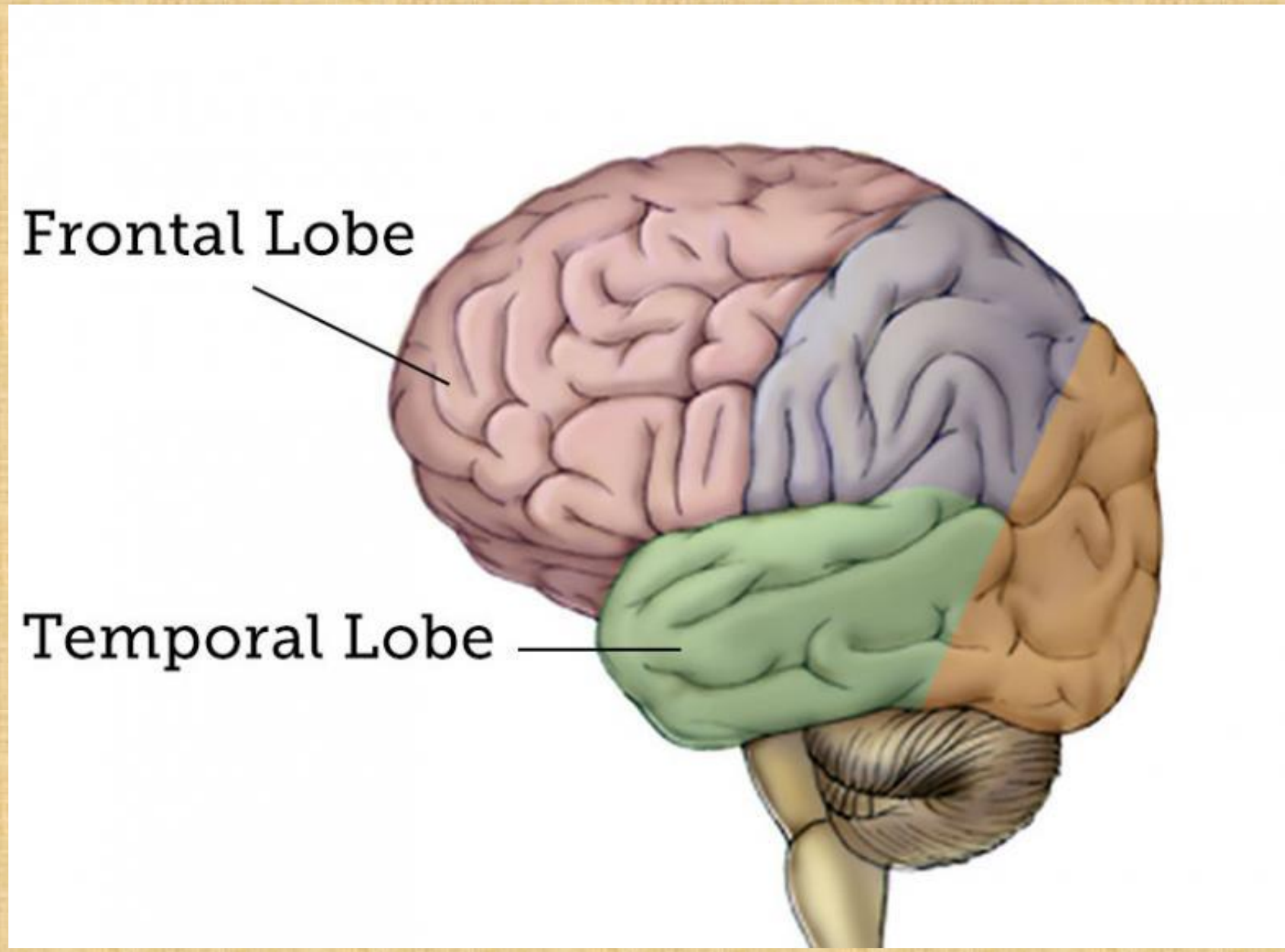
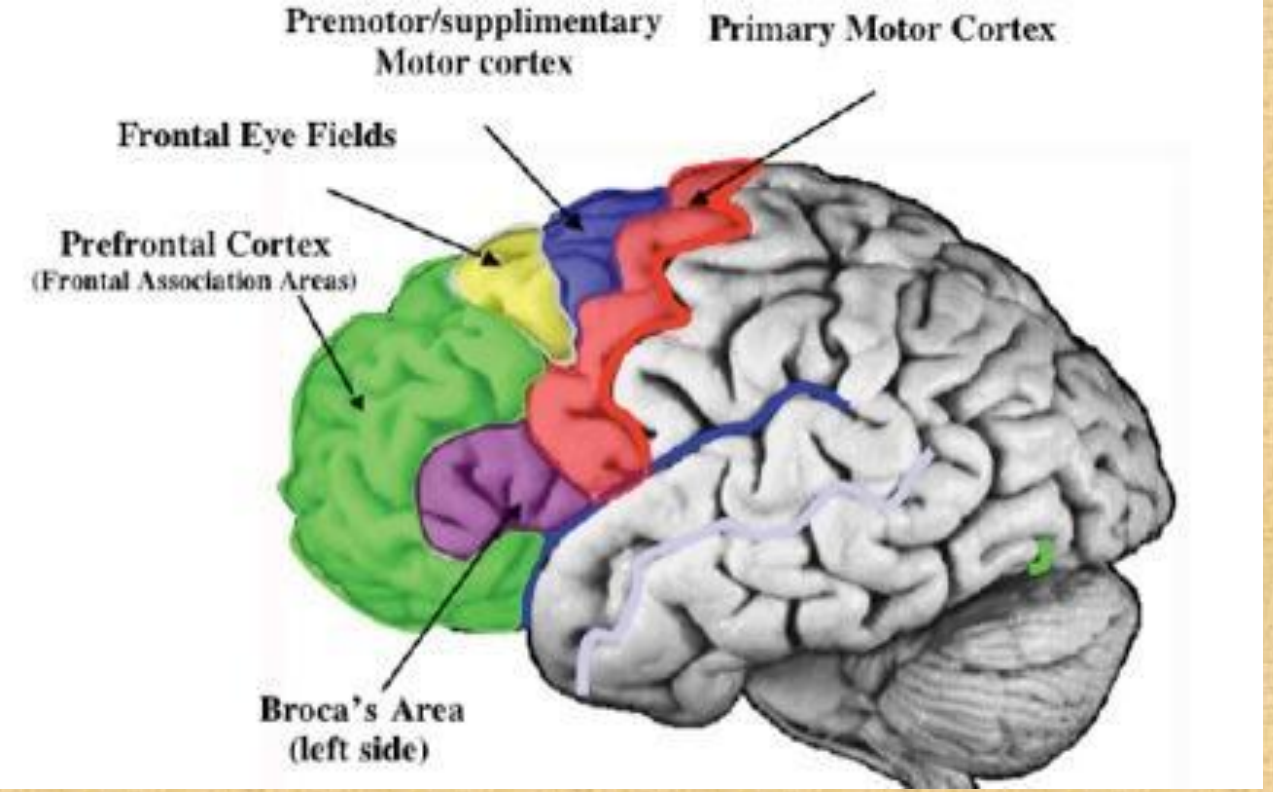
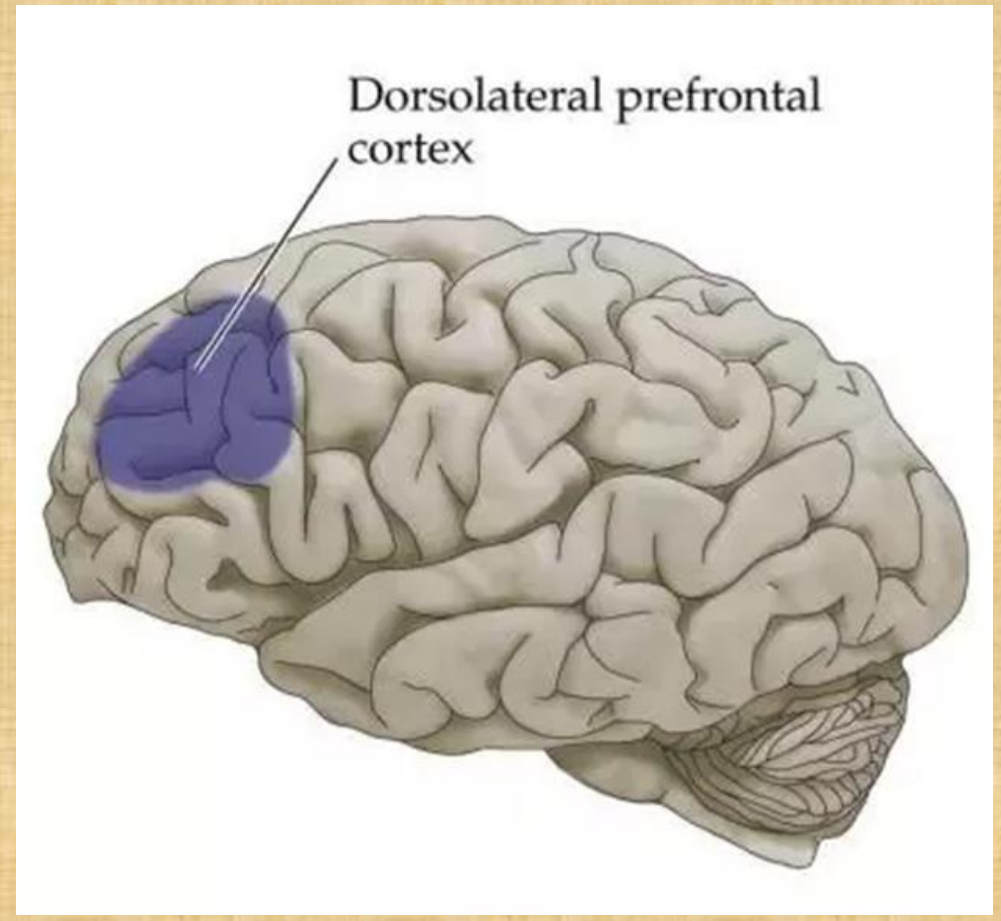
FRONTO-TEMPORAL DEMENTIA

