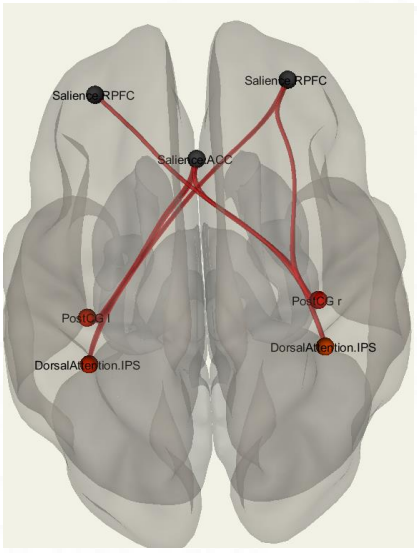
DMN network- ROI to ROI analysis: Default mode network show an increase in functional connectivity between right LPFC and posterior cingulate region and decrease in connectivity at MPFC, which is more prominent in the cognitive decline presentation group. In the post embolization group and non-cognitive decline group, the relative increase in functional connectivity at the posterior cingulate seed region. In the patient with high NP score, increase in connectivity between the left frontal pole and posterior cingulate region

2.Salience network: ROI to ROI analysis (p-FDR corrected <0.05)

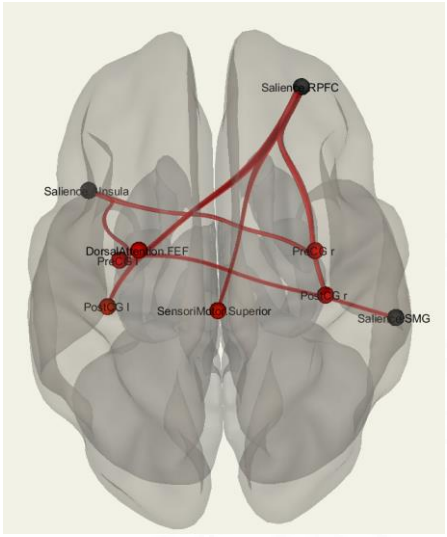
Patient > HC



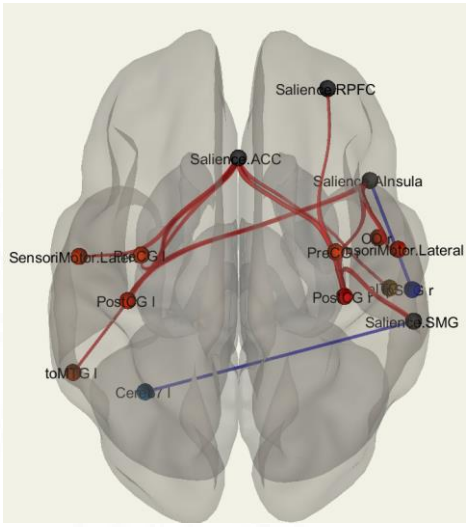
Post embolization > HC



Low NP patients > HC

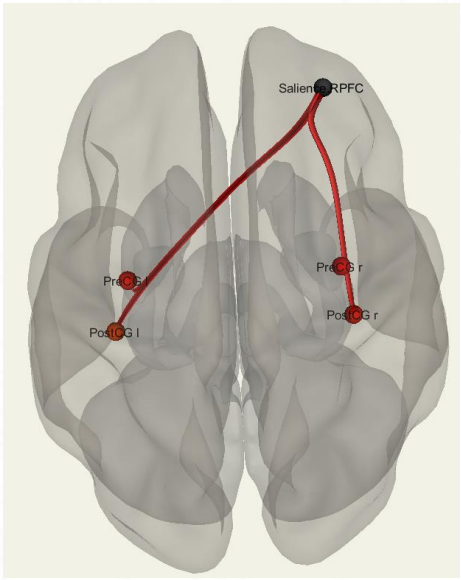


High NP patients > HC

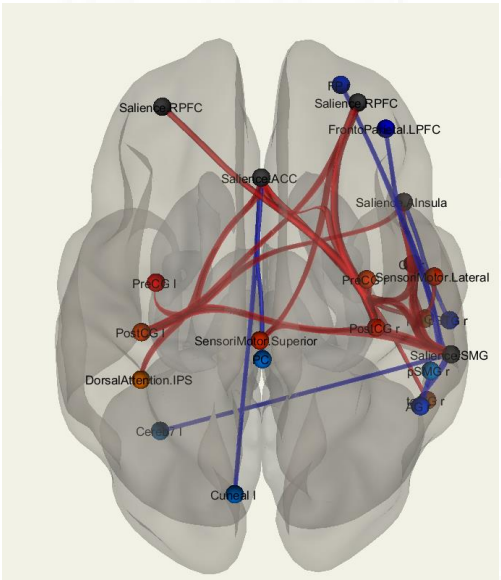


-

Cognitive decline presentation> HC



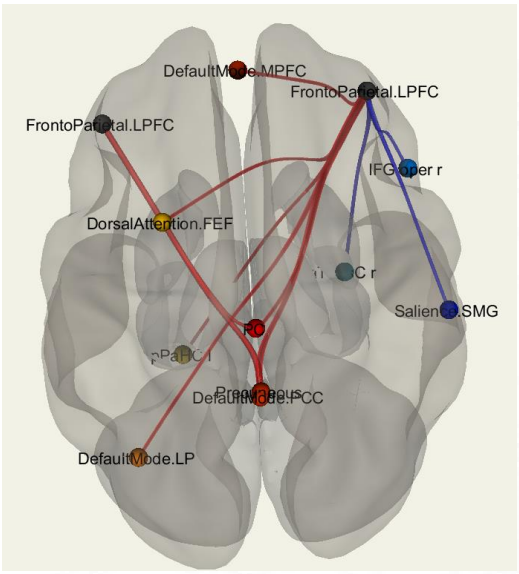
Non-cognitive presentation > HC



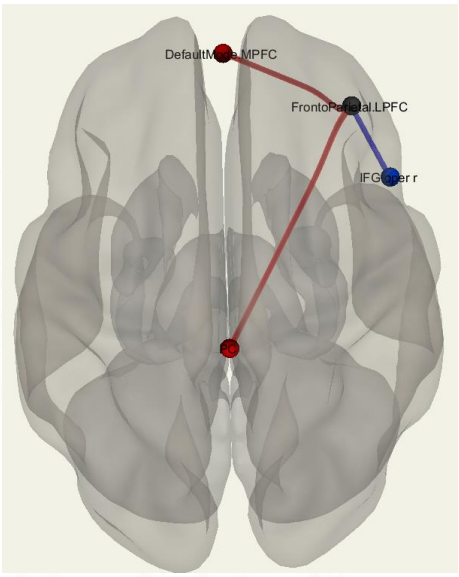
Salience network- ROI to ROI analysis: Salience network show an increase in functional connectivity at RPFC, which is more prominent in the cognitive decline presentation group. In the post embolization group, high NP score group, and non-cognitive decline group, the relative increase in functional connectivity at the anterior cingulate region.

3.Fronto-parietal network: ROI to ROI analysis (p-FDR corrected< 0.05)

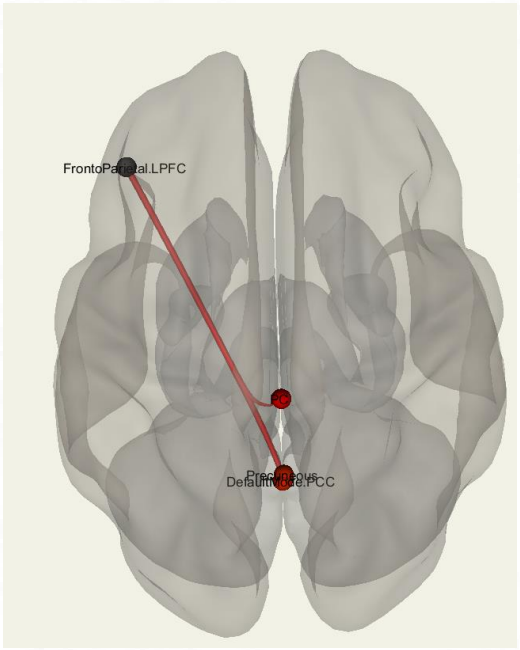
Patient > HC



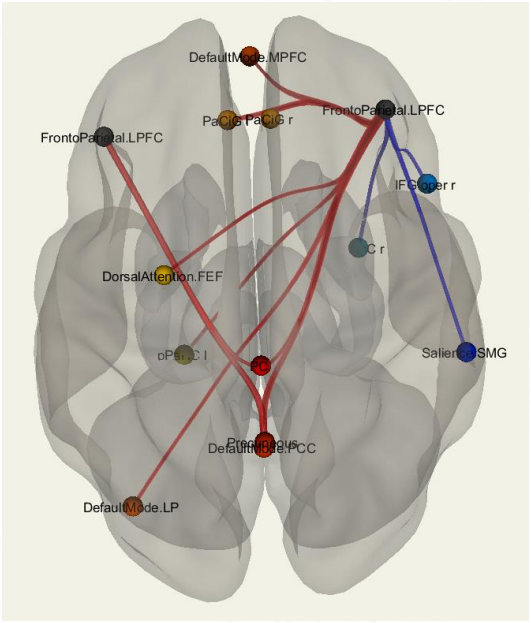
Low NP >HC



High NP patients > HC



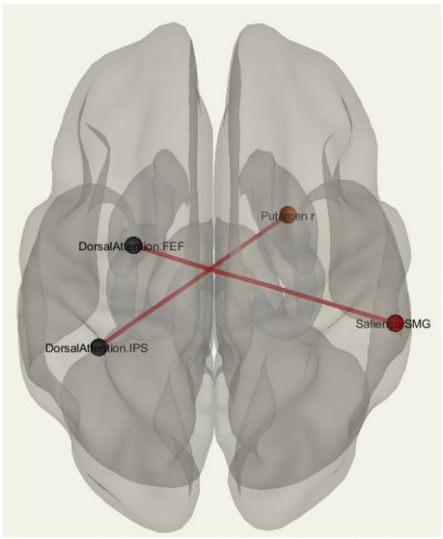
Non-cognitive presentation >HC



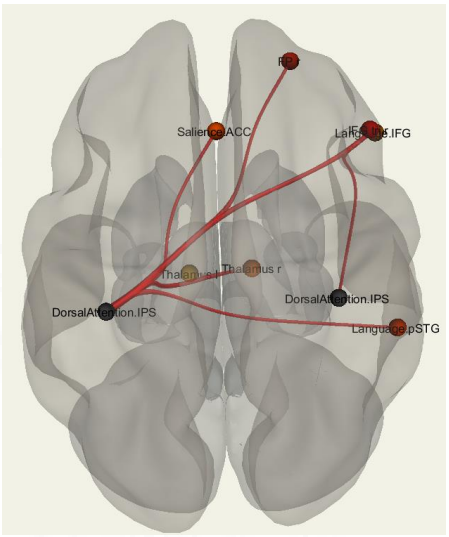
Fronto-parietal network- ROI to ROI analysis: Fronto-parietal network shows an increase in functional connectivity between right LPFC and PC-PCCC, MFPC. In the cognitive decline presentation group, this increase in functional connectivity is less prominent. In patients with high NP score and non-cognitive decline group, increase in functional connectivity between left LPFC and posterior cingulate seed region.

4.Dorsal attention network: ROI to ROI analysis (p-FDR corrected < 0.05)

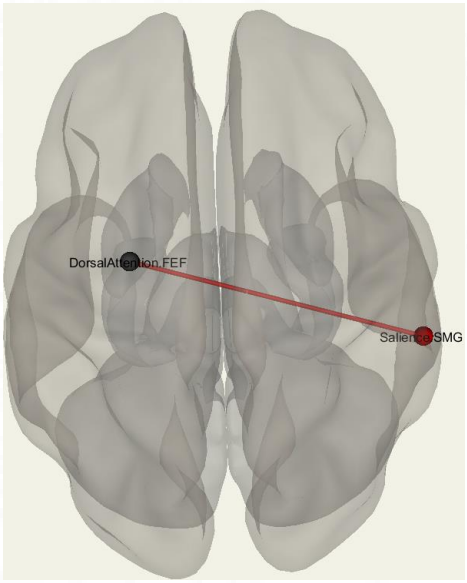
Patients > HC



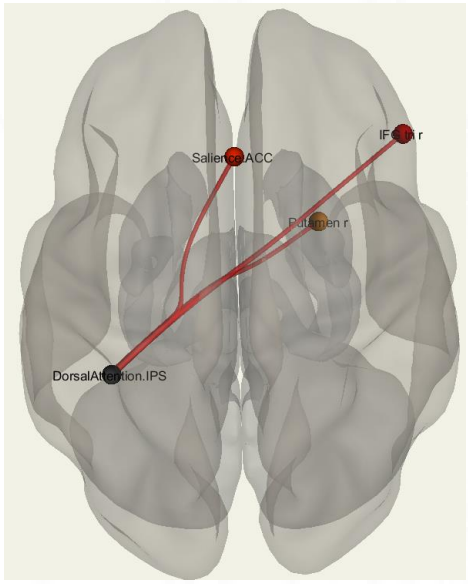
Post patients > HC



Low NP > HC



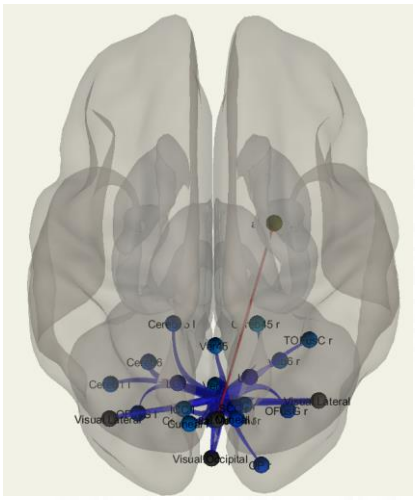
Non-cognitive presentation> HC



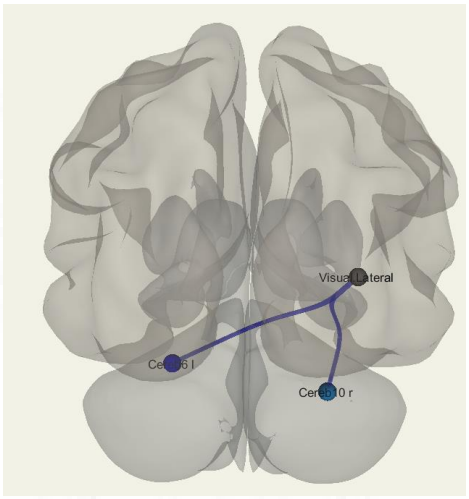
Dorsal attention network- ROI to ROI analysis: In the patient group, left IPS and left frontal eye field seed regions to show increased frontal connectivity. In post embolization, patient group and patient with non-cognitive decline presentation, more prominent functional connectivity.