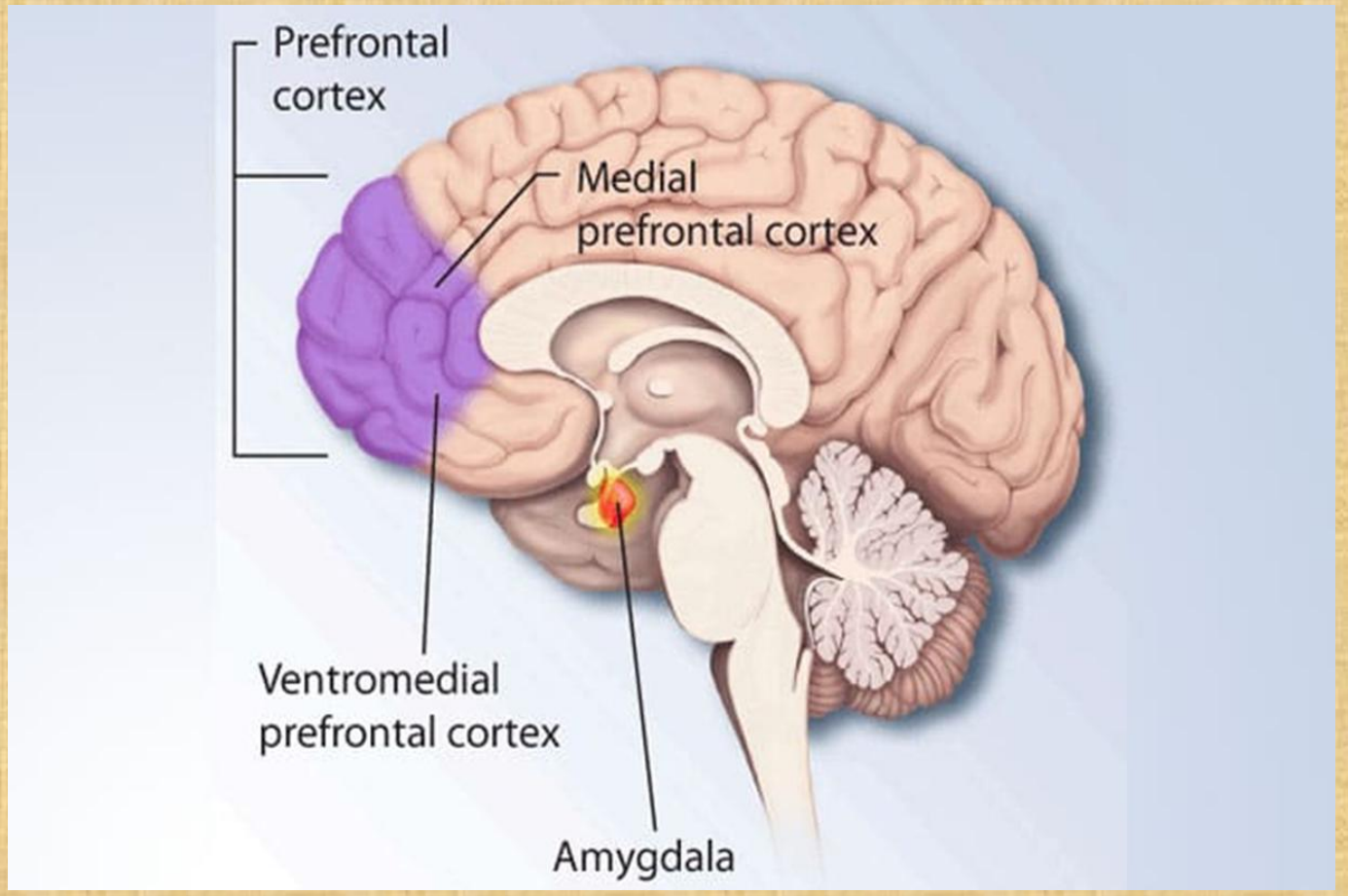
CHALLENGES IN DIAGNOSIS

Department of Psychiatry
BARC Hospital
Anushaktinagar


Frontal Lobe
Temporal Lobe


Premotor/supplimentary
Motor cortex
Primary Motor Cortex
Frontal Eye Fields
Prefrontal Cortex
(Frontal Association Areas)
Broca's Area
(left side)

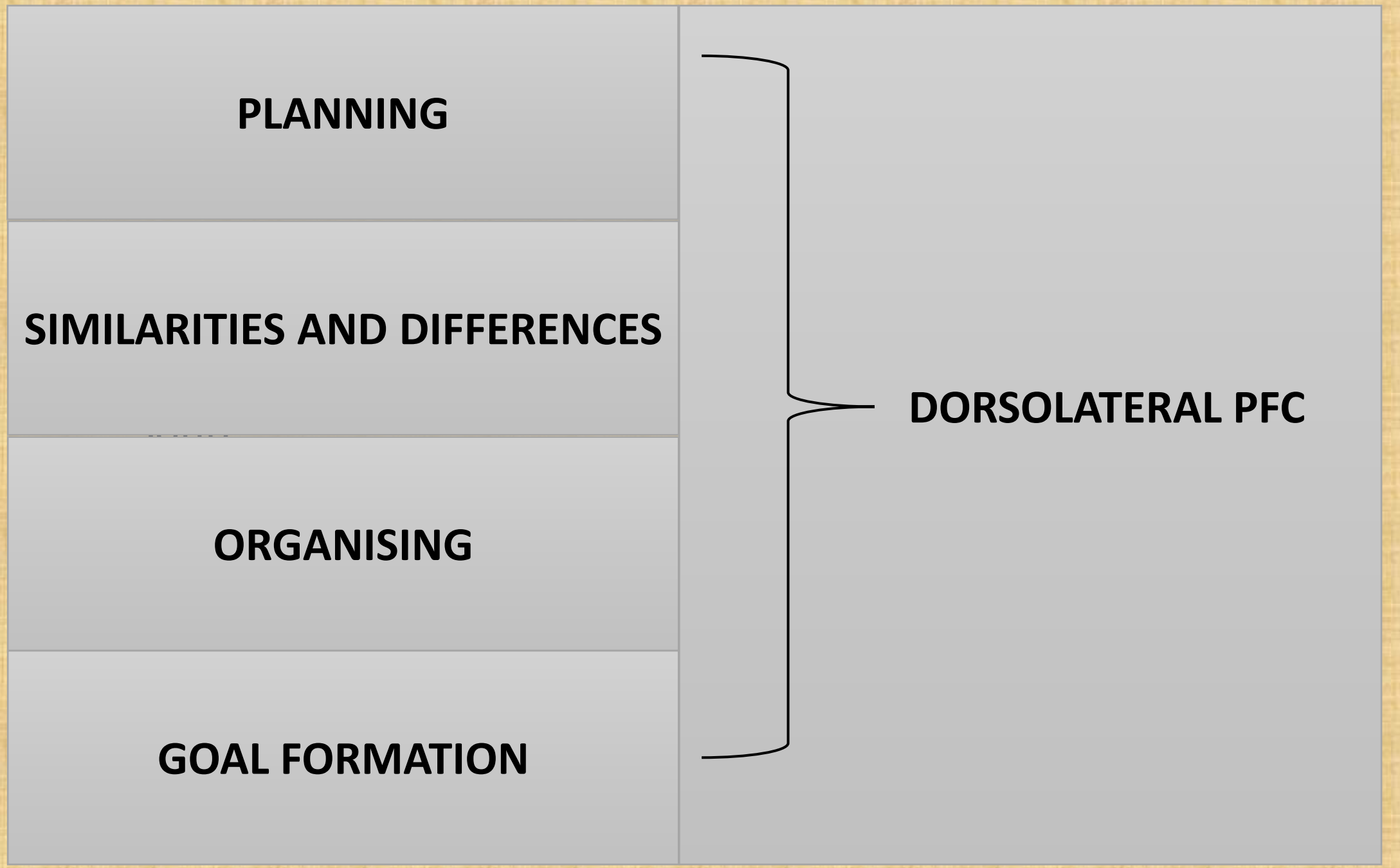

Dorsolateral prefrontal
cortex

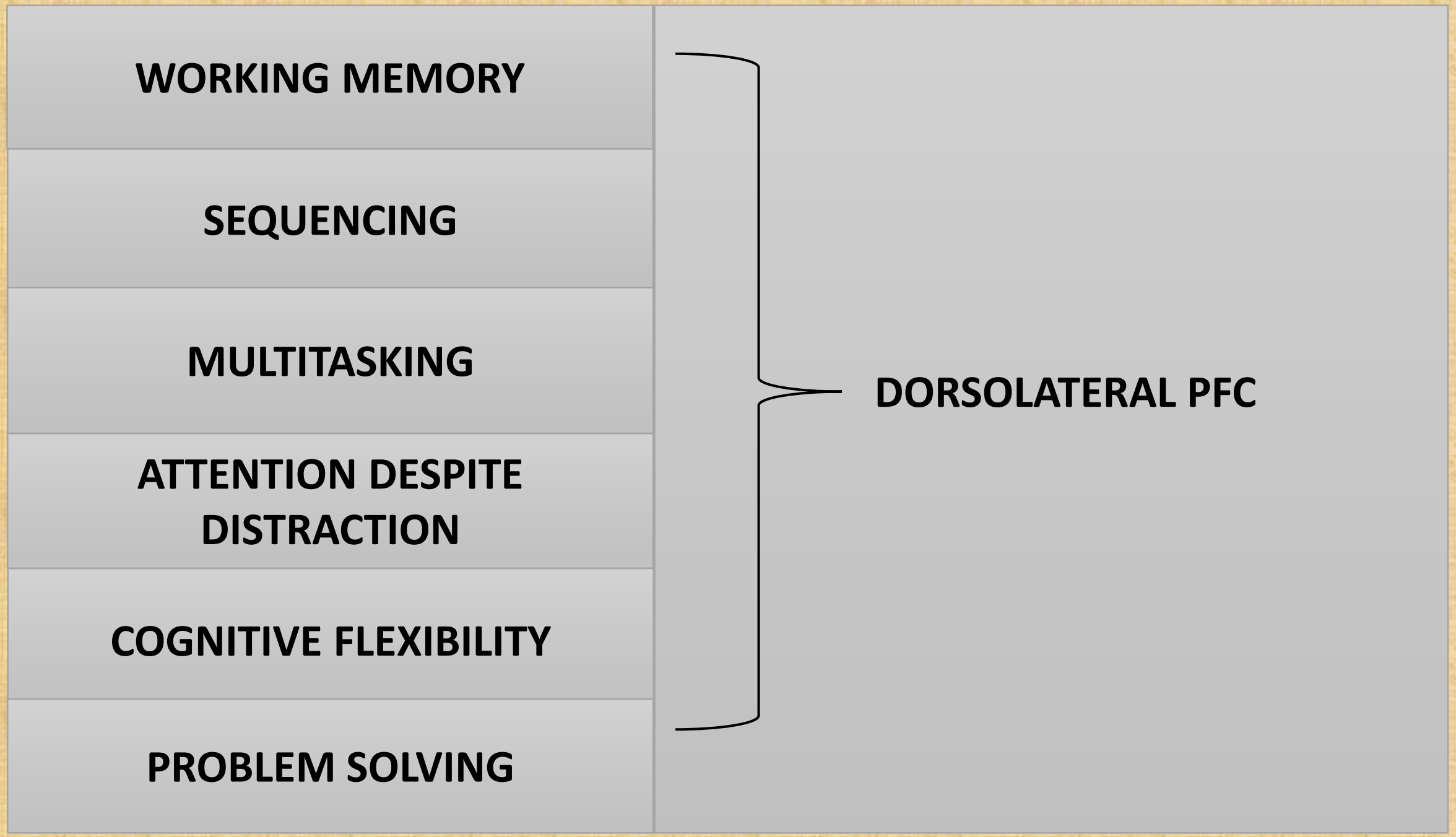

Prefrontal
cortex
Medial
prefrontal cortex
Ventromedial
prefrontal cortex
Amygdala