5. Visual network: ROI to ROI analysis (p-FDR corrected <0.05)

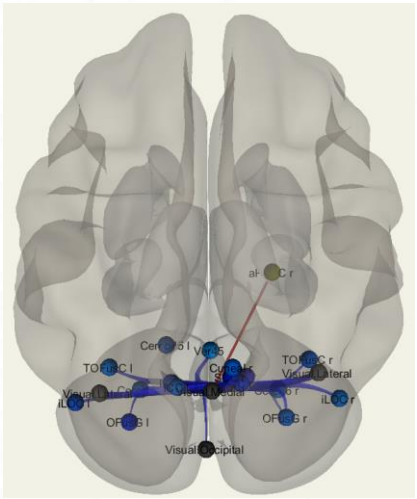
Patient > HC



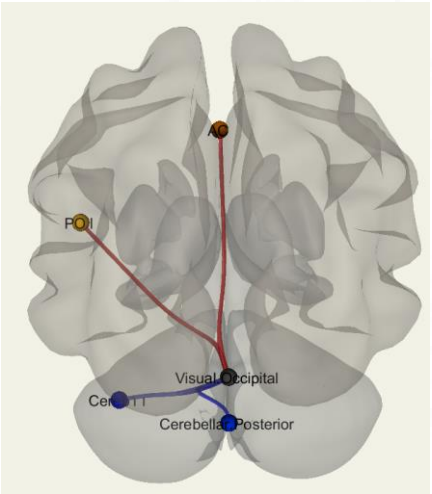
Post embolization > HC



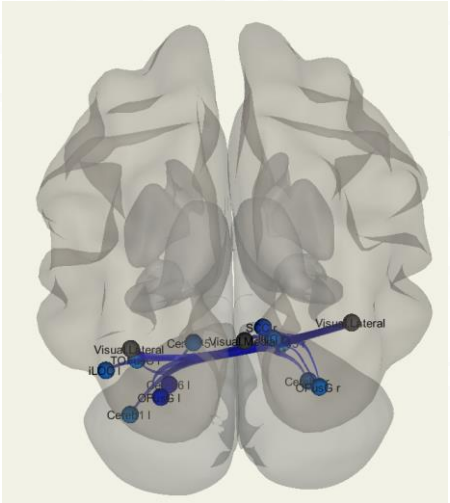
Low NP > HC



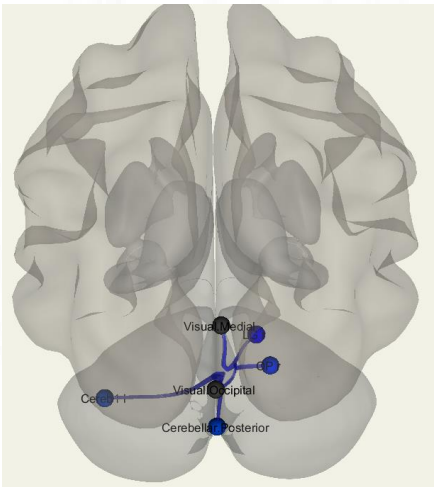
High NP > HC



Cognitive decline >HC



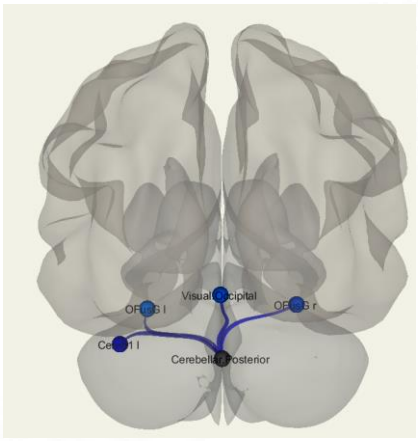
Non cognitive decline presentation> HC



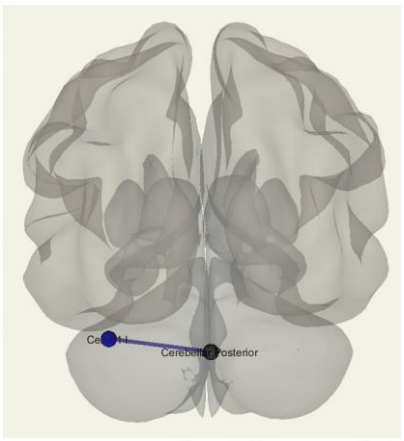
Visual network- ROI to ROI analysis: Visual network show global reduction in functional connectivity, which is more prominent in patients with low NP score, cognitive decline presentation group. Post embolization patient group, non-cognitive decline presentation group show a global reduction in occipital functional connectivity is less prominent.

6.Cerebellar network: ROI to ROI analysis (p-FDR corrected <0.05)

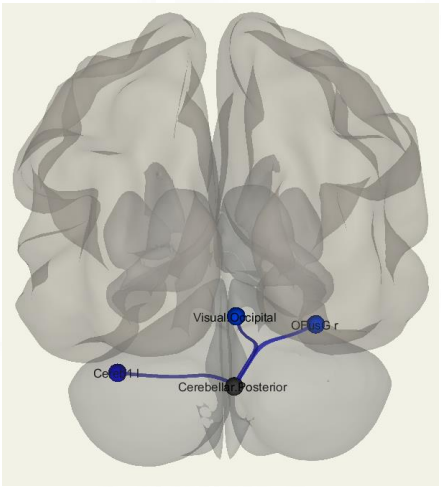
Patient > HC



High NP > HC



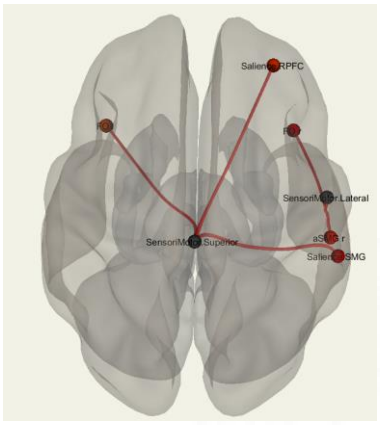
Non-cognitive decline >HC



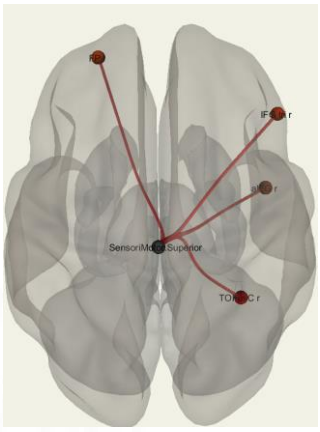
Cerebellar network- ROI to ROI analysis: Posterior cerebellum show decreased functional connectivity with the bilateral occipital and fusiform region in the patient group. Post embolization patient group show complete resolution of decrease in functional connectivity with bilateral occipital region

7.Sensori-motor network (p-FDR corrected <0.05)

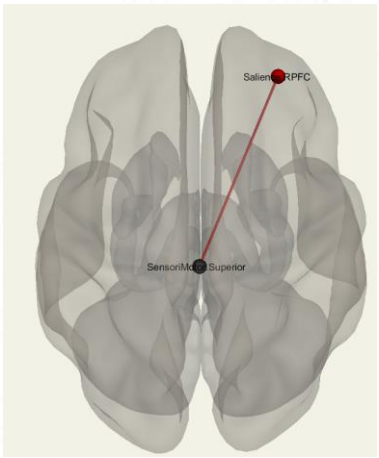
Patient > HC



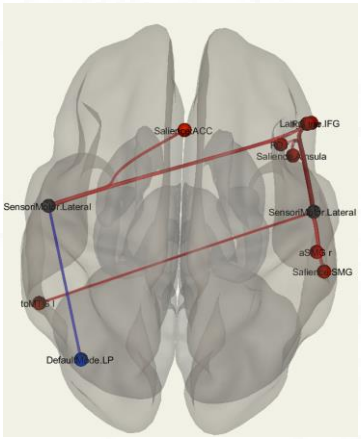
Post patients > HC



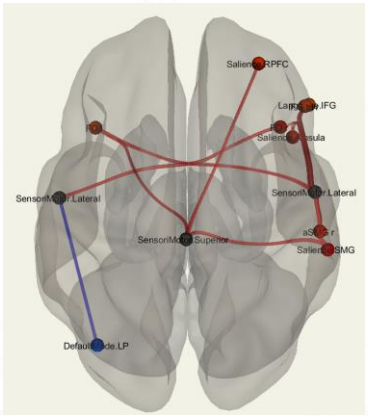
Low NP > HC



High NP > HC



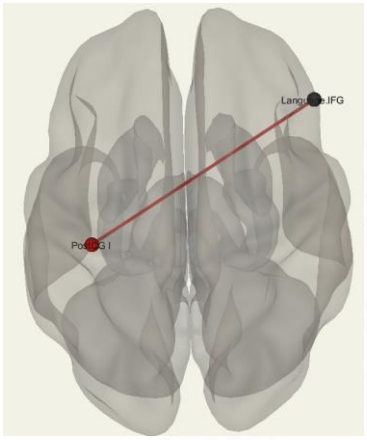
Non-cognitive > HC



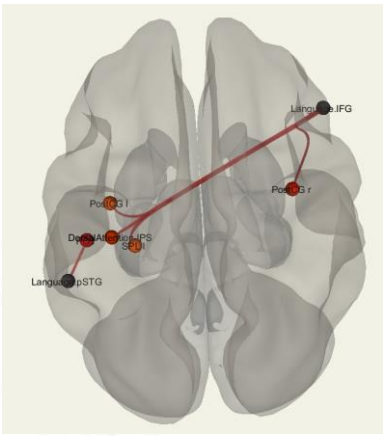
Sensori-motor network- ROI to ROI analysis: Increased connectivity at salience network seed points such as - right insula, right RPFC and right supramarginal gyrus. Salience, language network functional connectivity results suggest, sensorimotor network act as final compensatory out-put for salience network, i.e., increase the motor attention. This altered functional connectivity is less prominent in patients with cognitive decline presentation and patients with low neuropsychology score

8. Language network: ROI to ROI analysis (p-FDR corrected <0.05)

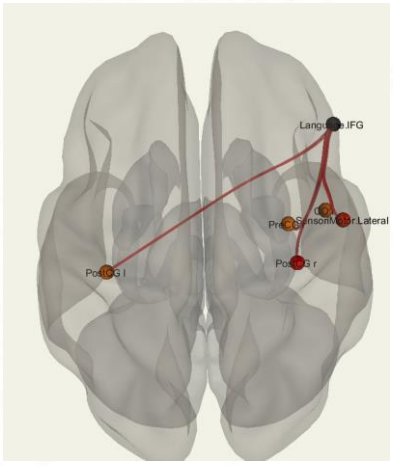
Patient > HC



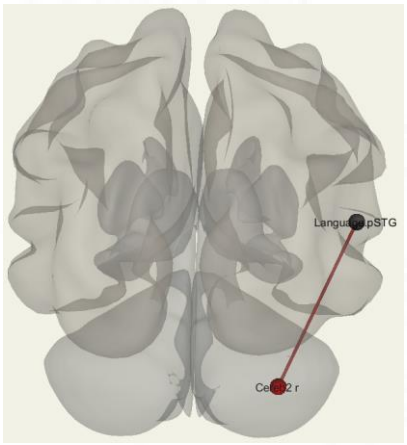
Post patients > HC



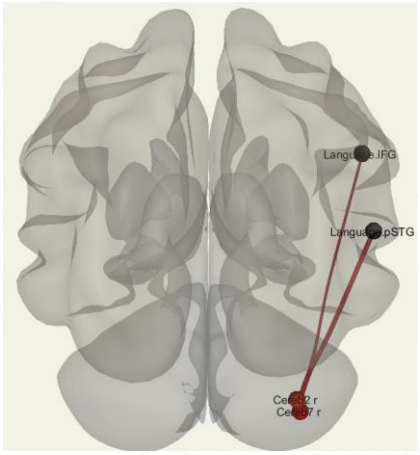
High NP > HC



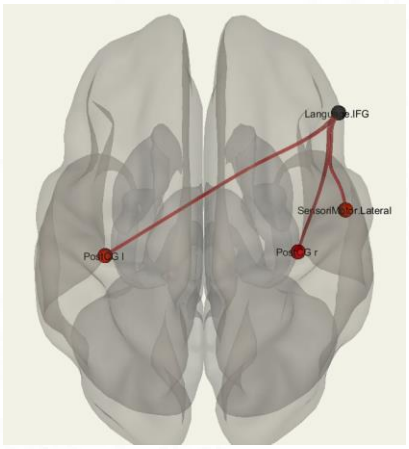
Low NP> HC



Cognitive decline>HC



Non-cognitive decline >HC



Language network-ROI to ROI analysis: Increased functional connectivity between right inferior frontal gyrus (IFG)and bilateral pre, and postcentral gyrus suggests that right inferior frontal gyrus act as intermediate in salience's network modulating activity over primary and SMAs**.** An increase in functional connectivity between right IFG with bilateral pre and postcentral gyrus was absent in patients

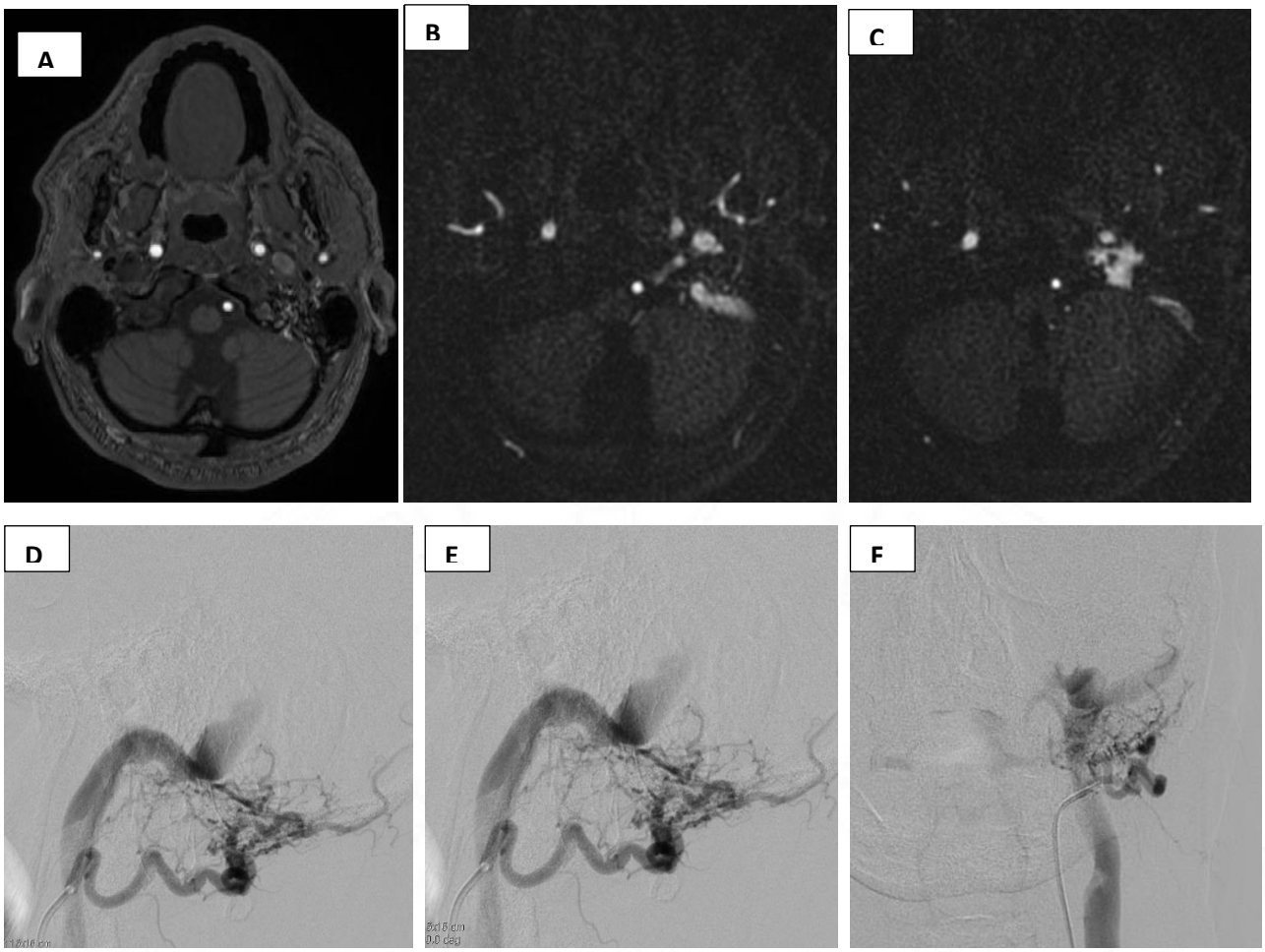
with cognitive decline presentation, and patients with low neuropsychology score with increased posterior cerebellar connectivity

3.Summary of connectivity changes in resting-state networks- ROI to ROI analysis: All seed regions from each resting-state network, as provided by the CONN toolbox, were used as seed areas and estimated the ROI-to-ROI functional connectivity (bivariate correlation measure) between seed and a set of 164 ROIs defining the Brodmann areas. Then, individual correlation maps were generated for each of these 8 networks.