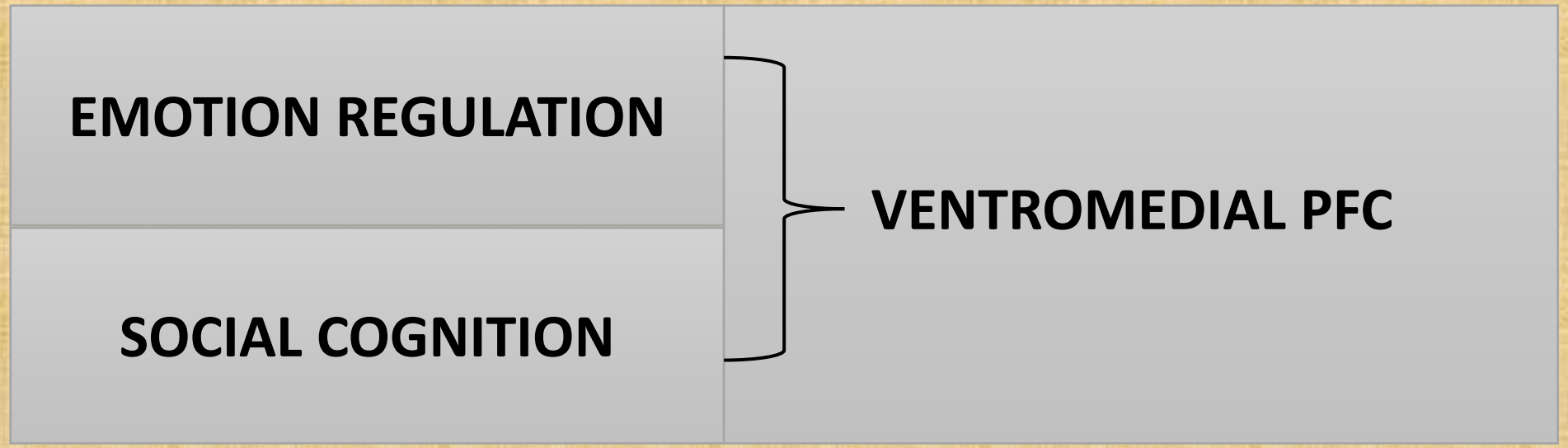
PLANNING

Menu:

- Masala Papad
- Salad
- Soup
- ? Starter
- Paneer Tikka Masala
- Butter Roti
- Custard

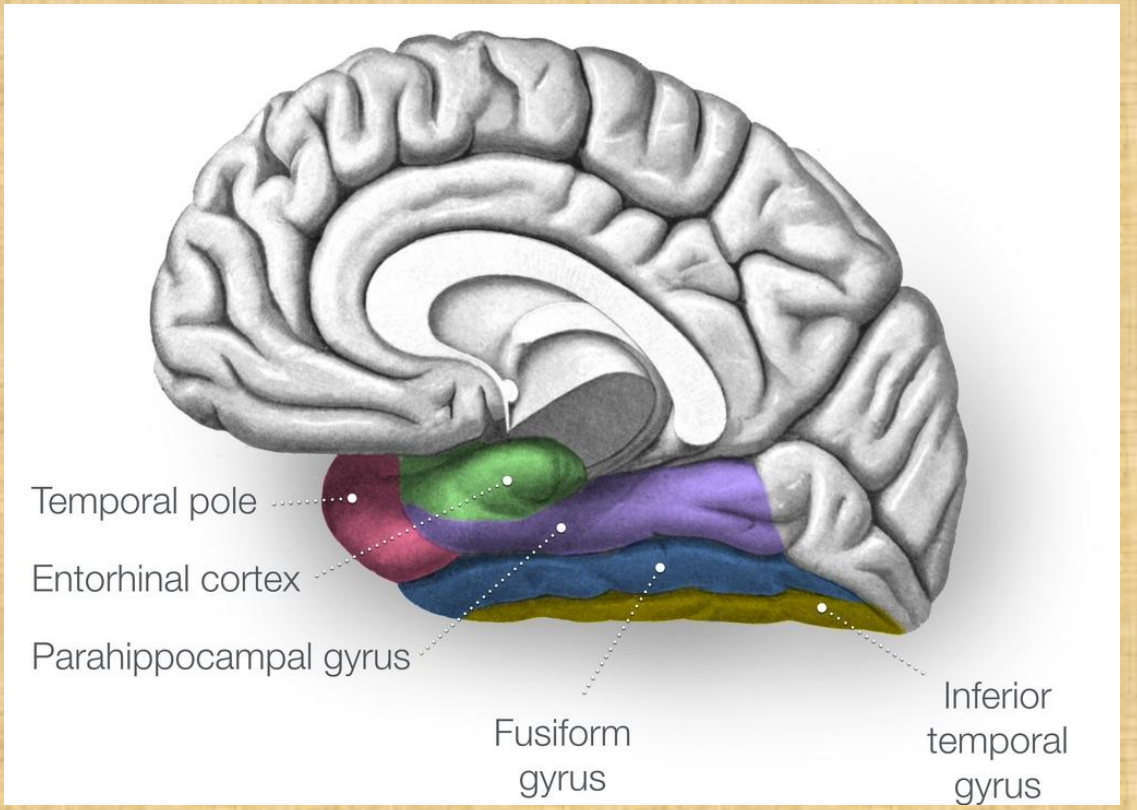

PLANNING
SIMILARITIES AND DIFFERENCES
ORGANISING
GOAL FORMATION
DORSOLATERAL PFC


WORKING MEMORY
SEQUENCING
MULTITASKING
ATTENTION DESPITE DISTRACTION
COGNITIVE FLEXIBILITY
PROBLEM SOLVING
DORSOLATERAL PFC


EMOTION REGULATION
SOCIAL COGNITION
VENTROMEDIAL PFC

Temporal Lobe

- Medial temporal lobe – Episodic memory
- Anterior temporal lobe – Semantic memory, language processing and social cognition



Episodic memory:

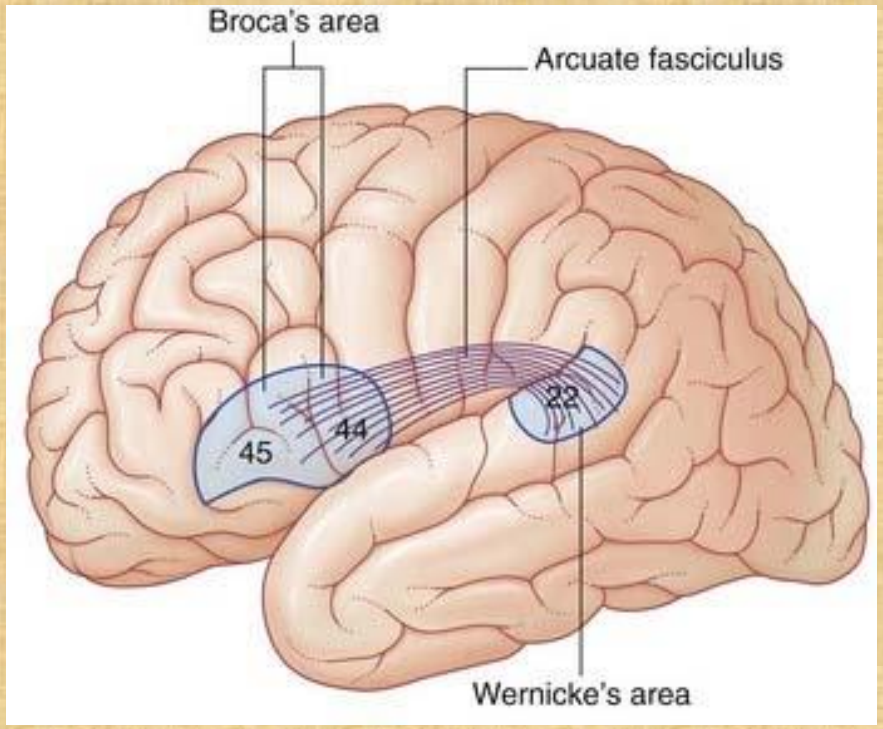
Long term memory that involves the recollection of specific events, situations and experiences.

Semantic memory:

Long term memory that includes knowledge of facts, meaning of words and objects, ideas, and concepts.

Fronto-temporal connections

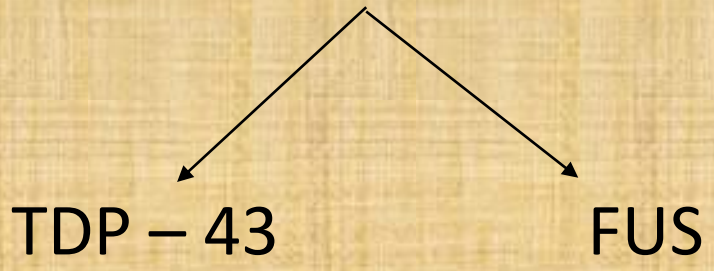
- Broca's area – Inferior frontal gyrus (speech production)
- Wernicke's area – Superior temporal gyrus (speech comprehension)



What happens in FTD?

- Neuronal loss, gliosis and microvacuolar changes

- Intracytoplasmic inclusions
  - TAU positive
  - TAU negative but Ubiquitin positive



Proteins involved

- Microtubule associated protein TAU (MAPT)
- Transactive response DNA binding protein (TDP-43)
- Tumour-associated protein fused in sarcoma (FUS)

FTD – TAU	FTD – TDP-43	FTD – FUS
Approx. 45%	Approx. 50%	Approx. 5%
Pick bodies	4 types of TDP-43	Early onset FTD
bvFTD, PSP	nfvPPA, svPPA, MND	Severe disinhibition, psychosis
MAPT mutation	C9orf72 and GRN gene mutations	Severe striatal atrophy

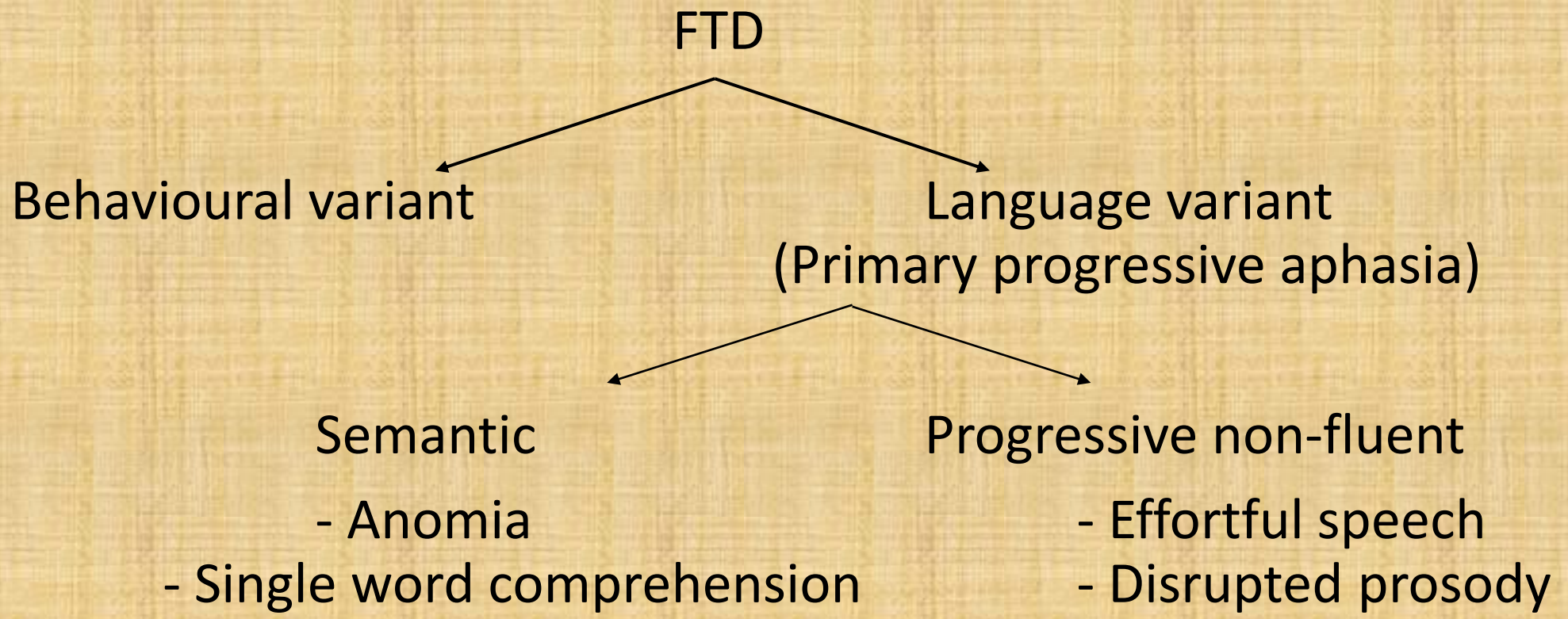
Genetics

- 30-50% cases are familial (Kurz et al., 2014)
- Autosomal Dominant transmission
- Genes involved:
    i. Gene for microtubule associated protein tau (MAPT)
    ii. Chromosome 9 open reading frame 72 (C9orf72)
    iii. Progranulin (GRN)
    iv. Charged multivescicular body protein 2B (CHMP2B)
    v. Valosin containing proteins (VCP)

Risk factors

- Diabetes
- Hypertension
- Smoking
- Obesity
- Dyslipidemia

Variants


FTD
Behavioural variant
Language variant
(Primary progressive aphasia)
Semantic
- Anomia
- Single word comprehension
Progressive non-fluent
- Effortful speech
- Disrupted prosody

Diagnostic criteria

(A) The criteria are met for major or mild neurocognitive disorder

(B) The disturbance has insidious onset and gradual progression.

(C) Either of (1) or (2)

(1) **Behavioural variant**

(a) Three or more of the following behavioural symptoms

i. Behavioural disinhibition

ii. Apathy or inertia

iii. Loss of sympathy or empathy

iv. Perseverative, stereotyped or compulsive/ritualistic behaviour

v. Hyperorality and dietary changes

(b) Prominent decline in social cognition and/or executive abilities

(2) **Language variant**

(a) Prominent decline in language ability, in the form of speech production, word finding, object naming, grammar or word comprehension.

(D) Relative sparing of learning and memory and perceptual motor functions

(E) The disturbance is not better explained by cerebrovascular disease, other neurodegenerative disease, the effects of substance or another mental, neurological or systemic disorder.

Overlapping syndromes

- Corticobasal syndrome (CBS)
- Progressive supranuclear palsy (PSP)
- Amyotropic lateral sclerosis (ALS)

Prognosis and Survival

- 6-11 years
- Rapid deterioration in FTD associated with MND

Case 1

- Mrs P, 48 year old , Hindi speaking, right handed, married female
- Education-5 th std
- Homemaker

Brought by husband and son with c/o

- Inappropriate laughing and crying
- Abnormal and repetitive behaviour
- Irrelevant talk
- Restlessness

3 MONTHS

- Taken to a private psychiatrist ---- started on antipsychotics
- Symptoms deteriorated with antipsychotics
- Developed severe Parkinsonian features

Clinical Features

- Repeating same questions
- Very anxious on minor issues
- Used to severely panic at times
- Very fearful in crowded places
- Interaction with others decreased
- Not bathing or grooming properly
- Would be roaming in home at night

- Pre morbid personality- Introvert , religious, anxious temperament
- No h/o fall, confusional episodes or visual hallucination
- No family history of dementia.
- No past history of any psychiatric illness

Physical examination

- ✓ Thin built
- ✓ Vitally stable
- ✓Severe EPR (Rigidity, akinesia,mild tremors)
- ✓ Severe motor restlessness (akathasia)
- ✓ CNS Examination - WNL
- ✓Systemic examination -WNL

Mental Status Examination

- Attention - Impaired
- Mood - Sad
- Mask like face with inappropriate grin
- Speech - slow, laboured with abnormal prosody.

  Comprehension was impaired , naming was intact

  Echolalia , Perseveration - present
- Thought- delusion or depressive cognition could not be elicited

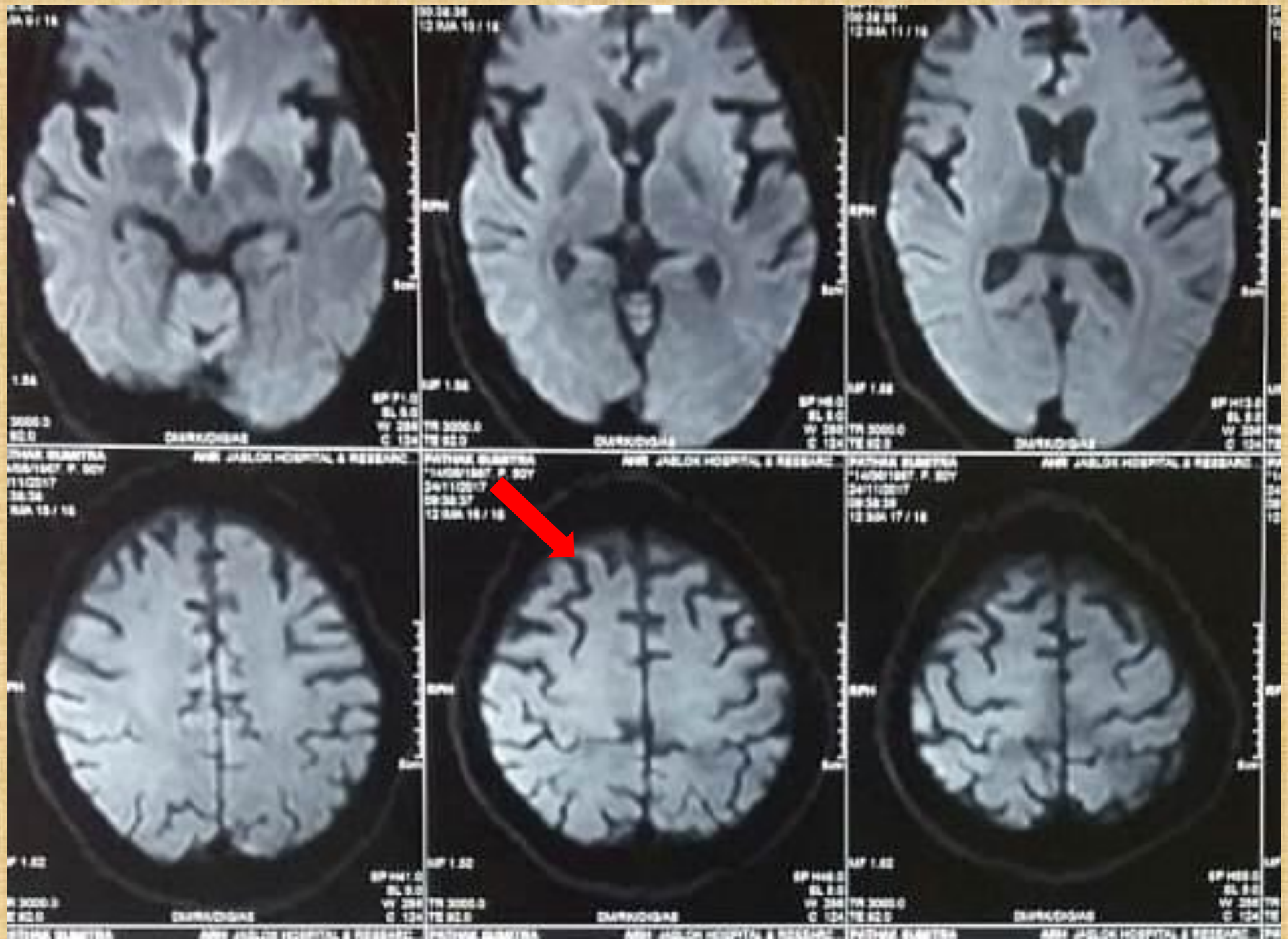
- No perceptual abnormality
- Oriented to T/P/P
- Immediate memory- Reg-2/3 Recall- 0/3
- Recent and remote memory was fairly intact
- Judgement - Impaired
- Insight - Absent

- CT Brain was done to rule out vascular etiology or Intracranial Space Occupying lesion
- Provisional diagnosis -