RSN	Pt> HC	Pt post >HC	L NP >HC	H NP >HC	Cog >NC	Non.cog>HC
DMN	↑Rt-LPFC (CBM &PCC ↓ MPFC (Amygdala)	↑ PCC (FP and CBM)	↑ Rt LPFC (CBM) ↓MPFC (Amygdala)	↑ CBM ↑ Frontal (No PC-PCC changes)	↓ MPFC (amygdala)	↑ Rt LPFC (CBM ,PCC FG) ↑ PCC (Lt FP and CBM)
Salience network (ACC)	↓ ACC-PCC ↑ RPFC (B/L pre and Pt CG)	↑ ACC ↑ Rt RPFC	↑ RPFC	↑ ACC ↑RPFC	↑ RPFC	↓ ACC-PCC ↑ RPFC ↑ ACC
Dorsal attention (Left IPS)	↑ Lt IPS and FEF	↑ Lt IPS	↑ Lt FEF	-	-	↑ Lt IPS
Fronto-parietal (Rt LPFC)	↑ LPFC(Rt) ↑ LPFC(Lt)	-	↑ PC-PCC	↑LPFC (left)		↑ LPFC(Rt) ↑ LPFC(Lt)
Visual (Rt Lat Occ)	↓ B/L Occ +FG	↓Visual lateral (Less prom)	↓ B/L Occ (More prom)	↓Visual occ (↑ ACC)	↓ B/L Occ (More prom)	↓ B/L Occ (Less prom)
Cerebellar (Post cerebellar)	↓ Post CBM	-	-	↓Post.CBM	-	↓Post CBM
Language (Right IFG)	↑PtCG(Left)	↑ PtCG(Left) DAN(IPS)	↑ CBM	↑ B/L PtCG	↑ CBM	↑ B/L Pre and Pt CG
Sensori-motor (Sensori-motor Superior)	↑ B/L FO, Rt RPFC, Rt SMG	↑ Rt IFG Lt FP	↑ Rt RPFC	↑ Rt SMG, ACC, Insula	-	↑ Rt insula, SMG, RPFC, B/L FO

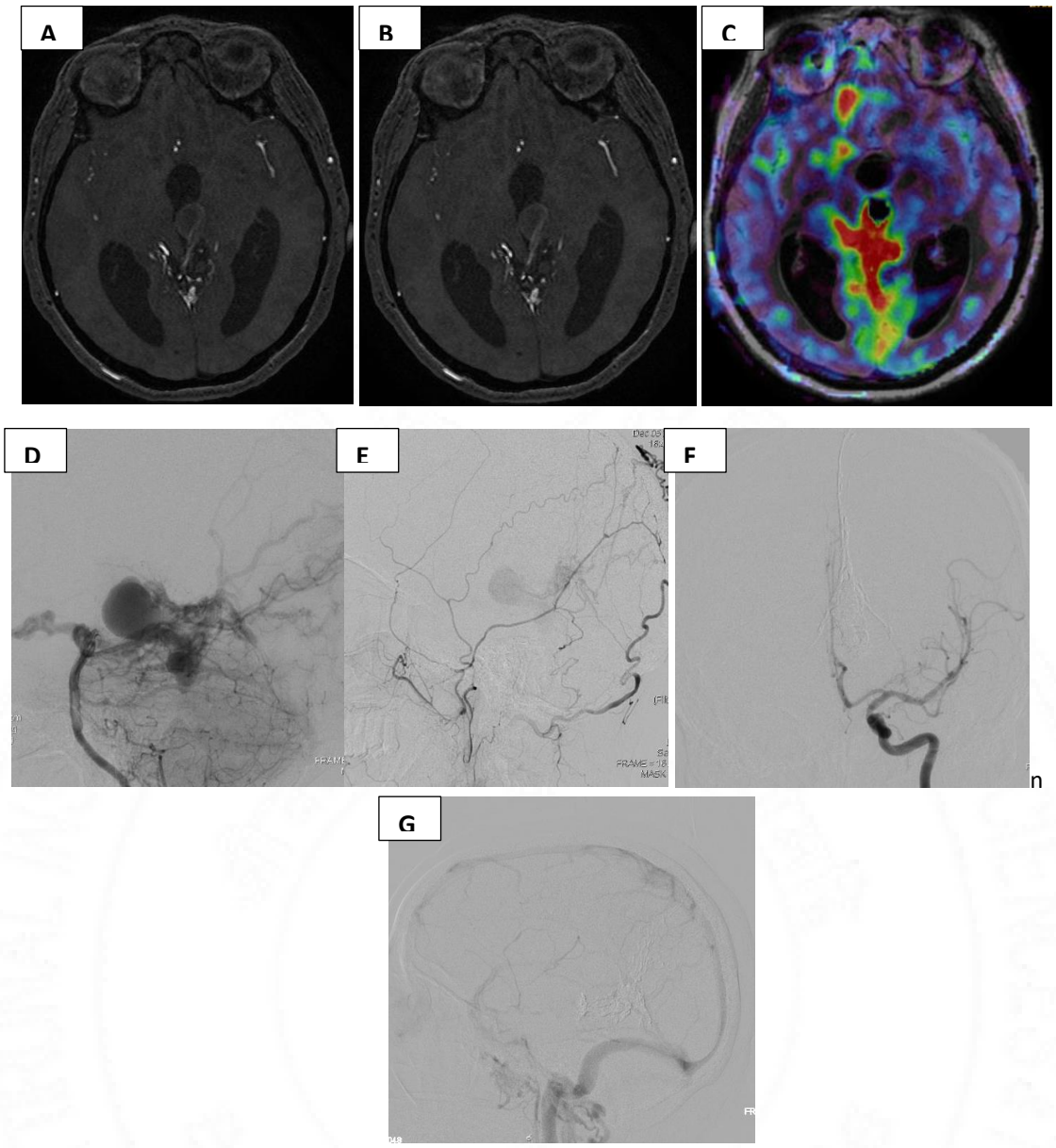
Abbreviations: LPFC-Lateral pre-frontal cortex, CBM-Cerebellum, PCC-Posterior cingulate, MPFC- Medial pre-frontal cortex, FG-Fusiform gyrus, ACC-Anterior cingulate, RPFC- Rostral pre-frontal cortex, prom-Prominent, PCG-Precentral gyrus, PtCG-Post central gyrus, IPS-Intra-parietal sulcus, FO- Frontal opercular, Post.CBM-Posterior cerebellum, SMG-Supra-marginal gyrus

Case illustrations: Case 1



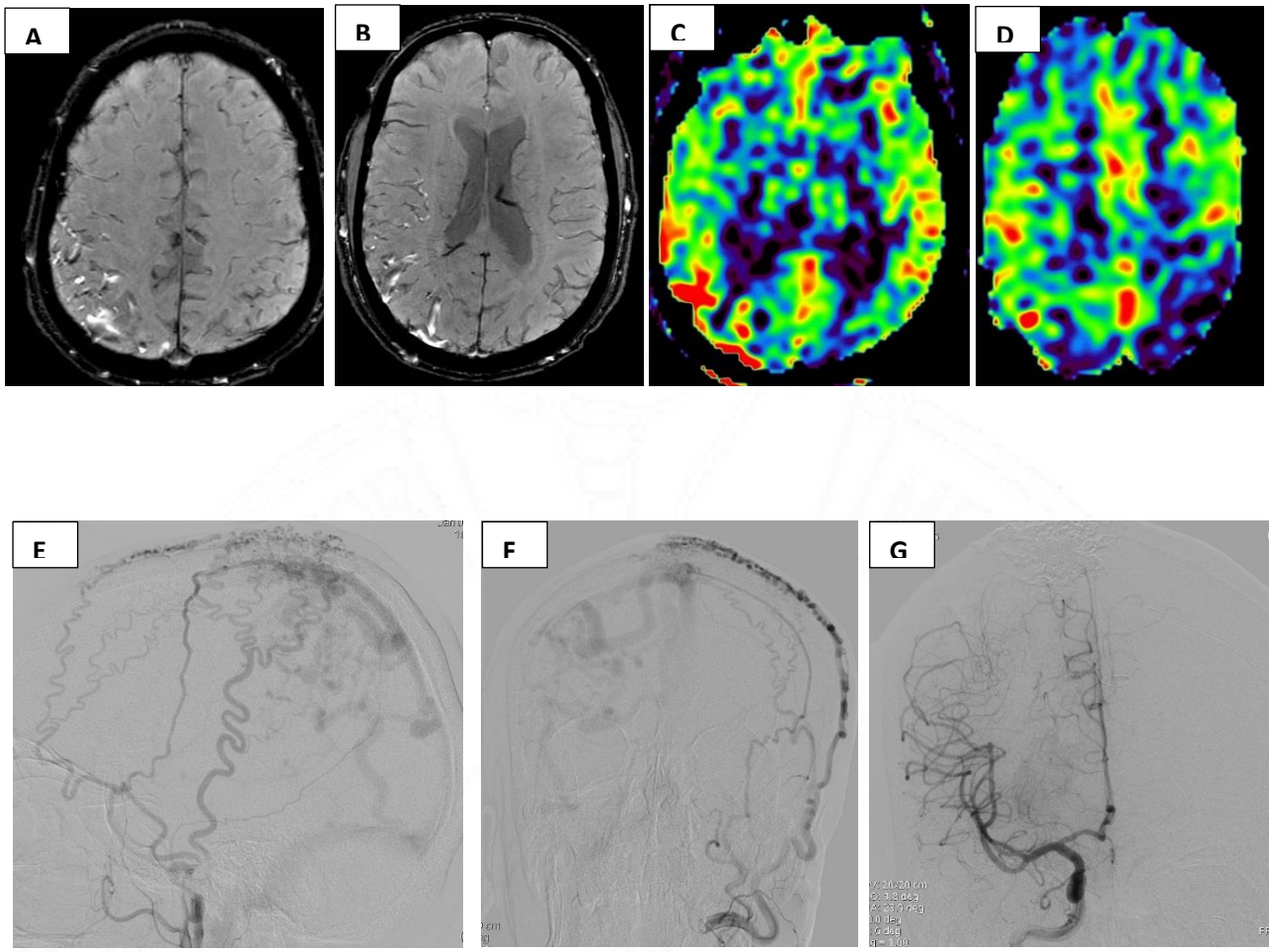
Case 1. Figure 1: 61-year-old Male, presented with complaints of headache and left sided tinnitus for 12 months. Baseline neuropsychological evaluation showed MMSE score of 30 & ACE score of 88, suggestive of no obvious cognitive impairment. **1st row: MRI images show (A- TOF MRA, B& C silent MRA) dural AV** fistula noted at the left sigmoid sinus-jugular fossa region with arterial feeders from occipital artery.2nd row: DSA images (D, E-Lateral angiogram and F- Frontal angiogram) show Cognard type 1 dural AVF at the left sigmoid-sinus jugular bulb region with arterial feeders from left occipital artery. No obvious retrograde drainage or cortical venous reflux. Patient is kept on conservative management in view of benign DAVF.

Case illustrations: Case 2



Case 2. Figure 1: 63-year-old female, presented with sub-acute onset of memory disturbances and headache for 2 months. Baseline neuropsychological evaluation showed MMSE score of 19 & ACE score of 37, suggestive of cognitive decline. **1st row: MRI images show (A, B-TOF MRA, C -ASL image) dural AV** fistula noted at the midline tentorial region with venous ASL signal along the straight sinus. 2nd and 3rd row: DSA images (D, E-Vertebral and ECA lateral angiogram and F, G- post embolization Frontal and lateral angiogram) show Cognard type 4 dural AVF at the midline tentorial region with arterial feeders from occipital artery and dural branches of PCA. Patient underwent onyx embolization with complete obliteration. Follow-up one-month NP scores are MMSE-27 & ACE score of 82, suggestive of cognitive improvement

Case illustrations: Case 3



Case 3. Figure 1: 44-year-old male, presented with 2 episodes of seizure over 2-month duration. Baseline neuropsychological evaluation showed MMSE score of 24 & ACE score of 76, suggestive of subclinical cognitive decline. **1st row: MRI images show (A, B- SWI, C, D - ASL image) pseudophelbitic pattern over right fronto-parietal convexity with** venous ASL signal along the superior sagittal sinus. 2nd row: DSA images (E, F- ECA lateral and frontal angiogram and G- post embolization Frontal angiogram) show Cognard type 2B dural AVF at the superior sagittal sinus region with arterial feeders from middle meningeal artery. Patient underwent onyx embolization with complete obliteration. Follow-up one-month NP scores are MMSE-30 & ACE score of 84, suggestive of cognitive improvement

DISCUSSION

Discussion:

Clinical presentation of intracranial dural arteriovenous fistula can vary from with benign to aggressive symptoms. Benign symptoms are headache, tinnitus, proptosis, chemosis, visual blurring secondary to raised ICA features. Aggressive symptoms include hemorrhage, non-hemorrhagic neurological features, including the focal neurological deficit, TIA, seizure, and dementia. Rarely perimedullary venous drainage leading to isolated congestive myelopathy as the initial manifestation of the dural arteriovenous fistula also has been described(1,25,26,76). The incidence of overall aggressive symptoms (including hemorrhagic and non-hemorrhagic) in this series is about 54.4%, similar to the reported incidence of aggressive symptoms in intermediate to higher grade fistula by Cognard et al. (77,78). Intracranial dural arteriovenous fistula presenting as the cognitive decline is a well-known entity. Incidence of the cognitive decline reported in literature ranging from 4 % to 12%. The Maximum reported incidence of cognitive decline presentation is about 21.4% from one of the earliest reports(79).

In our patient group, the cognitive decline presentation of the DAVF is about 30.3%, the highest of all reported incidences. If we consider sub-clinical cognitive decline cases revealed by neuropsychological evaluation (21.2%), the overall incidence of cognitive decline reaches up to 51.5 %. This really point to the need of early neuropsychological testing, especially in aggressive fistulas, to detect and treat these patients appropriately. Relative higher incidence in our group could be related to the following reasons, (i). Our study group predominantly contains aggressive dural fistula (Cognard grade II B to V or Borden grade II and III) about 87.9%, and benign fistula (Cognard grade I, IIA, or Borden grade I) contributes about 12.1%. (ii). Our center is one of the largest comprehensive neurovascular tertiary care treatment centers in South India, and higher incidence could be related to a referral bias of aggressive fistulas (iii). Others might be geographical and patient-related factors

Most of the classification systems of DAVF, including Cognard, Borden system based on the assessment of hemodynamic patterns, and there has always been attention towards the haemorrhagic neurological manifestations(43). Except for a few case series, no prior longitudinal studies have evaluated cognitive decline in dural arteriovenous fistula as a separate entity(31,33,42,77,80).

Risk factors for cognitive decline described are multisite dural arteriovenous fistula, fistula located at tentorium, and superior sagittal sinus. Imaging features described in dementia

associated with DAVF are diffuse white matter hyperintensity secondary to venous congestion, medullary vein dilatation, thalamic and brainstem edema (in thalamic dementia). Additional nuclear imaging features described are hypoperfusion of frontal and temporal lobes in SPECT studies. Most of these imaging features correlate to already manifested cognitive decline. No characteristic imaging predictor has been described until now, although cortical venous reflux is described as one of the risk factors for developing cognitive decline(34,36,39).

Further, cognitive decline in dural arteriovenous fistula results from reversible to irreversible structural changes. Cognitive decline showed immediate complete recovery in 33%, 55% recovered over time, and 6% patient showed progressive dysfunction(8). Kai et al., in 2009, reported reversibility of cerebrovascular reactivity on acetazolamide in SPECT study suggests in reversible cognitive disorder on treatment. The group without significant improvement showed loss of cerebrovascular reactivity on acetazolamide challenge and showed areas of hypoperfusion on the baseline and irreversible dementia associated with DAVF(28)

Resting-state fMRI is an investigational research tool by assessing connectivity changes, has been extensively testified in many of the neurodegenerative and neuropsychiatric disorders. Most of the studies show promising results about the identification of the neuro-cognitive disease process at a very earlier stage itself(12).

The current study has evaluated the feasibility of resting-state functional MRI in correlation with the neuropsychological changes in intra-cranial DAVF. The study provides valuable insight into the functional connectivity changes associated with intracranial DAVF and functional connectivity changes that are responsible for cognitive decline in such patients. To the best of our knowledge, no study to date, has evaluated the role of resting-state functional MRI in intracranial DAVF.

The patient group was selected from the interventional neuroradiology clinic at SCTIMST. Consecutive patients who were diagnosed to have intracranial DAVF on CT or MRI and confirmed on digital subtraction angiogram were selected for inclusion in the study. We stratified the patient group based on their clinical presentation and their neuropsychology score as two paired groups (i). Patients with cognitive decline presentation and non-cognitive decline presentation (ii). Patients with low neuropsychological performance and high neuropsychological performance group.

Further, we assessed the patient's post embolization rsfMRI and neuropsych scores at one-month follow-up to look for change in the status of functional connectivity and neuropsychology.

An equal number of healthy controls included in the study were comparable with the patients in terms of age and gender.

All the resting-state functional connectivity changes compared with age-matched healthy controls.

1. Although stratified patient groups didn't have an equal number, the comparison made at the whole control group because external comparison should be homogenous for meaningful interpretation.

2. A comparison of functional connectivity changes assessed in the CONN toolbox, based on a statistical test with mean low-frequency BOLD fluctuations in each group, will overcome this hindrance.

3. Another fact is a comparison of functional connectivity changes made with a wide range of standard healthy control resting-state connectivity, and the final result suggests *most specific connectivity changes* and results may be more reproducible.

1.Default mode network (DMN):

Resting-state functional connectivity analysis from group-ICA analysis, seed to voxel analysis (PCC as seed), and ROI to ROI analysis suggests, decreased connectivity at the pre-cuneus and posterior cingulate region is the primary core change. There is also reduced connectivity between the medial prefrontal cortex (MPFC) of DMN and PCC, suggests reduced anteroposterior connectivity. This reduced connectivity follows a particular trend, i.e., more reduced connectivity in patients with low neuropsychology score and patients with cognitive decline as presentation. There is also reduced connectivity between MPFC and its sub-cortical medial temporal sub-unit amygdala (81)

Possible compensatory mechanisms to overcome this reduced connectivity are (i). increased DMN -right posterior cerebellar connectivity (ii). Increased connectivity between PCC of DMN and bilateral Lateral prefrontal cortex (LPFC) of the frontoparietal network (iii). Decreased connectivity between the left lateral parietal region of DMN and postcentral gyrus (iv). Decreased connectivity between PCC of DMN and Intra-parietal sulcus of dorsal attention

network, right supra-marginal, and fronto-opercular seed regions of the salience network. These 'compensatory' mechanisms are seen to be minimal to absent in patients with low neuropsychology score and patients with cognitive decline.

In post embolization, follow-up patient group, reduction in functional connectivity at pre-cuneus- the posterior cingulate region is improved, and fewer residual compensatory connectivity changes (increased connectivity with cerebellum) as compared to HC, suggests normalization towards the base-line. In comparison patients before and after did not show any statistically significant difference at p-FEW 0.001 and p-FDR 0.05 within one month, even when there was significant improvement in their neuropsychological scores. This finding suggests that functional connectivity changes may take more time to reach baseline and to become statistically significant, which needs to be addressed in future follow up studies. Deficient functional connectivity at PCC in our patient group may be responsible for cognitive decline, similar to what is described in Alzheimer's disease pathogenesis(9).

2. Salience network(SN):

Resting-state functional connectivity analysis from group-ICA analysis, seed to voxel analysis (ACC as seed) and ROI to ROI analysis suggests, decreased connectivity at the dorsal anterior cingulate region and right anterior insula of salience network is the primary core change. Decreased connectivity clusters at the dorsal anterior cingulate region follow the particular trend that cluster size is more (i.e., more reduced connectivity) in patients group presented with cognitive decline and patient group with low neuropsychology score as compared to patient group with high neuropsychology score and non-cognitive decline.

The possible compensatory mechanisms to overcome reduced connectivity at anterior cingulate are (i). the increased bilateral rostral pre-frontal cortex (RPFC) -bilateral pre and postcentral gyrus, superior sensorimotor connectivity (ii). Increased ACC to bilateral pre, postcentral gyrus, and superior sensorimotor connectivity (iii). They possibly show increased functional connectivity of left insula and supra-marginal seeds of SN to dorsal attention network-frontal eye field to increase attention (iv). Decreased connectivity with PCC of DMN v) Increased functional connectivity with medial temporal sub-unit of left amygdala vi) increased connectivity with the posterior cerebellum.

Usually, this increase in connectivity between ACC and primary and supplementary motor areas occurs during conflict processing. Increased resting-state functional connectivity between the dorsal ACC, RPFC of the salience network, and the primary and SMAs support the

hypothesis that the salience network directs attention by modulating activity in diverse cortical regions(82). The same findings also explain the deactivation of the posterior cingulate seed region of the DMN, as task de-activation(83).

No statistical difference in connectivity changes were noted between pre and post embolization patient groups. However, in the post embolization group, as compared to HC, the reduced connectivity cluster is at dorsal ACC is less prominent to absent and there is residual increased connectivity cluster at the rostral prefrontal cortex and bilateral postcentral gyrus and dorsal attention network.

'Compensatory mechanisms' acting at both DMN and SN seed points suggest the functional connectivity offers a flexible and powerful way to evaluate the functional integration of various brain regions involved in cognitive processing(12).

3.Fronto-parietal network:

Resting-state functional connectivity analysis from group-ICA analysis, seed to voxel analysis (right LPFC as seed), and ROI to ROI analysis suggests, increased connectivity at the pre-cuneus and posterior cingulate region is primary core change, suggests frontoparietal network primarily acting as a 'compensatory' network for DMN. Further FPCNa predominantly noted around the LPFC, show more vital connectivity with DMN in mento-cognitive awareness(68). A decrease in functional connectivity between right opercular and supra-marginal gyrus seed regions of SN, suggests anti-correlation with salience network.

An increase in functional connectivity with posterior cingulate and left lateral parietal seed points of DMN were absent in patients with cognitive decline presentation and with low neuropsychology scores, suggests that this 'compensatory failure' may result in cognitive worsening.

4.Dorsal attention network (DAN):

Resting-state functional connectivity analysis from group-ICA analysis, seed to voxel analysis (left intra-parietal sulcus used as seed) and ROI to ROI analysis suggests, increased connectivity at the bilateral rostral pre-frontal region and right supramarginal gyrus is primary core change, suggests dorsal attention network primarily acting as a 'compensatory' network for salience network. Seed to voxel analysis revealed increased connectivity of left IPS with at ACC, right insular region further suggests DAN acting as a 'compensatory network', to increase attention to external stimuli.

An increase in functional connectivity with posterior cingulate and left lateral parietal seed points of DMN were absent in patients with cognitive decline presentation, and with low neuropsychology scores, suggesting again the 'compensatory failure' resulting in cognitive decline.

5.Visual network (VN):

Functional connectivity analysis from group-ICA analysis, seed to voxel analysis (right lateral occipital used as seed) and ROI to ROI analysis suggests, global decreased connectivity at bilateral posterior fusiform region, bilateral medial and lateral visual regions is the primary core change.

Decreased connectivity clusters at the visual network follow the particular trend that decreases in connectivity cluster more concentrated over the bilateral posterior fusiform region in patients group presented with cognitive decline and with low neuropsychology score as compared to the lateral occipital region in the group of patients with high neuropsychology score and non-cognitive decline. This finding suggests the role of posterior fusiform gyrus in visual cognition(72). The decrease in connectivity cluster is less prominent in patients with high neuropsychology score and non-cognitive decline group.

'Compensatory' mechanisms to overcome reduced connectivity in pan-visual networks are (i) increased functional connectivity with ACC (ii). decreased connectivity with the posterior cerebellar region. These 'compensatory' mechanisms are minimal to absent in patients with low neuropsychology score and patients with cognitive decline.

No statistical difference in connectivity changes between pre and post embolization patient groups were noted. However, in the post embolization group as compared to HC, the pan visual reduced connectivity cluster is less prominent to absent and with residual decreased connectivity with the posterior cerebellar region.

6. Cerebellar network:

Functional connectivity analysis from group-ICA analysis, seed to voxel analysis (posterior cerebellar region used as seed) and ROI to ROI analysis suggests, decreased connectivity at left

lateral visual regions and bilateral fusiform gyrus is the primary core change, suggests it act again as a possible compensatory network for the visual network. This decrease in functional connectivity with lateral visual and fusiform gyrus was absent in patients with cognitive decline presentation suggests the possibility of this compensatory failure results in cognitive worsening.

7. Language network:

Functional connectivity analysis from group-ICA analysis, seed to voxel analysis (right inferior frontal gyrus used as seed) and ROI to ROI analysis suggests, increased connectivity at anterior cingulate and right supramarginal gyrus is the primary core change, suggesting language network primarily acting as a possible compensatory network for salience network. There is also decreased connectivity between bilateral anterior fusiform gyrus and occipital regions, which may be related to anti-correlation for DMN connection with anterior fusiform gyrus.

Seed to voxel and ROI to ROI analysis suggests increased functional connectivity between right inferior frontal gyrus (IFG)and bilateral pre, and postcentral gyrus suggests that right inferior frontal gyrus possibly acts as intermediate in salience's network modulating activity over primary sensory motor areas and SMAs.

An increase in functional connectivity between right IFG with bilateral pre and postcentral gyrus was absent in patients with cognitive decline presentation, and patients with low neuropsychology score further suggest a compensatory failure in these patients.

8. Sensorimotor network:

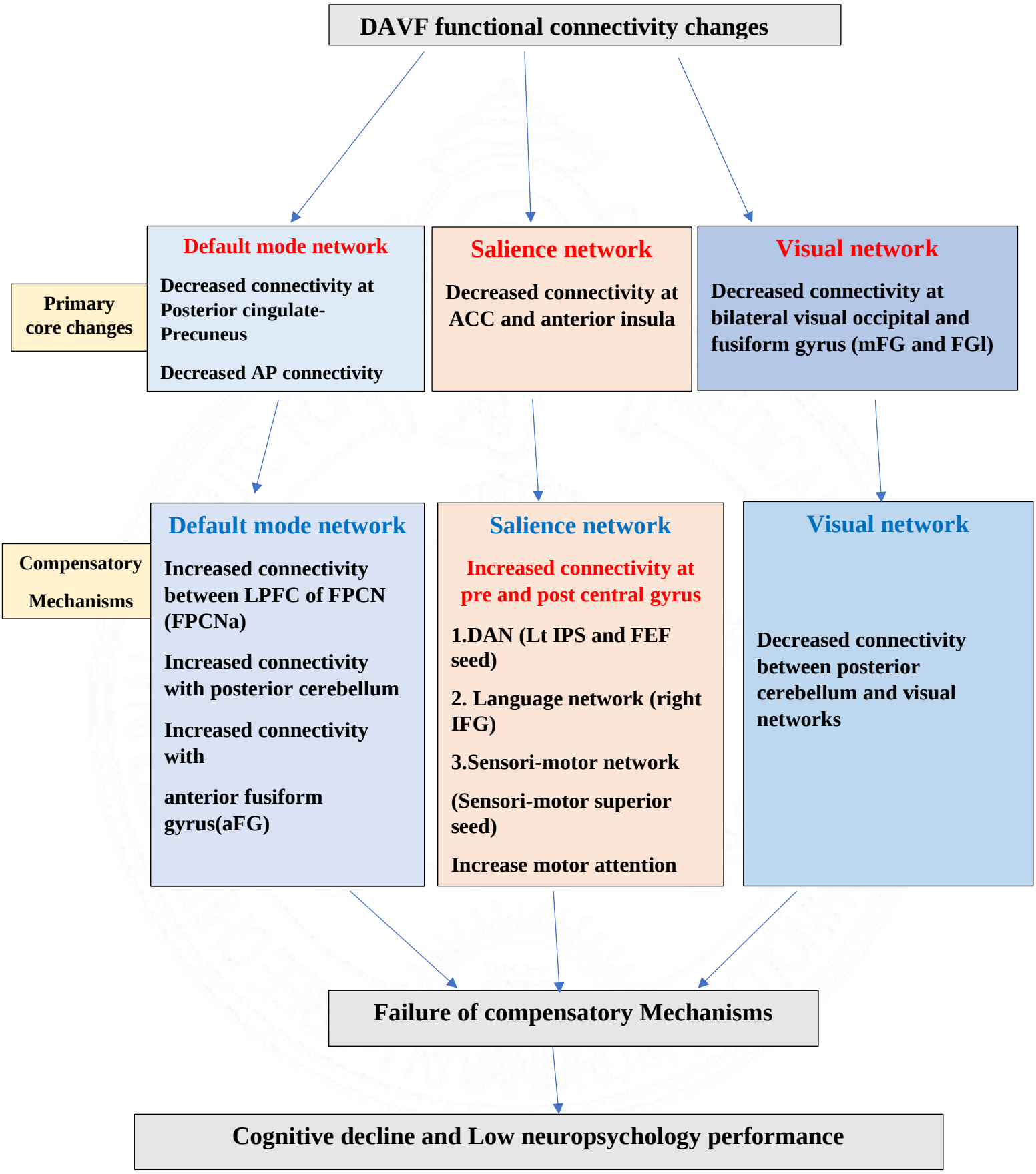
Functional connectivity analysis from group-ICA analysis, seed to voxel analysis (right inferior frontal gyrus used as seed) and ROI to ROI analysis suggests, increased connectivity at salience network seed points such as -ACC, right insula, right RPFC and right supramarginal gyrus and decreased connectivity with left insula and left supramarginal gyrus. Salience, language network functional connectivity results suggest, sensorimotor network act as final 'compensatory' out-put for salience network, i.e., increase the motor attention. This altered functional connectivity is less prominent in patients with cognitive decline presentation and patients with low neuropsychology score.

Overall, resting-state networks (RSNs) connectivity changes suggest that primary core functional areas affected in DAVF patients are the **posterior cingulate region of the default**

mode network, anterior cingulate, and anterior insular region of the salience network, bilateral visual network- lateral visual and fusiform regions.

To compensate for these immediate changes, secondary orchestration of the **task-negative** – frontoparietal control network (FPCNa), **task-positive** – dorsal attention, language, and sensorimotor network interplay with each other to maintain the activity of the default mode and salience network. Also, the cerebellar network appears to compensates for the visual network.

Loss of harmony of these compensatory networks may result in cognitive decline presentation along with low neuropsychology.


DAVF functional connectivity changes
Primary core changes
Default mode network
Decreased connectivity at Posterior cingulate-Precuneus
Decreased AP connectivity
Salience network
Decreased connectivity at ACC and anterior insula
Visual network
Decreased connectivity at bilateral visual occipital and fusiform gyrus (mFG and FGl)
Compensatory Mechanisms
Default mode network
Increased connectivity between LPFC of FPCN (FPCNa)
Increased connectivity with posterior cerebellum
Increased connectivity with
anterior fusiform gyrus(aFG)
Salience network
Increased connectivity at pre and post central gyrus
1.DAN (Lt IPS and FEF seed)
2. Language network (right IFG)
3.Sensori-motor network
(Sensori-motor superior seed)
Increase motor attention
Visual network
Decreased connectivity between posterior cerebellum and visual networks
Failure of compensatory Mechanisms
Cognitive decline and Low neuropsychology performance

Limitations of the study:

The present study has a few limitations.

1. Our study was carried out in a relatively limited number of subjects, especially benign intra-cranial dural arterio-venous fistulas. Further studies with large samples of benign DAVF are warranted to confirm the existence of the proposed mechanism of compensatory connectivity changes and the failure of which leading on to cognitive decline.

2. Not all patients underwent endovascular management at the time of completion of this study and a few patients were lost to follow-up. This might have affected the statistical inferences due to the reduced number in the post embolization arm.

3. Although our results follow the regular trend in connectivity changes, confounded connectivity differences secondary to absent arteriovenous pulsations in the post-embolization arm, resulting in neurovascular coupling differences and differential physiological noise, cannot be completely ruled out in studies like this. Cerebrovascular autoregulation, glial-vascular uncoupling predominantly affects graph metrics, which will be analysed in the subsequent studies on this.

4. There was no significant difference in functional connectivity between pre and post embolization group of patients on direct comparison suggesting that, such changes may take more time than the short one month follow up done in the present study. A continuation study to address this is already underway with long term follow up rsfMRI strategies.

5. Multi-band echo-planar resting-state fMRI might have resulted in a more significant number of data sampling points within a short time and possibly could have improved the statistically results. Future studies are envisaged on these lines.

SUMMARY AND CONCLUSIONS

Summary and conclusions:

The study examined the resting-state functional connectivity changes associated with intracranial dural arteriovenous fistula compared to healthy controls. The study is the first of its kind in patients with intracranial DAVF. Further, we have evaluated the functional connectivity changes associated with cognitive decline presentation and low neuropsychology scores performance in patient subgroups in this condition.

Our study revealed that significant resting-state functional connectivity changes at the default mode network, salience network, and visual networks is seen patients with DAVF. These primary functional connectivity changes noted in the patient group irrespective of their clinical presentation and neuropsychology scores, suggests that primary functional connectivity changes at default mode network, salience network, and visual network are noted even at the earlier stage of the disease.

A higher strength of functional connectivity changes at the DMN, salience network and visual networks correlate with disease severity, i.e., in patients with cognitive decline presentation and low neuropsychology scores, strength of connectivity changes were higher (more decreased functional connectivity) as compared to patients with the non-cognitive decline and high neuropsychology score performance.

In the default mode network (DMN), the reduced functional connectivity epicenter at the pre-cuneus -posterior cingulate region (PC-PCC) and with deficient anteroposterior connectivity between posterior cingulate and medial prefrontal cortex (MPFC) seed regions. Strength of reduced functional connectivity at these regions correlated with cognitive decline.

In the salience network (SN), the poor functional connectivity was noted at the anterior cingulate cortex (ACC) and anterior insular region (AI). Further, in the salience network also, the strength of poor functional connectivity at these regions correlated with cognitive decline.

In a visual network (VN), the deficient functional connectivity was noted at lateral visual occipital regions and bilateral posterior parts of the fusiform gyrus. In visual networks also the strength of poor connectivity at fusiform gyrus and lateral visual regions correlated with cognitive decline.

Although deficient resting-state functional connectivity changes at DMN, Salience, and visual network started even at the earlier stage of the disease, few ‘compensatory’ resting-state connectivity changes might have helped to overcome these deficits of resting-state networks in

non- cognitive decline group of patients. Compensatory functional connectivity changes for deficient task-negative DMN predominantly occurs through the bilateral lateral pre-frontal cortex (LPFC) of the frontoparietal network (also called FPCN1), as discussed previously.