  Fronto-temporal dementia with drug induced parkinsonism and akathisia

MRI

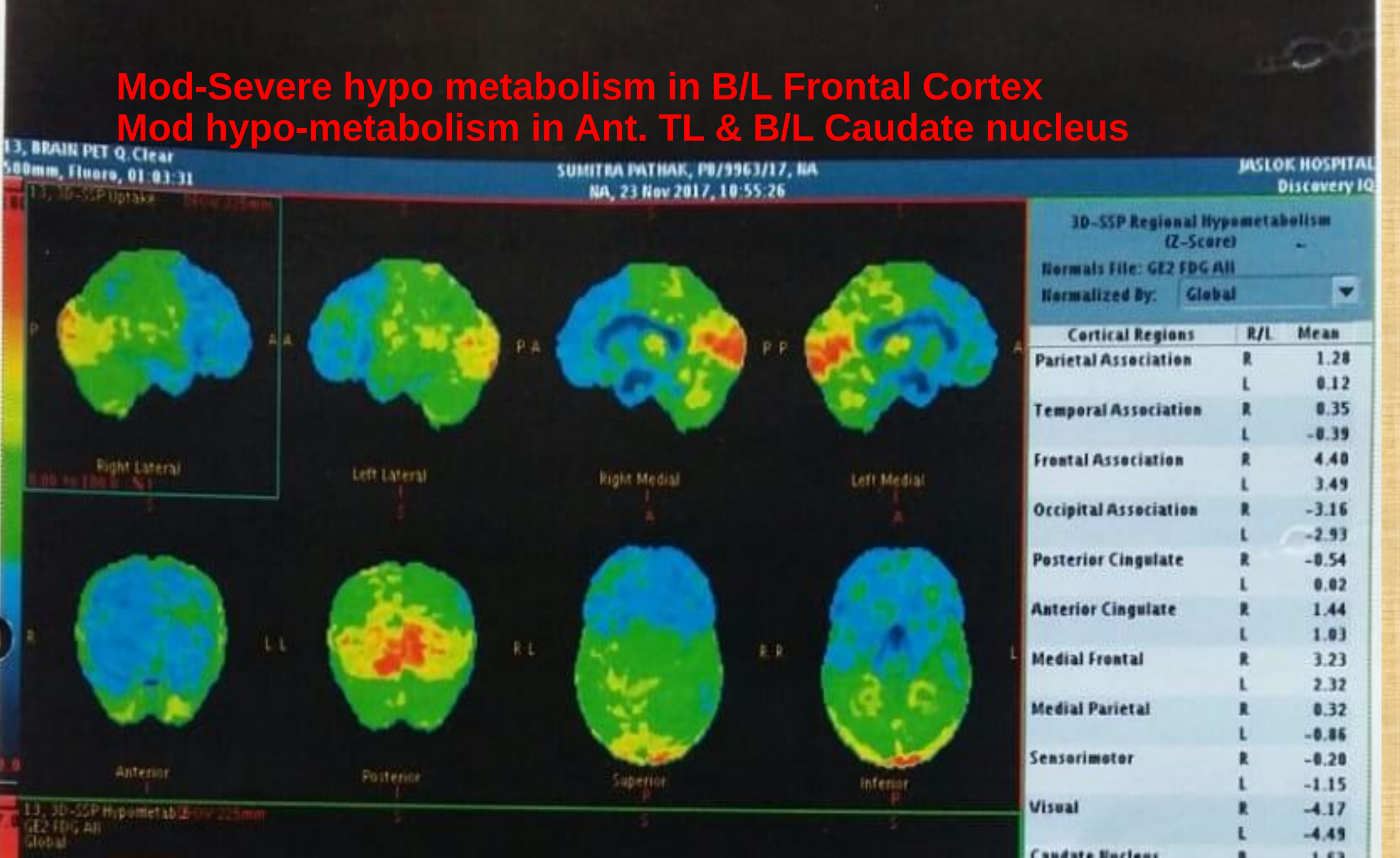
- Atrophy of Frontal and Temporal lobe with widening of lateral and third ventricle
- Loss of differentiation between Pars Reticulata and Pars Compacta, findings may be seen in Parkinsons disease



Treatment

- T. Syndopa 125 mg ½ TDS
- T. Quetiapine 25 mg raised to 37.5 mg
- C Rivastigmine 1.5 mg BD hiked to 4.5 mg

Mod-Severe hypo metabolism in B/L Frontal Cortex
Mod hypo-metabolism in Ant. TL & B/L Caudate nucleus



Cortical Regions	R/L	Mean
Parietal Association	R	1.28
	L	0.12
Temporal Association	R	0.35
	L	-0.39
Frontal Association	R	4.40
	L	3.49
Occipital Association	R	-3.16
	L	-2.93
Posterior Cingulate	R	-0.54
	L	0.02
Anterior Cingulate	R	1.44
	L	1.03
Medial Frontal	R	3.23
	L	2.32
Medial Parietal	R	0.32
	L	-0.86
Sensorimotor	R	-0.20
	L	-1.15
Visual	R	-4.17
	L	-4.49
Caudate Nucleus	R	1.53

Factors pointing towards FTD

- ✓Young age of onset
- ✓Rapid progress
- ✓Behavioural/psychotic symptoms
- ✓Language impairment (speech apraxia)
- ✓Executive dysfunction
- ✓Intolerance to psychotropics

I DON’T FEEL & NEITHER DO I CARE

Case 2

- Mr D, 59yr married male, Education-10th std, Electrician
- Chief complains-
  - Fearfulness
  - Decreased Communication
  - Decreased sleep

  } Since 1.5 years (age of onset of symptoms 57 y)

- Stressor- Altercation with Elder Brother

Clinical features

- Decreased communication
- Decreased interest
- Avoid going for walk or meeting friends
- Peep out of window
- Decreased sleep

- Family history of psychosis in elder brother
- No past psychiatric illness
- No substance use
- Pre morbid personality-

  Social, Extrovert, Bright and Cheerful, Adjustable, Foresighted

MSE

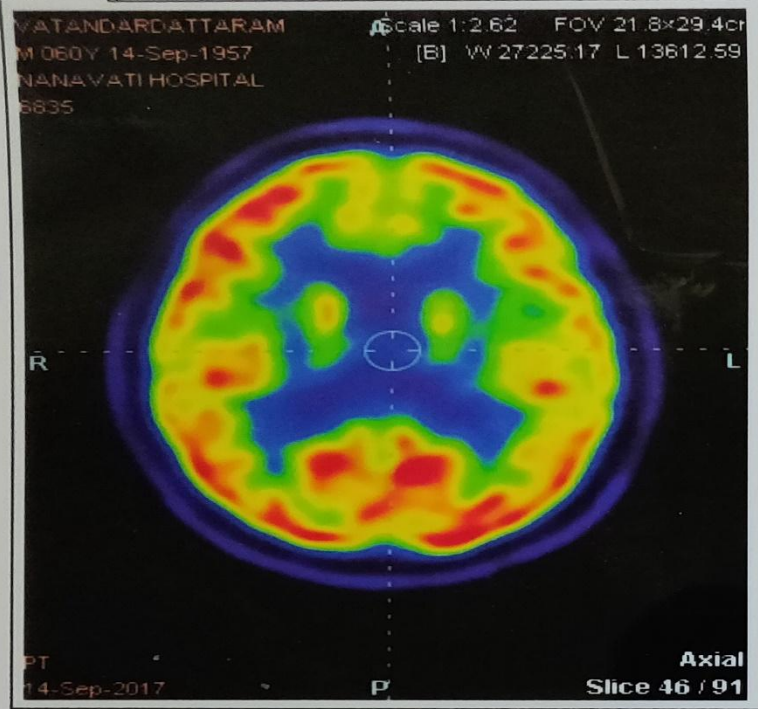
- Well dressed & well groomed
- Conscious, not very co-operative, minimally communicating, Very guarded, psychomotor retardation noted
- Attention-Active- aroused, not well sustained
- Passive attention- heightened
- Rapport- established with difficulty
- Mood: okay. Affect: anxious and restricted in range
- Speech and thought- decreased speech output, low volume,
- Could not elicit any depressive cognition, delusion or suicidal ideation.
- Memory-immediate, recent, remote -intact
- No perceptual abnormality
- Absent insight