Deficient functional connectivity at the task-positive- salience network is possibly overcome by increased connectivity with bilateral pre and postcentral gyrus suggesting motor recruitment. This motor recruitment occurs through task-positive networks such as dorsal attention network (DAN), Language network (LN), and sensorimotor network (SMN).

Deficient functional connectivity changes at the visual network is overcome by decreased functional connectivity between the posterior cerebellum and visual networks.

Post embolization follow-up at one-month**,** deficient functional connectivity is less prominent and fewer residual compensatory connectivity changes suggests, that there will be reorganization of these network on treatment and which needs to be confirmed by long term follow up studies.

In conclusion, resting-state functional MRI in patients with intracranial dural arteriovenous fistula shows functional connectivity changes related to cognitive decline. When there is the failure of compensatory network changes (Fronto-parietal, Dorsal attention, Language, sensorimotor and cerebellar networks) or increase in primary network changes at default mode network, salience network, and visual network, the patient presents with cognitive decline. This finding might be of interest in patient selection for early embolization of DAVF to reverse or prevent cognitive decline in such patients.

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ANNEXURES

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Study Proforma for Patients with Dural AV fistula Patients

Hospital no.

Study ID:

Father/Mother/Spouse's name:

DOB, yrs:

Sex: M ☐ F ☐

Address H.No.:

Street/Locality:

Vill/Twn/City:

PIN: Rural ☐ Urban ☐

Telephone No.

Education, yrs:

Primary/Secondary ☐ 10thStd ☐ 12thStd ☐ Graduate ☐ Post-graduate ☐

Occupation:

Marital status: Unmarried ☐ Married ☐ Divorced ☐ Widowed ☐

Monthly income (Rs):

Religion:

Height: Weight:

Clinical history:

1. Presenting symptoms

2. Evolution: Onset, progress and number of episodes

3. Other relevant neurologic history

4. Other relevant history (Past history of significant other illness, family history, treatment history)

5. Clinical findings

Angiographic (DSA) findings:

1. Fistulous points: Number, location, classification(Cognard & Borden)

2. Cortical venous reflex

3. Pseudophelbitic pattern

Pre-treatment nneuropsychological evaluation:

1. Addenbrooke's Cognitive Examination- III for Attention, Memory, Verbal Fluency, Language and Visuospatial abilities.
2. Clinical Dementia Rating Scale
3. Weschler Memory Scale-III

Embolization details:

1. Complete/ partial embolization
2. Materials used
3. Duration from the pre-treatment neuropsychological, rs-fMRI evaluation

Post-treatment neuropsychological evaluation:

Pre-treatment rs-fMRI findings:

Post-treatment rs-fMRI findings:

} Group level analysis

Study Proforma for Healthy Subjects

Study ID:

Father/Mother/Spouse's name:

DOB, yrs:

Sex: M ☐ F ☐

Address H.No.:

Street/Locality:

Vill/Twn/City:

PIN: Rural ☐ Urban ☐

Telephone No.

Education, yrs:

Primary/Secondary ☐ 10th Std ☐ 12th Std ☐ Graduate ☐ Post-graduate ☐

Occupation:

Marital status: Unmarried ☐ Married ☐ Divorced ☐ Widowed ☐

Monthly income (Rs):

Religion:

Height: Weight:

Neuropsychological evaluation:

1. Addenbrooke's Cognitive Examination- III for Attention, Memory, Verbal Fluency, Language and Visuospatial abilities.
2. Clinical Dementia Rating Scale
3. Weschler Memory Scale-III

SREE CHITHRA THIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY – TRIVANDRUM

PATIENT INFORMATION SHEET AND STUDY CONSENT FORM FOR ADVANCED NEUROIMAGING FROM PATIENTS

Study title: "Role of resting state functional magnetic resonance imaging in patients with intracranial dural arteriovenous fistula"

Investigators:

Principal Investigator:	Dr. Sabarish S. S
Co-Principle investigator:	Dr. Bejoy Thomas
Co-investigator:	Dr. Santhosh kumar K
Co-investigator:	Dr Ramsekhar N. Menon

This consent form is meant to invite you for the participation in a research study conducting at Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST) on "Role of resting state functional magnetic resonance imaging in patients with intracranial dural arteriovenous fistula "

Purpose of the study

The study is conducted to explore the utility of resting state functional magnetic resonance imaging in intracranial dural arterio-venous fistula. It helps to understand the brain functional connectivity changes in individuals with dural arterio-venous fistula.

Kindly take time to read this information carefully and to decide whether you wish or not to participate. The Principal Investigator will help you by explaining all the procedures involved in the study to the patient and clear all his/her doubts regarding resting state fMRI within 10-15 minutes. If you have decided to participate, you will be asked to fill in, sign and date this information and consent form and to keep it as useful reference on study details and personal contacts.

Nature of the procedure

Resting state fMRI is an advanced imaging technique to understand how brain functions during a resting state in the brain. It uses certain frequency of waves and magnetic fields to image the brain. These particular tests will not be done in patients with cardiac pacemakers, stents or other metallic devices. You may feel nervous about being in a small space when you are in the Magnetic Resonance scanner; however you will be able to communicate with us throughout the scan and can tell us whenever you want the scan to be stopped or interrupted.

If you take part, what will you have to do?

On the day of the Magnetic Resonance Imaging (MRI) investigations, you will be accompanied to the MRI room, where the scan is performed. The scan uses a large magnet to obtain the scans and does not use radiation like X-rays. A scan session will take about half an hour. During the recording, you will be asked to lie on your back on a table with your head positioned in a padded headrest. Further, you will be requested to keep eye closed calmly, not to feel asleep. The principal investigator and the technicians will provide you with the necessary instructions and help during the recording.

The information that we obtain from this investigation will help us to better understand the nature of the functional abnormalities, in patients with intracranial dAVF. However, if we identify any clinically relevant information, it will be communicated to your treating physician for appropriate decision making. Your participation is entirely voluntary and decision will in no way influence your current treatment at SCTIMST. Absolute confidentiality of data shall be maintained. No expenses shall be incurred as a result of your participation in the study.

Can you withdraw from this study after it starts?

You have right to withdraw consent at any stage of study and this will not affect your usual treatment in this institute in any way.

Do you have to undergo any blood tests and invasive placing an intravenous cannula and / or administration of any medications or agents such as contrast media?

No need to undergo any blood tests, invasive placement of intravenous cannula, administration of medications or contrast media

Contact for Further Information:

In case if the subject wants more information about the study and the participant's right at any time of the research, you will be free to contact any one among the Research team. Please contact the Principal Investigator, Dr. Sabarish. S. S, Senior Resident**,** Dept of IS&IR (contact No: Ph: 9994270566, Mail ID: sabarish@sctimst.ac.in, Sabarish.ss.dr@gmail.com) or Co Principal Investigator, Dr Bejoy Thomas, Professor, Dept of IS&IR (contact No: Ph: 9447719481, Mail ID: bejoy@sctimst.ac.in)

We thank you very much for agreeing to participate in this study.

INFORMED CONSENT FORM

Participant's name: Date of Birth / Age (in years):

I_____
son/daughter of _____ (Please tick boxes)

- Declare that I have read the above information provided to me regarding the study: "Role of resting state fMRI in intracranial Dural AV fistula patients" and have clarified the doubts that I had [ ]
- I also understand that my participation in this study is entirely voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected [ ]
- I also understand that the neuroimaging is being done to explore the utility of resting state fMRI in functional connectivity changes of intracranial dAVF[ ]
- I understand that the results of the data obtained will not be disclosed to me, however, if some additional information, which will require modification of the treatment, is identified, that will be communicated to the treating physician for appropriate decision making [ ]
- I understand that no expenses will be incurred by me for participating in this study and my identity will not be revealed in any information released to third parties or published [ ]
- I voluntarily agree to take part in this study [ ]
- I received a copy of this signed consent form [ ]

Name:	Name of witness:
Signature:	Relation to participant:
Date:	Date:

(Person Obtaining Consent)

I attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged participant to ask questions and that all questions asked were answered.

_____ _____

Name and Signature of Principal Investigator with date

SREE CHITHRA THIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY – TRIVANDRUM

PATIENT INFORMATION SHEET AND STUDY CONSENT FORM FOR ADVANCED NEUROIMAGING FROM HEALTHY VOLUNTEERS

Study title: "Role of resting state functional magnetic resonance imaging in intracranial Dural arterio-venous fistula patients."

Investigators:

Principal Investigator:	Dr. Sabarish S. S
Co-Principle investigator:	Dr. Bejoy Thomas
Co-investigator:	Dr. Santhosh kumar K
Co-investigator:	Dr Ramsekhar N. Menon

This consent form is meant to invite you for participation in a research study conducting at Sree Chitra Tirunal Institute for Medical Sciences and Technology on "Role of resting state functional magnetic resonance imaging in patients with intracranial Dural AV fistula"

Purpose of the study

The study is conducted to explore the utility of resting state magnetic resonance imaging brain functional connectivity changes in dural arterio-venous fistula patients. It helps to understand the neuronal and biochemical bases of working memory deficits in individuals with MCI. We seek your consent to take part in this study for comparison as a person free of neurological illness.

Kindly take time to read this information carefully and to decide whether you wish or not to participate. The Principal Investigator will help you by explaining all the procedures involved in the study to the research participant and clear all his/her doubts regarding resting state fMRI within 10-15 minutes. If you have decided to participate, you will be asked to fill in, sign and date this information and consent form and to keep it as useful reference on study details and personal contacts.

Nature of procedure

Resting state fMRI is an advanced imaging technique to understand how brain functions and how the neurochemicals change during a task in the brain, which uses certain frequency of waves and magnetic fields to image the brain. It does not involve any ionizing radiation. These particular tests will not be done in individuals with cardiac pacemakers, stents or other metallic devices. You may feel nervous about being in a small space when you are in the Magnetic Resonance scanner; however you will be able to communicate with us throughout the scan and can tell us whenever you want the scan to be stopped or interrupted.

If you take part, what will you have to do?

On the day of the Magnetic Resonance Imaging (MRI) investigations, you will be accompanied to the MRI room, where the scan is performed. The scan uses a large magnet to obtain the scans

and does not use radiation like X-rays. A scan session will take about half an hour. During the recording, you will be asked to lie on your back on a table with your head positioned in a padded headrest. Further, you will be requested to keep eye closed calmly, not to feel asleep. The principal investigator and the technicians will provide you with the necessary instructions and help during the recording.

The information that we obtain out of such an investigation will help us to better understand the nature of the functional and biochemical changes during the working memory, in normal healthy subjects. Your participation is entirely voluntary. Absolute confidentiality of the data shall be maintained. No expenses shall be incurred as a result of your participation in the study. However, any brain abnormalities discovered during the scan may be diagnosed free of cost, but the treatment thereafter will be your responsibility.

Can you withdraw from this study after it starts?

You have right to withdraw consent at any stage of study.

Do you have to undergo any blood tests and invasive placing an intravenous cannula and / or administration of any medications or agents such as contrast media?

No need to undergo any blood tests, invasive placement of intravenous cannula, administration of medications or contrast media

Contact for Further Information:

In case, if the you want more information about the study and the participant's right at any time of the research, you will be free to contact any one among the Research team. Please contact the Principal Investigator, Dr. Sabarish. S. S, Senior Resident**,** Dept of IS&IR (contact No: Ph: 9994270566) or Co Principal Investigator, Dr Bejoy Thomas, Professor, Dept of IS&IR (contact No: Ph: 9447719481, bejoy@sctimst.ac.in)

We thank you very much for agreeing to participate in this study.

INFORMED CONSENT FORM

Participant's name: Date of Birth / Age (in years):

I_____
son/daughter of _____ (Please tick boxes)

- Declare that I have read the above information provided to me regarding the study: "Role of resting state fMRI in intracranial Dural AV fistula patients" and have clarified any doubts that I had [ ]
- I also understand that my participation in this study is entirely voluntary and that that I am free to withdraw at any time without giving any reason [ ]
- I also understand that the neuroimaging is being done to explore the utility of resting state fMRI in functional connectivity changes of intracranial dAVF [ ]
- I understand that the results of the data obtained will not be disclosed to me. [ ]
- I understand that no expenses will be incurred by me for participating in this study and my identity will not be revealed in any information released to third parties or published [ ]
- I voluntarily agree to take part in this study [ ]
- I received a copy of this signed consent form [ ]

Name: Name of witness:
Signature: Relation to participant:
Date: Date:

(Person Obtaining Consent)

I, attest that the requirements for informed consent for the medical research project described in this form have been satisfied. I have discussed the research project with the participant and explained to him or her in nontechnical terms all of the information contained in this informed consent form, including any risks and adverse reactions that may reasonably be expected to occur. I further certify that I encouraged participant to ask questions and that all questions asked were answered.

_____ _____

Name and Signature of Principal Investigator with date

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ സയൻസ് ആന്റ് ടെക്നോളജി, തിരുവനന്തപുരം

ആധുനീകമായ ന്യൂറോ ചിത്രീകരണത്തിന് രോഗികൾക്കുള്ള വിവരണപത്രം

പഠനശീർഷകം.

തലയ്ക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളിൽ, വിശ്രമാവസ്ഥയിലുള്ള ഫങ്ഷണൽ മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തിന്റെ പങ്ക്

ഗവേഷകർ

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സഹ-ഗവേഷക	ഡോ. സ്മിത
സഹ-ഗവേഷകൻ	പി ജി രാജേഷ്

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ സയൻസ് ആന്റ് ടെക്നോളജിയിൽ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളുടെ, തലയ്ക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളിൽ, വിശ്രമാവസ്ഥയിലുള്ള ഫങ്ഷണൽ മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തിന്റെ പങ്ക് പരിശോധിക്കുന്ന ഗവേഷണ പഠനത്തിൽ താങ്കളുടെ പങ്കാളിത്തം ക്ഷണിക്കുന്നതിന് ഉദ്ദേശിച്ചുള്ള സമ്മതപത്രമാണിത്.

പഠനത്തിന്റെ ഉദ്ദേശം?

തലയോട്ടിക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയിൽ, തലയ്ക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളിൽ, വിശ്രമാവസ്ഥയിലുള്ള ഫങ്ഷണൽ മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തിന്റെ ഉപയോഗക്ഷമത പരിശോധിക്കാനാണ് ഈ പഠനം നടത്തുന്നത്. ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള വ്യക്തികളിലെ തലച്ചോറിന്റെ പ്രവർത്തനപരമായ ബന്ധത്തിന്റെ മാറ്റങ്ങൾ മനസ്സിലാക്കാൻ ഇത് സഹായിക്കും.

വിവരങ്ങൾ ശ്രദ്ധാപൂർവ്വം വായിക്കാൻ ദയവായി സമയമെടുക്കുകയുംപങ്കെടുക്കണോവേണ്ടയോ എന്ന് താങ്കൾ തീരുമാനിക്കുകയും ചെയ്യുക. പ്രധാന ഗവേഷകൻ പഠനത്തിലുൾപ്പെട്ടിട്ടുള്ള എല്ലാ നടപടികളും രോഗിയോട് വിശദീകരിക്കുകയും അദ്ദേഹത്തിന് തലയ്ക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളിൽ, വിശ്രമാവസ്ഥയിലുള്ള ഫങ്ഷണൽ മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തെപ്പറ്റിയുള്ള സംശയങ്ങൾ 10-15 മിനിട്ടിനകം ദൂരീകരിക്കുകയും ചെയ്യും. താങ്കൾ പങ്കെടുക്കാൻ തീരുമാനിച്ചാൽ, ഈ കാര്യവിവരണ സമ്മതപത്രം പൂരിപ്പിക്കുകയും ഒപ്പും തിയതിയും നൽകുകയും പഠന വിശദാംശങ്ങളുടെയും വ്യക്തിബന്ധങ്ങളുടെയും ഗുണകരമായ ആധാരമായി സൂക്ഷിക്കുകയും ചെയ്യുക.

നടപടിയുടെ സ്വഭാവം?

വിശ്രമാവസ്ഥയിലുള്ള എഫ്എംആർഐ തലച്ചോറ് വിശ്രമാവസ്ഥയിൽ എങ്ങിനെ പ്രവർത്തിക്കുന്നു എന്ന് മനസ്സിലാക്കാനുള്ള ആധുനീകമായ ചിത്രികരണ സങ്കേതമാണ്. അത് ചില ഫ്രീക്വൻസിയിലുള്ള തരംഗങ്ങളും, കാന്തികമണ്ഡലവും തലച്ചോറിന്റെ ചിത്രീകരണത്തിനായി ഉപയോഗിക്കുന്നു. ഹൃദയത്തിനുള്ള പേസ്മേക്കർ, സ്റ്റെന്റ്, അല്ലെങ്കിൽ മറ്റ് ലോഹ ഉപകരണങ്ങൾ എന്നിവയുള്ളവരിൽ ഈ പ്രത്യേക പരിശോധന നടത്തില്ല. മാഗ്നറ്റിക് റെസൊണൻസ് സ്കാനറിൽ താങ്കൾക്ക് ഇടുങ്ങിയ സ്ഥലത്തുള്ള ബുദ്ധിമുട്ടനുഭവപ്പെട്ടേക്കാം, എന്തായാലും സ്കാനിലുടനീളം താങ്കൾക്ക് ഞങ്ങളോട്

ബന്ധപ്പെടാനും താങ്കൾക്കാവശ്യമുള്ളപ്പോൾ സ്കാൻ നിർത്തുകയോ തടസ്സപ്പെടുത്തുകയോ ചെയ്യാനും കഴിയും.

പങ്കെടുക്കുന്നു എങ്കിൽ താങ്കളെന്ത് ചെയ്യണം?

മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തിന്റെ പരിശോധനാ ദിവസം താങ്കളെ സ്ക്ൻ ചെയ്യുന്ന എംആർഐ മുറിയിലേക്ക് കൊണ്ടുപോകും, സ്കാനിന് ചിത്രങ്ങൾ ലഭിക്കാൻ വലിയ ഒരു കാന്തം ഉപയോഗിക്കുന്നു എക്സ്-റേ പോലെ റേഡിയേഷനുപയോഗിക്കുന്നില്ല. ഒരു സ്കാൻ ഘട്ടം അരമണിക്കൂറെടുക്കും. സ്കാൻ രേഖപ്പെടുത്തുന്ന സമയത്ത് താങ്കളോട് ഒരു മേശയിൽ ശബ്ദനിരോധികളുള്ള ഒരു തലയിണയിൽ തല ക്രമീകരിച്ച് വച്ച് മലർന്ന് കിടക്കാൻ ആവശ്യപ്പെടും. എന്നിട്ട് താങ്കളോട് കണ്ണുകൾ അടച്ച് ,ശാന്തമായി, എന്നാൽ ഉറങ്ങാതിരിക്കാൻ അഭ്യർത്ഥിക്കും. സ്കാൻ രേഖപ്പെടുത്തുന്ന സമയത്ത് പ്രധാന ഗവേഷകനും സാങ്കേതീക വിദഗ്ധരും വേണ്ടുന്ന നിർദ്ദേശങ്ങൾ നൽകുകയും താങ്കളെ സഹായിക്കുകയും ചയ്യും.

ഈ പരിശോധനയിൽനിന്നും ലഭിക്കുന്ന വവരങ്ങൾ തലയോട്ടിക്കുള്ളിൽ ഡിഎവിഎഫ് ഉള്ള രോഗികളുടെ പ്രവർത്തനപരമായ അസാധാരണത്വം മനസിലാക്കാൻ ഞങ്ങളെ സഹായിക്കും. എന്നിരുന്നാലും വൈദ്യശാസ്ത്രപരമായി പ്രസക്തമായ എന്തെങ്കിലും വിവരങ്ങൾ ഞങ്ങൾ കണ്ടെത്തിയാൽ താങ്കളെ ചികിത്സിക്കുന്ന ഡോക്ടർക്ക് വേണ്ടുന്ന തീരുമാനമെടുക്കാനായി അത് നൽകും. താങ്കളുടെ പങ്കാളിത്തം തികച്ചും സ്വമേധയായാണ്, തീരുമാനം താങ്കളുടെ SCTIMST യിലെ ഇപ്പോഴത്തെ ചികിത്സയെ ഒരുവിധത്തിലും ബാധിക്കില്ല. വിവരങ്ങളുടെ പരിപൂർണ്ണ രഹസ്യ സ്വഭാവം നിലനിർത്തും. പങ്കെടുക്കുന്നതുകൊണ്ട്. താങ്കൾക്ക് ഒരു ചിലവുമുണ്ടാകില്ല.

പഠനം ആരംഭിച്ചശേഷം താങ്കൾക്ക് പിൻമാറാമോ?

പഠനത്തിന്റെ ഏത് ഘട്ടത്തിലും താങ്കൾക്ക് സമ്മതം പിൻവലിക്കാം, അത് താങ്കളുടെ സാധാരണ ചികിത്സയെ ഒരു വിധത്തിലും ബാധിക്കില്ല.

താങ്കൾക്ക് രക്തപരിശോധനകളോ, ശരീരത്തിൽകടന്നുള്ള അശുദ്ധരക്തക്കുഴലിൽ കടത്തുന്ന കുഴലുകളോ/ അല്ലെങ്കിൽ ഏതെങ്കിലും തരത്തിലുള്ള മരുന്നുകളോ ചിത്രീകരണത്തിനായുള്ള മരുന്നുകളോ നൽകുമോ?

രക്തപരിശോധനകളോ, ശരീരത്തിൽ കടന്നുള്ള അശുദ്ധരക്തക്കുഴലിൽ വയ്ക്കുന്ന കുഴലുകളോ ഏതെങ്കിലും തരത്തിലുള്ള മരുന്നുകളോ ചിത്രീകരണത്തിനായുള്ള മരുന്നുകളോ വേണ്ടതില്ല.

കൂടുതൽ വിവരങ്ങൾക്ക് ബന്ധപ്പെടാൻ

രോഗിക്ക് പഠനത്തെപ്പറ്റിയും പങ്കാളിയുടെ അവകാശങ്ങളെപ്പറ്റിയും കൂടുതൽ വിവരങ്ങൾ ആവശ്യമെങ്കിൽ ഗവേഷണ സംഘത്തിലെ ഏതൊരാളെയും ബന്ധപ്പെടാം.

ദയവായി പ്രധാന ഗവേഷകനെ ബന്ധപ്പെടുക. ഡോ. ശബരീഷ് എസ് എസ്, സീനിയർ റസിഡന്റ്, ഡിപ്പാർട്ടമെന്റ് ഓഫ് ഐഎസ് & ഐആർ (ബന്ധപ്പെടാനുള്ള ഫോൺ നമ്പർ. 9994270566) email. sabharish@sctimst.ac.in, sabarishss@gmail.com, ഉപപ്രധാനഗവേഷകൻ ഡോ. ബിജോയ് തോമസ്, പ്രൊഫസർ, ഡിപ്പാർട്ടമെന്റ് ഓഫ് ഐഎസ് & ഐആർ, ഫോൺ. 9447719481, email. bejoy@sctimst.ac.in,

ഡോ. മാല രാമനാഥൻ മെമ്പർ സെക്രട്ടറി ഐഇസി (ഫോൺ നമ്പർ 0471-2524234)

പഠനത്തിൽ പങ്കെടുക്കാൻ സമ്മതിച്ചതിന് താങ്കൾക്ക് വളരെ നന്ദി

കാര്യബോധത്തോടെയുള്ള സമ്മതപത്രം

പങ്കെടുക്കുന്നയാളുടെ പേര്.....മകൻ/മകൾ..... (ദയവായി (ബോക്സുകളിൽ ശരി അടയാളമിടുക)

- തലയ്ക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളിൽ, വിശ്രമാവസ്ഥയിലുള്ള ഫങ്ഷണൽ മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തിന്റെ പങ്ക് എന്ന പഠനസംബന്ധമായി എനിക്കുനൽകിയ വിവരങ്ങൾ വായിച്ചുഎന്നും എനിക്കുണ്ടായ സംശയങ്ങൽ ദുരീകരിച്ചു എന്നും ഞാൻ പ്രസ്താവിക്കുന്നു. [ ]

- എന്റെ ഈ പഠനത്തിലുള്ള പങ്കാളിത്തം സ്വമേധയായുള്ളതാണെന്നും, എനിക്ക് ഒരു കാരണവും കൂടാതെ ഏതുസമയത്തും, എനിക്കുള്ള വൈദ്യശുശ്രൂഷയെയോ നിയമപരമായ അവകാശങ്ങളെയോ ബാധിക്കാതെ പിൻവാങ്ങാമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- തലയോട്ടിക്കുള്ളിലെ ഡിഎവിഎഫിന്റെ പ്രവർത്തിപരമായ ബന്ധത്തിലുള്ള മാറ്റങ്ങൾ കണ്ടെത്തുന്നതിലുള്ള വിശ്രമാവസ്ഥയിലുള്ള ഫങ്ഷണൽ മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തിന്റെ പ്രയോജനക്ഷമത പരിശോധിക്കാനാണ് ന്യൂറോ ചിത്രീകരണം നടത്തുന്നത് എന്നും ഞാൻ മനസ്സിലാക്കി [ ]
- ശേഖരിച്ചവിവരങ്ങൾ എന്നോട് വെളിപ്പെടുത്തില്ലെന്നും, എന്നിരുന്നാലും, ചികിത്സ പരിഷ്ക്കരിക്കാനിടയാക്കുന്ന എന്തെങ്കിലും വിവരങ്ങൾ കണ്ടെത്തിയാൽ അത് വേണ്ടുന്ന തീരുമാനമെടുക്കാനായി ചികിത്സിക്കുന്ന ഡോക്ടർക്ക് നൽകുമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു.
- പഠനത്തിൽ പങ്കെടുക്കുന്നതുകൊണ്ട് എനിക്ക് ചിലവൊന്നും ഉണ്ടാകില്ലെന്നും, മൂന്നാം കക്ഷികൾക്കോ പ്രസിദ്ധീകരണത്തിനോ നൽകുമ്പോൾ എന്റെ വ്യക്തിവിവരങ്ങൾ വെളിപ്പെടുത്തുകയില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- സ്വമേധയാ പഠനത്തിൽ പങ്കെടുക്കാൻ ഞാൻ സമ്മതിക്കുന്നു. [ ]
- സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു പ്രതി എനിക്ക് കിട്ടി. [ ]

പേര് സാക്ഷിയുടെ പേര്

ഒപ്പ്/ രോഗിയുടെ വിരലടയാളം/ ഒപ്പ്

തീയതി തീയതി

രോഗിയുമായുള്ള ബന്ധം

(സമ്മതം വാങ്ങുന്നയാൾ)

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണപദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകടസാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെ ചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതപത്രം വാങ്ങുന്ന ആളുടെ പേരും ഒപ്പും

ഡോ ശാന്തകുമാർ എസ് (ഫോൺ. 442357488)

സീനിയർ റസിഡന്റ്

പഠനവുമായി ബന്ധമില്ലാത്ത വ്യക്തിയെ ബന്ധപ്പെടുന്നതിന് ദയവായി സ്ഥാപനത്തിലെ നൈതീക കമ്മിറ്റി മെംമ്പർ സെക്രട്ടറി ഡോ. മാല രാമനാഥനെ ബന്ധപ്പെടാം. ഫോൺ 04712524234, email: iec.mem.sec@sctimst.ac.in

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ സയൻസ് ആന്റ് ടെക്നോളജി, തിരുവനന്തപുരം

ആധുനീകമായ ന്യൂറോ ചിത്രീകരണത്തിന് ആരോഗ്യമുള്ള സന്നദ്ധപ്രവർത്തകർക്കുള്ള വിവരണപത്രം

പഠനശീർഷകം.

തലയ്ക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളിൽ, വിശ്രമാവസ്ഥയിലുള്ള ഫങ്ഷണൽ മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തിന്റെ പങ്ക്

ഗവേഷകർ

പ്രധാന ഗവേഷകൻ	**ഡോ. ശബരീഷ് എസ് എസ്**
സഹ-ഗവേഷകൻ	**ഡോ. ബിജോയ് തോമസ്**
സഹ-ഗവേഷകൻ	**ഡോ. സന്തോഷ്കുമാർ കെന്നത്ത്**
സഹ-ഗവേഷകൻ	**ഡോ. ജയദേവൻ**
സഹ-ഗവേഷകൻ	**ഡോ. റാം ശേഖർ മേനോൻ**
സഹ-ഗവേഷക	**ഡോ. സ്മിത**
സഹ-ഗവേഷകൻ	**പി. ജി രാജേഷ്**

ശ്രീ ചിത്ര തിരുനാൾ ഇൻസ്റ്റിറ്റ്യൂട്ട് ഫോർ സയൻസ് ആന്റ് ടെക്നോളജിയിൽ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളുടെ, തലയ്ക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളിൽ, വിശ്രമാവസ്ഥയിലുള്ള ഫങ്ഷണൽ മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തിന്റെ പങ്ക് പരിശോധിക്കുന്ന ഗവേഷണ പഠനത്തിൽ താങ്കളുടെ പങ്കാളിത്തം ക്ഷണിക്കുന്നതിന് ഉദ്ദേശിച്ചുള്ള സമ്മതപത്രമാണിത്.

പഠനത്തിന്റെ ഉദ്ദേശം?

തലയോട്ടിക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയിൽ, തലയ്ക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളിൽ, വിശ്രമാവസ്ഥയിലുള്ള ഫങ്ഷണൽ മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തിന്റെ ഉപയോഗക്ഷമത പരിശോധിക്കാനാണ് ഈ പഠനം നടത്തുന്നത്. എം സിഐ യുള്ള വ്യക്തികളിലെ പ്രവർത്തനക്ഷമമായ ഓർമ്മയുടെ ദൗർബല്യങ്ങളുടെ ന്യൂറോണലും ബയോകെമിക്കലുമായ അടിസ്ഥാനം മനസ്സിലാക്കാൻ ഇത് സഹായിക്കും. ന്യൂറോളജിക്കലായ അസുഖമില്ലാത്തയാളെന്ന നിലയിൽ താരതമ്യത്തിനായി ഈ പഠനത്തിൽ പങ്കെടുക്കാൻ താങ്കൾ സമ്മതിക്കണമെന്ന് അഭ്യർത്ഥിക്കുന്നു.

വിവരങ്ങൾ ശ്രദ്ധാപൂർവ്വം വായിക്കാൻ ദയവായി സമയമെടുക്കുകയുംപങ്കെടുക്കണോവേണ്ടയോ എന്ന് താങ്കൾ തീരുമാനിക്കുകയും ചെയ്യുക. പ്രധാന ഗവേഷകൻ പഠനത്തിലുൾപ്പെട്ടിട്ടുള്ള എല്ലാ നടപടികളും താങ്കളോട് വിശദീകരിക്കുകയും വിശ്രമാവസ്ഥയിലുള്ള ഫങ്ഷണൽ മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തെപ്പറ്റിയുള്ള സംശയങ്ങൾ 10-15 മിനിട്ടിനകം ദൂരീകരിക്കുകയും ചെയ്യും. താങ്കൾ പങ്കെടുക്കാൻ തീരുമാനിച്ചാൽ, ഈ കാര്യവിവരണ സമ്മതപത്രം പൂരിപ്പിക്കുകയും ഒപ്പും തീയതിയും നൽകുകയും പഠന വിശദാംശങ്ങളുടെയും വ്യക്തി ബന്ധങ്ങളുടെയും ഗുണകരമായ ആധാരമായി സൂക്ഷിക്കുകയും ചെയ്യുക.

നടപടിയുടെ സ്വഭാവം?

വിശ്രമാവസ്ഥയിലുള്ള എഫ്എംആർഐ തലച്ചോറ് വിശ്രമാവസ്ഥയിൽ എങ്ങിനെ പ്രവർത്തിക്കുന്നു എന്ന് മനസ്സിലാക്കാനുള്ള ആധുനീകമായ ചിത്രീകരണ സങ്കേതമാണ്. അത് ചില ഫ്രീക്വൻസിയിലുള്ള തരംഗങ്ങളും, കാന്തിക മണ്ഡലവും തലച്ചോറിന്റെ ചിത്രീകരണത്തിനായി ഉപയോഗിക്കുന്നു. ഇതിൽ അയണൈസിംഗ് റേഡിയേഷനുപയോഗിക്കുന്നില്ല. ഹൃദയത്തിനുള്ള പേസ്മേക്കർ, സ്റ്റെന്റ്, അല്ലെങ്കിൽ മറ്റ് ലോഹ ഉപകരണങ്ങൾ എന്നിവയുള്ളവരിൽ ഈ പ്രത്യേക പരിശോധന നടത്തില്ല. മാഗ്നറ്റിക് റെസൊണൻസ് സ്കാനറിൽ താങ്കൾക്ക് ഇടുങ്ങിയ സ്ഥലത്തുള്ള ബുദ്ധിമുട്ടനുഭവപ്പെട്ടേക്കാം, എന്തായാലും സ്കാനിലുടനീളം താങ്കൾക്ക് ഞങ്ങളോട് ബന്ധപ്പെടാനും താങ്കൾക്കാവശ്യമുള്ളപ്പോൾ സ്കാൻ നിർത്തുകയോ തടസ്സപ്പെടുത്തുകയോ ചെയ്യാനും കഴിയും.

പങ്കെടുക്കുന്നു എങ്കിൽ താങ്കളെന്ത് ചെയ്യണം?

മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തിന്റെ പരിശോധനാ ദിവസം താങ്കളെ സ്ക്രീൻ ചെയ്യുന്ന എംആർഐ മുറിയിലേക്ക് കൊണ്ടുപോകും, സ്കാനിന് ചിത്രങ്ങൾ ലഭിക്കാൻ വലിയ ഒരു കാന്തം ഉപയോഗിക്കുന്നു എക്സ്-റേ പോലെ റേഡിയേഷനുപയോഗിക്കുന്നില്ല. ഒരു സ്കാൻ ഘട്ടം അരമണിക്കൂറെടുക്കും. സ്കാൻ രേഖപ്പെടുത്തുനനസമയത്ത് താങ്കളോട് ഒരു മേശയിൽ ശബ്ദനിരോധമുള്ള ഒരു തലയിണയിൽ തലക്രമപ്പെടുത്തി വച്ച് മലർന്ന് കിടക്കാൻ ആവശ്യപ്പെടും. എന്നിട്ട് താങ്കളോട് കണ്ണുകൾ അടച്ച് ,ശാന്തമായി, എന്നാൽ ഉറങ്ങാതിരിക്കാൻ അഭ്യർത്ഥിക്കും. സ്ക്രീൻ രേഖപ്പെടുത്തുന്ന സമയത്ത് പ്രധാന ഗവേഷകനും സാങ്കേതികവിദഗ്ധരും വേണ്ടുന്ന നിർദ്ദേശങ്ങൾ നൽകുകയും താങ്കളെ സഹായിക്കുകയും ചെയ്യും.

ഈ പരിശോധനയിൽനിന്നും ലഭിക്കുന്ന വവരങ്ങൾ ആരോഗ്യമുള്ള വ്യക്തികളിൽ പ്രവർത്തിക്കുന്ന ഓർമ്മയുടെ പ്രവർത്തനത്തിന്റെ സ്വഭാവവും ബയോകെമിക്കൽ മാറ്റങ്ങളും മനസിലാക്കാൻ ഞങ്ങളെ സഹായിക്കും. താങ്കളുടെ പങ്കാളിത്തം തികച്ചും സ്വമേധയാ ആണ്. വിവരങ്ങളുടെ പരിപൂർണ്ണ രഹസ്യ സ്വഭാവം നിലനിർത്തും. പങ്കെടുക്കുന്നതുകൊണ്ട്. താങ്കൾക്ക് ഒരു ചിലവുമുണ്ടാകില്ല. എന്നിരുന്നാലും സ്കാനിങ്ങിനിടയിൽ തലച്ചോറിൽ എന്തെങ്കിലും അസാധാരണത്വം കണ്ടെത്തിയാൽ രോഗനിൽണ്ണയം സൗജന്യമാണെങ്കിലും അതിനുശേഷമുള്ള ചികിത്സ താങ്കളുടെ ഉത്തരവാദിത്വത്തിലായിരിക്കും.

പഠനം ആരംഭിച്ചശേഷം താങ്കൾക്ക് പിൻമാറാമോ?

പഠനത്തിന്റെ ഏത് ഘട്ടത്തിലും താങ്കൾക്ക് സമ്മതം പിൻവലിക്കാം,

താങ്കൾക്ക് രക്തപരിശോധനകളോ, ശരീരത്തിൽകടന്നുള്ള അശുദ്ധരക്തക്കുഴലിൽ കടത്തുന്ന കുഴലുകളോ/ അല്ലെങ്കിൽ ഏതെങ്കിലും തരത്തിലുള്ള മരുന്നുകളോ ചിത്രീകരണത്തിനായുള്ള മരുന്നുകളോ നൽകുമോ?

രക്തപരിശോധനകളോ, ശരീരത്തിൽ കടന്നുള്ള അശുദ്ധരക്തക്കുഴലിൽ വയ്ക്കുന്ന കുഴലുകളോ ഏതെങ്കിലും തരത്തിലുള്ള മരുന്നുകളോ ചിത്രീകരണത്തിനായുള്ള മരുന്നുകളോ വേണ്ടതില്ല.

കൂടുതൽ വിവരങ്ങൾക്ക് ബന്ധപ്പെടാൻ

രോഗിക്ക് പഠനത്തെപ്പറ്റിയും പങ്കാളിയുടെ അവകാശങ്ങളെപ്പറ്റിയും കൂടുതൽ വിവരങ്ങൾ ആവശ്യമെങ്കിൽ ഗവേഷണ സംഘത്തിലെ ഏതൊരാളെയും ബന്ധപ്പെടാം.

ദയവായി പ്രധാന ഗവേഷകനെ ബന്ധപ്പെടുക. ഡോ. ശബരീഷ് എസ് എസ്, സീനിയർ റസിഡന്റ്, ഡിപ്പാർട്ടമെന്റ് ഓഫ് ഐഎസ് & ഐആർ (ബന്ധപ്പെടാനുള്ള ഫോൺ നമ്പർ. 9994270566) email. sabharish@sctimst.ac.in, sabarishss@gmail.com, സഹ- പ്രധാനഗവേഷകൻ ഡോ. വിജോയ് തോമസ്, പ്രൊഫസർ, ഡിപ്പാർട്ടമെന്റ് ഓഫ് ഐഎസ് & ഐആർ, ഫോൺ. 9447719481, email. bejoy@sctimst.ac.in

ഡോ. മാല രാമനാഥൻ മെമ്പർ സെക്രട്ടറി ഐഇസി (ഫോൺ നമ്പർ 0471-2524234)

പഠനത്തിൽ പങ്കെടുക്കാൻ സമ്മതിച്ചതിന് താങ്കൾക്ക് വളരെ നന്ദി

കാര്യബോധത്തോടെയുള്ള സമ്മതപത്രം

പങ്കെടുക്കുന്നയാളുടെ പേര്.....മകൻ/മകൾ..... (ദയവായി (ബോക്സുകളിൽ ശരി അടയാളമിടുക)

- തലയ്ക്കുള്ളിലെ ഡ്യൂറൽ ആർട്ടിരിയോ വീനസ് ഫിസ്റ്റുലയുള്ള രോഗികളിൽ, വിശ്രമാവസ്ഥയിലുള്ള ഫങ്ഷണൽ മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തിന്റെ പങ്ക് എന്ന പഠനസംബന്ധമായി എനിക്കുനൽകിയ വിവരങ്ങൾ വായിച്ചുഎന്നും എനിക്കുണ്ടായ സംശയങ്ങൽ ദൂരീകരിച്ചു എന്നും ഞാൻ പ്രസ്താവിക്കുന്നു. [ ]

- എന്റെ ഈ പഠനത്തിലുള്ള പങ്കാളിത്തം സ്വമേധയായുള്ളതാണെന്നും, എനിക്ക് ഒരു കാരണവും കൂടാതെ ഏതുസമയത്തും, പിൻവാങ്ങാമെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- തലയോട്ടിക്കുള്ളിലെ ഡിഎവിഎഫിന്റെ പ്രവർത്തിപരമായ ബന്ധത്തിലുള്ള മാറ്റങ്ങൾ കണ്ടെത്തുന്നതിലുള്ള വിശ്രമാവസ്ഥയിലുള്ള ഫങ്ഷണൽ മാഗ്നറ്റിക് റെസൊണൻസ് ചിത്രീകരണത്തിന്റെ [ ]
  പ്രയോജനക്ഷമത പരിശോധിക്കാനാണ് ന്യൂറോ ചിത്രീകരണം നടത്തുന്നത് എന്നും ഞാൻ മനസ്സിലാക്കി
- ശേഖരിച്ചവിവരങ്ങൾ എന്നോട് വെളിപ്പെടുത്തില്ലെന്നും, ഞാൻ മനസ്സിലാക്കുന്നു.
- പഠനത്തിൽ പങ്കെടുക്കുന്നതുകൊണ്ട് എനിക്ക് ചിലവൊന്നും ഉണ്ടാകില്ലെന്നും, മൂന്നാം കക്ഷികൾക്കോ പ്രസിദ്ധീകരണത്തിനോ നൽകുമ്പോൾ എന്റെ വ്യക്തിവിവരങ്ങൾ വെളിപ്പെടുത്തുകയില്ലെന്നും ഞാൻ മനസ്സിലാക്കുന്നു. [ ]
- സ്വമേധയാ പഠനത്തിൽ പങ്കെടുക്കാൻ ഞാൻ സമ്മതിക്കുന്നു. [ ]
- സമ്മതപത്രത്തിന്റെ ഒപ്പിട്ട ഒരു പ്രതി എനിക്ക് കിട്ടി. [ ]

പേര് സാക്ഷിയുടെ പേര്

ഒപ്പ്/ രോഗിയുടെ വിരലടയാളം/ ഒപ്പ്

തീയതി തീയതി

രോഗിയുമായുള്ള ബന്ധം

(സമ്മതം വാങ്ങുന്നയാൾ)

മെഡിക്കൽ റിസർച്ച് പ്രോജക്ടിനാവശ്യമായ സമ്മതപത്രത്തിനു വേണ്ടുന്ന എല്ലാ ഘടകങ്ങളും തൃപ്തികരമായി നിർവഹിച്ചിരിക്കുന്നുവെന്ന് ഞാൻ ബോധ്യപ്പെടുത്തുന്നു. പഠനപങ്കാളിയുമായി ഗവേഷണപദ്ധതിയെപ്പറ്റി സാങ്കേതികേതര പദങ്ങളുപയോഗിച്ച് എല്ലാ വിവരങ്ങളെപ്പറ്റിയും ചർച്ച നടത്തുകയും പ്രതീക്ഷിക്കാവുന്ന അപകടസാധ്യതകളും പാർശ്വഫലങ്ങളും വിശദീകരിക്കുകയും ചെയ്തു. പങ്കാളിയെ ചോദ്യങ്ങൾ ചോദിക്കാൻ പ്രേരിപ്പിക്കുകയും എല്ലാ ചോദ്യങ്ങൾക്കും ഉത്തരം നൽകുകയും ചെയ്തു എന്നും ഞാൻ സാക്ഷ്യപ്പെടുത്തുന്നു.

സമ്മതപത്രം വാങ്ങുന്ന ആളുടെ പേരും ഒപ്പും

ഡോ ശാന്തകുമാർ എസ് (ഫോൺ. 442357488)

സീനിയർ റസിഡന്റ്

പഠനവുമായി ബന്ധമില്ലാത്ത വ്യക്തിയെ ബന്ധപ്പെടുന്നതിന് ദയവായി സ്ഥാപനത്തിലെ നൈതീക കമ്മിറ്റി മെംമ്പർ സെക്രട്ടറി ഡോ. മാല രാമനാഥനെ ബന്ധപ്പെടാം. ഫോൺ 04712524234, email: iec.mem.sec@sctimst.ac.in

Master chart

Age	Sex	Sex	Duration	Duration	Presentati	Benign/ag	MRI bleed	MRI bleed	Cognard	Borden	Cognard + Single site	Single/Mu	Site of DAI Site	Embolization	statu	Managem	Embolic m	Clinical syn	MRI bleed	Risk factor	Risk factor	Circula	Lt ant	Post	
39	M	1	7 months	7 Head ache	1	1	0	No	5	3	Type 3	Single	1 Lt pterione	5 Complete embolisa		1 Squid 12		Improvem	No	Nil		0	5	5.5	5
59	F	2	9 months	9 Head ache	1	1	0	No	5	3	Type 3	Single	1 Right para	5 Complete embolisa		1 Coiling		Improved	No	H/O HTN		3	6.8	7	7
45	M	1	2 months	2 Headache,	3	2	0	No	5	3	Type 3(SSS multi		2 Superior sa	1 Complete embolisa		1 Squid 18		Improved	No	H/O HTN a		3	7	7.5	7.5
13	F	2	8 months	8 Headache	1	1	0	No	3	2	Type 2 B(T	Single	1 Torcula-R	4 Complete embolisa		1 Squid and		Improved	No	Nil		0	8	8.5	9
44	M	1	3 months	3 Seizure an	4	2	0	No	3	2	Type 2B(SS	Single	1 Mid SSS	1 Complete embolisa		1 Onyx 18		Improved	No	H/O DM		3	7	6.5	6
69	M	1	2 months	2 Slurring of	5	2	1	Yes	3	2	Type 2B(Lt S	Single	1 Lt TS-SS wi	3 Complete embolisa		1 Onyx 18		Improved	Yes	Nil		0	6.5	8	6.5
68	M	1	1 month	1 Seizures ai	3	2	0	No	4	2	Type 2 A+t	Single	1 Torcula- Le	4 Not yet embolized		0 Nil		Nil	No	CVT, DM, I		1			
28	M	1	1 month	1 Seizures ai	3	2	0	No	4	2	Type 2 A+t	Multisite	2 Rt TS-SS, P	1 3 times embolized		2 Glue + Onyx		Improved	No	Nil		0	14	11.5	12
47	M	1	3 months	3 Seizures ai	5	2	1	Yes	4	2	Type 2A+B	Single	1 Lt TS-SS w	3 Complete embolisa		1 PVA		Improved	Yes	Nil		0	5	5.5	5.8
43	M	1	1 month	1 GTCS and i	5	2	1	Yes	4	2	Type 2A+B	Single	1 Rt TS-SS	3 Complete embolisa		1 Onyx 18		Improved	Yes	Nil		0	6.5	5.5	5
53	F	2	3 months	3 Memory d	3	2	0	No	6	3	Type 4	Single	1 Tentorial C	2 Complete embolisa		1 Onyx 18		Improved	No	Nil		0	6	6.5	6
49	M	1	7 months	7 Headache,	1	1	0	No	4	2	Type 2A+B	Multisite	2 Right trans	3 Significant reductio		2 Onyx 18		Improved	No	H/O HTN,		3	6.5	6	6.8
61	M	1	12 months	12 Headache	1	1	0	No	1	1	Type 1 (Lt	Single	1 Left TS-SS	3 Conservative mana		0		Tinnitus in	No	Nil		0	3.5	4	4
52	M	1	1 month	1 Sudden on	5	2	1	Yes(SAH)	5	3	Type 3(Lt S	Single	1 Lt sphenoi	5 Complete embolisa		1 Onyx		Improved	Yes(SAH)	H/O HTN a		3	4	6	4.8
39	M	1	6 months	6 Headache	1	1	0	No	1	1	Type 1(TS	Single	1 Mid SSS ar	1 Significant reductio		2 PVA		Improved	No	H/O CVT		1	5	5	5.5
37	M	1	12 months	12 Headache,	1	1	0	No	1	1	Type 1	Single	1 Rt TS-Torc	4 Conservative mana		0			No	H/O CVT		1	4	4	4.2
53	M	1	2 months	2 Seizures ai	4	2	0	No	5	3	Type 3	Single	1 Lt paracav	5 Complete embolisa		1 Squid		Improved	No	H/O RTA		2	6	7	6.5
53	M	1	1 month	1 Headache	3	2	1	Yes	3	2	Type 2B	Single	1 Lt TS-SS	3 Complete embolisa		1 Onyx and		Improved	Yes	Nil		0	5	5.5	6
41	M	1	5 months	5 Gradual vis	1	1	0	No	4	2	Type 2 A+t	Multisite	2 Torcula an	4 Significant reductio		2 Squid 18		Improved	No	CVT, Prote		1	5	6	6.5
57	F	2	2 months	2 Tinnitus ar	4	2	0	No	3	2	Type 2B(R	Single	1 Rt TS-SS	3 Significant reductio		2 Onyx		Improved	No	Rt cerebell		4	7	8	8
52	M	1	1 month	1 Headache	1	1	0	No	5	3	Type 3(RT	Single	1 Right TS - Si	3 Complete embolisa		1 PVA		Improved	No	HTN and D		3	5.5	6	6
38	M	1	4 months	4 Headache	3	2	1	Yes	3	2	Type 2 B(T	Single	1 Right TS-Si	3 Complete embolisa		1 PVA		Improved	Yes	H/O RTA		2	8	7	6.5
45	M	1	12 months	12 Headache	1	1	0	No	4	2	Type 2A+B	Single	1 Mid SSS	1 Complete embolisa		1 Onyx 18		Improved	No	H/O Ca bre		4	5	5.5	5.5
38	M	1	9 months	9 Headache	1	1	0	No	4	2	Type 2 A+t	Single	1 Torcula-Rt	4 Significant reductio		2 Onyx and		Headache	No	H/O CVT		1	9	8.2	10
47	M	1	7 months	7 Headache,	1	1	0		4	2	Type 2A+B	Single	1 Right para	5 Lost F/U		0				Nil		0	3.5	4	4
70	M	1	4 months	4 Headache,	5	2	1	Yes	5	3	Type 3	Single	1 Torcula-TS	4 Expired venous sac		0		Pt expired	Yes	HTN, DM		3			
40	M	1	3 months	3 Tremors, r	3	2	0	No	4	2	Type 2 A+t	Single	1 Right TS	4 Complete embolisa		1 Onyx		Tremors in	No	H/o CVT ai		1	10	10	11
24	M	1	24 months	24 Headache,	3	2	0	No	4	2	Type 2 A+t	Multisite	2 Lt TS-SS, Tr	5 Significant reductio		2 Squid and		Slowness i	No	H/O CVT, I		1	7	7.5	7
24	M	1	18 months	18 Headache	1	1	0	No	2	1	Type 2A	Single	1 Mid SSS	1 Complete embolisa		1 Onyx		Improved	No	H/O traum		2	5	5	5.5
68	M	1	6 months	6 Memory d	3	2	0	No	3	2	Type 2B(W	Multisite	2 Mid SSS, Tr	1 Significant reductio		2 Onyx and		Improved	No	H/O CVT		1	8	8.2	8.5
28	M	1	24 months	24 Headache,	1	1	0	No	3	2	Type 2B	Single	1 Tentorial C	2 Complete embolisa		1 Squid 12		Improved	No	Nil		0	5	5	6
40	M	1	8 months	8 Seizures, H	1	1	0	No	5	3	Type 3(Rt	Multisite	2 Rt parietal	5 Complete embolisa		1 Squid 18		Improved	No	H/O CVT		1	7	6.5	5
50	M	1	6months	6 Seizure, he	3	2	0	No	4	2	Type 2A+B	Single	1 Tentorial C	4 Lost F/U		1			No	Nil		0	6	5.5	6

Pat vs con	MMSE	Addenbro	RAVLT-Im	RAVLT-De	RAVLT-Re	WMS-Verbral Imm	WMS- Verbal delay	WMS- Visı	WMS- Visı	WMS- Dig	Forward	Reverse	Semantic	TRAIL A	TRAIL B	RMT-Facie
1	26	77	5	7	14	18	9	21	21	7	4	3	41	174	265	20
1	26	54	4	5	12	14	5	5	5	7	4	3	38	245	305	12
1	24	72	4	6	11	4	2	0	0	8	4	4	47	276	330	9
1	26	70	3	6	12	15	7	17	17	9	5	4	34	145	345	11
1	28	76	4	5	13	11	2	7	7	11	6	5	41	84	306	17
1	26	80	3	3	15	20	7	20	14	7	4	3	33	93	206	9
1	23	72	2	4	8	4	3	11	7	5	3	2	34	145	321	11
1	26	80	1	3	4	16	3	14	11	10	6	4	37	134	341	14
1	24	78	3	4	9	15	6	23	11	6	4	2	35	119	352	15
1	25	86	3	5	13	4	3	0	0	6	4	2	28	66	190	17
1	19	37	1	0	0	0	0	0	0	5	3	2	27	270	500	14
1	23	53	1	5	12	6	2	17	11	9	5	4	22	95	278	15
1	30	88	3	12	14	32	32	35	31	7	4	3	46	78	180	21
1	23	78	3	4	12	20	25	25	30	11	6	5	33	64	235	13
1	28	76	4	9	11	17	10	26	7	9	5	4	23	143	256	19
1	30	84	4	11	13	36	36	31	31	10	6	4	25	90	320	21
1	21	65	1	0	0	0	0	7	7	10	6	4	31	200	370	7
1	18	57	2	0	0	4	3	7	0	3	2	1	26	310	354	14
1	30	83	4	8	11	16	7	33	31	10	5	5	48	153	309	20
1	21	68	2	4	7	11	5	27	21	7	4	3	27	134	256	13
1	24	78	4	5	11	7	0	14	14	7	4	3	23	180	270	16
1	27	77	3	0	8	15	0	15	0	5	3	2	49	120	360	9
1	24	56	2	5	7	13	4	23	21	6	3	3	21	123	346	13
1	26	78	3	15	14	45	45	0	0	6	3	3	0			
1	24	61	2	6	9	18	11	25	27	7	4	3	23	156	245	13
1	17	46	2	0	0	2	0	3	0	5	3	2	11	210	430	15
1	10	40	3	0	0	0	0	0	0	4	2	2	0			
1	21	86	2	5	7	4	2	21	21	10	6	4	32	125	347	23
1	28	87	4	11	13	35	32	7	7	14	7	7	51	68	150	16
1	23	70	4	2	11	13	9	0	0	8	4	4	34	243	500	19
1	30	98	7	10	11	38	34	33	33	14	7	7	40	98	141	23
1	24	74	2	4	7	14	12	9	12	9	5	4	17	146	245	11
1	24	72	2	4	6	4	0	11	7	9	5	4	15	175	311	15

Cognard t	Single site	Present sy	Cognard	Presentati	Post vs co	MMSE Post	Addenbrok	RVLT-Imm	RAVLT-De	RAVLT-Recog post	WMS-Verl	WMS-Ver delay	WMS-Visu	WMS-Visu	WMS-Digi	Forward p	Reverse p	Semantic	TRAIL A P(	TRAIL B P(	RMT-Facie
Type 3	Single	Head ache	5	1	1	29	86	5	9	14	35	13	28	28	8	5	3	43	120	210	22
Type 2 B(T	Single	Headache	3	1	1	28	88	4	8	14	24	24	24	24	10	5	5	38	139	234	15
Type 2B(SS	Single	Seizure an	3	4	1	30	84	4	9	14	27	27	24	24	11	6	5	43	85	224	19
Type 2B(Lt	Single	Slurring of	3	5	1	30	87	4	8	15	29	29	31	28	8	5	3	37	110	180	13
Type 2 A+E	Multisite	Seizures ar	4	3	1	30	93	2	9	9	21	24	31	28	11	6	5	39	145	185	18
Type 2A+B	Single	Seizures ar	4	5	1	28	88	3	5	12	28	30	28	25	7	4	3	41	75	210	16
Type 2A+B	Single	GTCS and a	4	5	1	30	92	4	7	15	35	37	25	25	7	4	3	39	70	170	18
Type 3(Lt s	Single	Sudden on	5	5	1	29	87	4	8	15	32	36	31	29	13	8	5	37	61	210	15
Type 1(TS	Single	Headache	1	1	1	30	85	3	11	13	38	39	35	31	10	5	5	28	123	196	20
Type 3	Single	Seizures ar	5	4	1	24	83	3	6	6	21	31	31	29	12	6	6	33	174	310	12
Type 2B	Single	Headache	3	3	1	26	79	3	6	6	23	28	27	27	8	4	4	28	158	245	15
Type 2 A+E	Single	Gradual vis	4	1	1	30	96	4	8	13	21	29	38	31	13	7	6	49	98	120	22
Type 3	Single	Headache	5	1	1	30	92	4	7	12	31	33	34	29	11	6	5	28	135	189	18
Type 2 B	Single	Headache	3	3	1	29	90	3	5	11	27	29	27	27	9	5	4	49	95	254	12
Type 2A+B	Single	Headache	4	1	1	28	78	3	6	9	29	29	28	25	9	5	4	25	100	310	17
Type 2 A+E	Single	Headache	4	1	1	30	84	4	15	14	29	27	0	0	9	5	4				
Type 2 A+E	Single	Tremors, n	4	3	1	26	68	3	5	7	23	22	0	0	7	4	3				
Type 2 A+E	Multisite	Headache,	4	3	1	28	88	3	7	9	22	27	31	27	11	6	5	39	105	258	23
Type 2B(M	Multisite	Memory d	3	3	1	26	84	4	7	13	31	31	33	31	11	6	5	39	185	360	20
Type 2B	Single	Headache,	3	1	1	30	98	7	11	15	37	37	39	34	14	7	7	44	105	153	24

Pat vs con	MMSE	Addenbro	RAVLT-Im	RAVLT-De	RAVLT-Re	WMS-Verbral Imm	WMS- Verbal delay	WMS- Visi	WMS- Visi	WMS- Dig	Forward	Reverse	Semantic	TRAIL A	TRAIL B	RMT-Facie
2	30	96	7	12	14	38	38	41	41	17	9	8	54	76	150	21
2	30	93	5	10	15	31	34	36	36	17	9	8	52	63	132	22
2	30	99	8	14	14	40	39	41	41	16	8	8	55	72	134	24
2	29	93	10	10	12	35	28	41	41	16	8	8	54	60	108	19
2	30	97	6	12	14	34	38	32	29	16	9	7	54	18	97	22
2	30	97	7	13	15	38	38	41	41	12	6	6	54	59	149	21
2	30	98	4	15	13	30	21	41	41	11	6	5	55	60	75	21
2	30	94	5	12	15	21	34	41	39	21	11	10	55	60	60	25
2	30	94	8	11	15	41	27	38	32	12	11	11	54	68	160	23
2	30	98	9	12	13	35	35	37	37	15	8	7	55	60	145	21
2	30	94	8	14	14	41	38	41	41	17	9	8	54	72	158	24
2	30	96	6	12	15	37	36	41	41	18	9	9	53	69	145	24
2	30	97	7	11	14	43	34	37	35	19	10	9	54	65	99	23
2	30	96	6	14	12	39	38	39	37	17	9	8	51	75	125	21
2	30	95	8	13	15	42	41	41	39	17	9	8	51	72	122	23
2	30	91	6	11	13	36	36	36	36	16	8	8	54	56	90	21
2	30	92	7	14	15	44	41	38	36	15	8	7	53	58	134	22
2	30	90	6	13	14	35	36	34	34	14	7	7	51	74	121	21
2	30	99	5	12	12	41	40	32	32	13	7	6	52	58	68	21
2	30	97	8	14	15	43	37	36	34	16	8	8	54	74	75	23
2	30	95	7	14	15	41	39	39	37	17	9	8	49	61	79	20
2	30	94	8	11	13	39	37	38	34	18	9	9	52	45	71	25
2	30	93	7	12	14	44	41	37	34	17	9	8	54	48	142	23
2	30	91	8	13	14	43	42	36	35	15	9	6	55	77	103	22
2	30	93	6	12	15	35	34	38	37	16	9	7	51	54	74	21
2	30	91	5	11	14	41	40	37	35	17	9	8	53	65	78	22
2	30	94	7	10	12	36	34	37	35	15	8	7	52	78	114	24
2	30	92	4	11	14	35	37	35	35	17	9	8	53	58	83	21
2	30	93	7	10	12	37	39	38	35	16	8	8	52	74	124	22
2	30	95	6	14	15	44	41	41	41	18	10	8	51	69	112	25
2	30	92	8	13	15	31	36	37	35	15	8	7	53	58	115	22
2	30	94	7	13	15	38	40	35	35	16	8	8	52	53	87	21
2	30	91	6	13	14	43	41	37	37	15	8	7	51	65	95	23

Key to Master chart

Sex: 1- Male, 2-Female

Clinical presentation: 1-Headache, visual 2-Tinnitus 3-Cognitive, dementia 4-Seizures 5-Hemorrhage

Symptoms: 1- Benign symptoms 2-Aggressive symptoms

Location of fistula: 1-SSS 2-Tentorial 3-TS-SS 4-Torcular 5-Convexity 6-Cavernous

Cognard classification:

Grade 1 – 1, Grade 2A-2, Grade 2B-3, Grade 2A+B-4, Grade 3- 5, Grade 4- 6, Grade 5-7

Borden classification: Grade 1-1, Grade 2-2, Grade 3-3

ABBREVIATIONS

AD-Alzheimer's disease

AFNI- Analysis of functional neuro-images

ALFF-Amplitude of Low Frequency Fluctuations

AI- anterior Insula'

ACC-Anterior cingulate cortex

AV-Arterio-venous

AVF-Arterio-venous fistula

BOLD- Blood oxygen level dependent

CCF-Carotico-Cavernous Fistula

CIS- Clinical Isolated symptom

CSF- Cerebro Spinal Fluid

CT-Computed Tomography

DLPFC- Dorsolateral prefrontal cortex

DAN-Dorsal attention network

DAVF-Dural arterio-venous fistula

DMN-Default mode network

FDR- False Discovery Rate

FEF-Frontal eye field

FSL- FMRIB's software library

FPCN- Fronto-parietal control network

FTD- Fronto-temporal Dementia

FWE- Family-wise error

GIFT- Group ICA od fMRI tool box software

GLM-General linear model

GM-Gray matter

GSR- Global signal regression

HP-Hippocampus

LVR- Lepto-meningeal reflux

LPFC-Lateral pre-frontal cortex

IEC- Intuitional Ethics committee

IFG-Inferior frontal gyrus

ICA- Independent component analysis

ICP- Intra-Cranial Pressure

MFG-Middle frontal gyrus

MMSE-Mini-mental state examination

MNI-Montreal neurological institute

MMP-Matrix metallo-proteins

MPFC-Medial pre-frontal cortex

MRI-Magnetic resonance imaging

VEGF- Vascular Endothelial Growth Factor

PC-Precuneus

PCC-Posterior cingulate cortex

PET- Positron emission tomography

ReHo- Regional homogeneity

ROI- Region of interest

RPFC-Rostral pre-frontal cortex

RSN- Resting state networks

rsfMRI- resting state functional magnetic resonance imaging

SMA- Supplementary motor area

SMN- Sensori-motor network

SN-Salience network

SSS-Superior sagittal sinus

SPECT- Single positron emission tomography

SPM- Statistical para-metric mapping

TIA- Transient ischemic attack

TR- Time of repetition

TS-SS- Transverse sinus-sigmoid sinus

RPFC- Rostral pre-frontal cortex

VENs- Von Economo’s neuron

VOG- Vein of Galen

VN- Visual network

IEC Approval form

श्री चित्रा तिरुनाल आयुर्विज्ञान और प्रौद्योगिकी संस्थान, त्रिवेन्द्रम
तिरुवनन्तपुरम - ६९५०११, केरल, इंडिया
SREE CHITRA TIRUNAL INSTITUTE FOR MEDICAL SCIENCES AND TECHNOLOGY, TRIVANDRUM
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Institutional Ethics Committee
(IEC Regn No. ECR/189/Inst/KL/2013/RR-16)

SCT/IEC/1240/AUGUST-2018 28.08.2018

Dr. Sabarish S S
Resident
Department of IS & IR
SCTIMST, Thiruvananthapuram

Dear Dr. Sabarish,

The Institutional Ethics Committee reviewed and discussed your application to conduct the study entitled "ROLE OF RESTING STATE FUNCTIONAL MAGNETIC RESONANCE IMAGING IN PATIENTS WITH DURAL ARTERIOVENOUS FISTULA (IEC/1240)" on 17th August, 2018.

The following documents were reviewed:

Original submission

1. *Covering letter addressed to the IEC, SCTIMST dated 18.07.2018 with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Declaration Form*
7. *Patient Information Sheet and Consent Form in English and Malayalam*
8. *CV of Principal Investigator and Co- Principal Investigators*

Revised submission

1. *Covering letter addressed to the IEC, SCTIMST dated 23.08.2018 with checklist*
2. *TAC Approval Letter*
3. *IEC Application Form*
4. *Project Proposal*
5. *Proforma*
6. *Declaration Form*
7. *Forwarding Letter from the HOD*
8. *Patient Information Sheet and Consent Form in English and Malayalam*
9. *CV of Principal Investigator and Co- Principal Investigators*

The following members of the Ethics Committee were present at the meeting held on 17th August, 2018 at G. Parthasarathi Board Room, AMCHSS, SCTIMST

SL. No.	Member Name	Highest Degree	Gender	Scientific /Non Scientific	Affiliation with Institution(s)
1.	Dr. R V G Menon	M Tech, PhD	Male	Lay Person (Chairman)	No
2.	Dr. V. Raman Kutty	M D, M Phil, M P H	Male	Health Sciences Expert/Clinician	Yes
3.	Dr. K R S Krishnan	M.E., Ph.D.	Male	Medical Technology	Yes
4.	Dr. Rema M. N	MD	Female	Basic Medical Scientist	No
5.	Dr. Mala Ramanathan	PhD	Female	Social Scientist (Member Secretary)	Yes

IEC Decision

The IEC approved the conduct of the study in the present form.

Remarks:

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information/informed consent and asks to be provided a copy of the final report.

There was no member of the study team who participated in voting / decision making process. The ethics committee is organized and operated according to the requirements of Good Clinical Practice and the requirements of the Indian Council of Medical Research (ICMR).

Sincerely,

Mala Ramanathan
Member Secretary, IEC