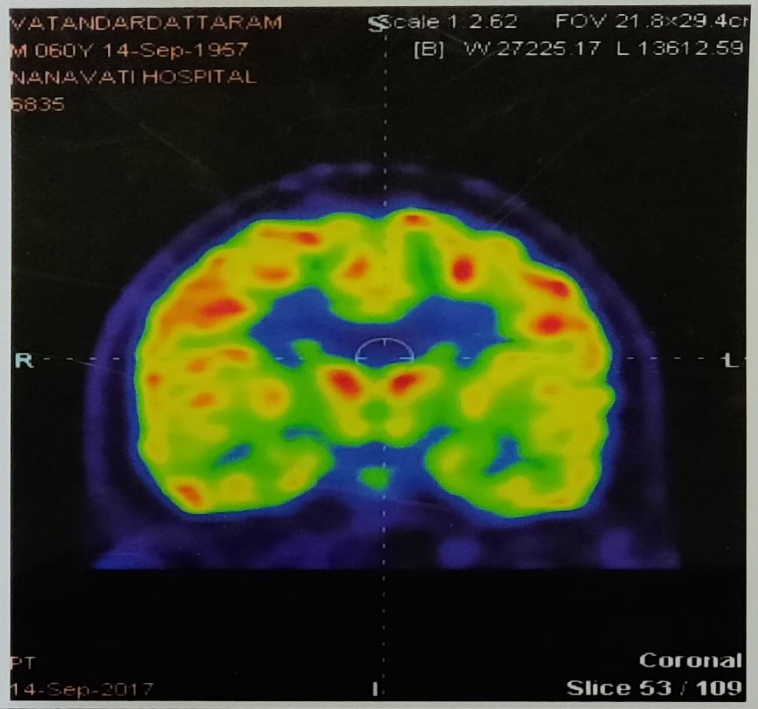
Case review-

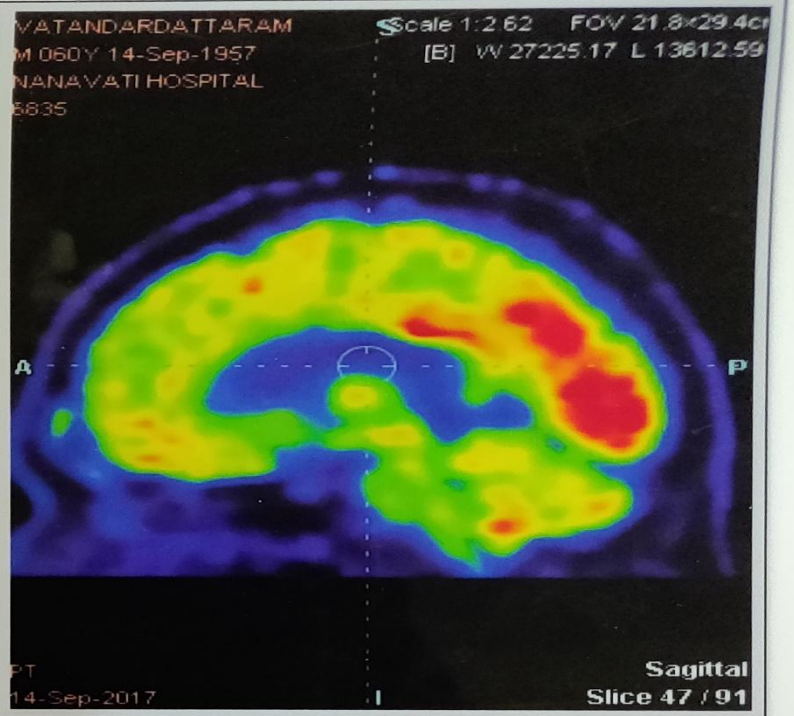
- Rigid pattern in daily routine
- Change in pre morbid-personality- Rigid, Stingy, Insensitive, Asocial

- **MMSE**- 26/30
- **FAB**- 15
- **ACE**- 86/100 -Attention 17/18
  Memory 18/26
  Fluency 10/14
  Language 25/26
  Visual-spatial orientation- 16/16
- **FDG-PET**- Reduced FDG uptake in B/L mesial temporal structures
  Diffuse Cortico-cerebral atrophy
  Reduced FDG uptake in left cerebellar hemisphere

Uptake | Cortical Uptake



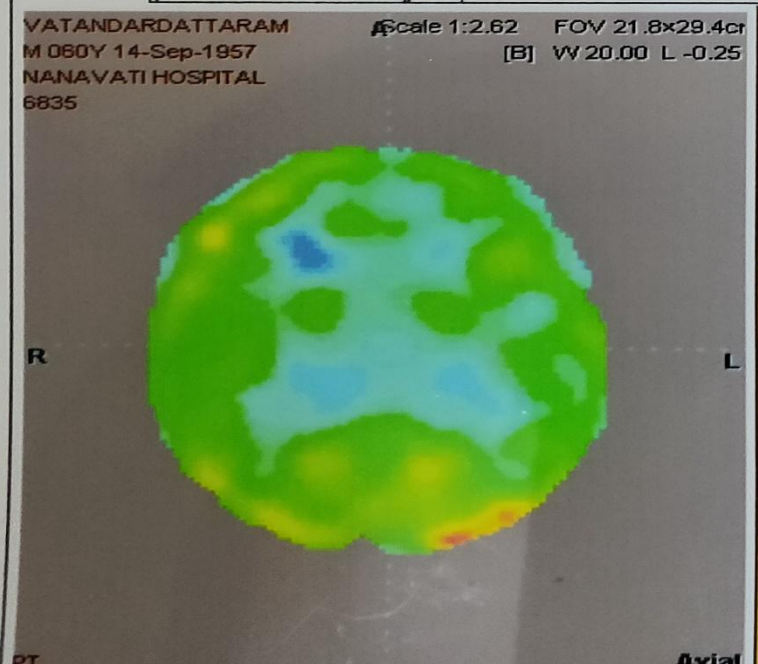


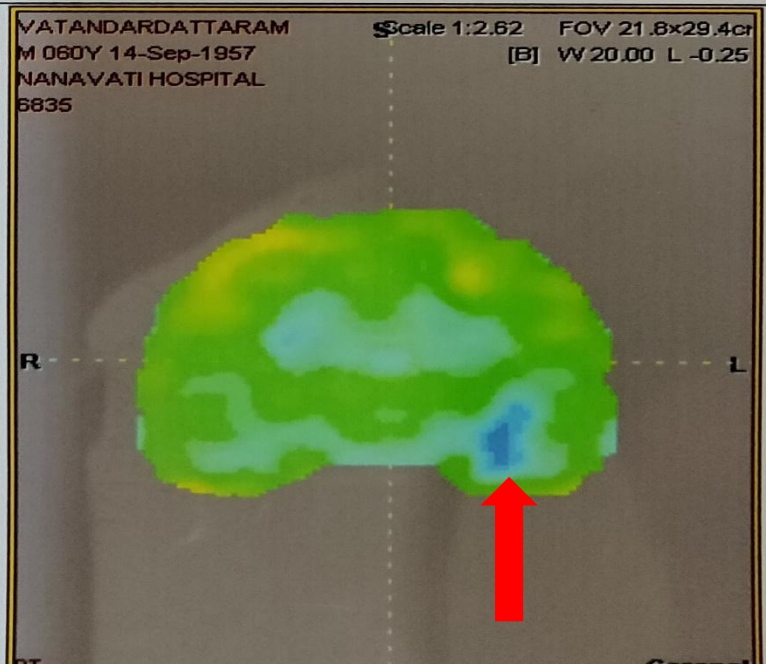


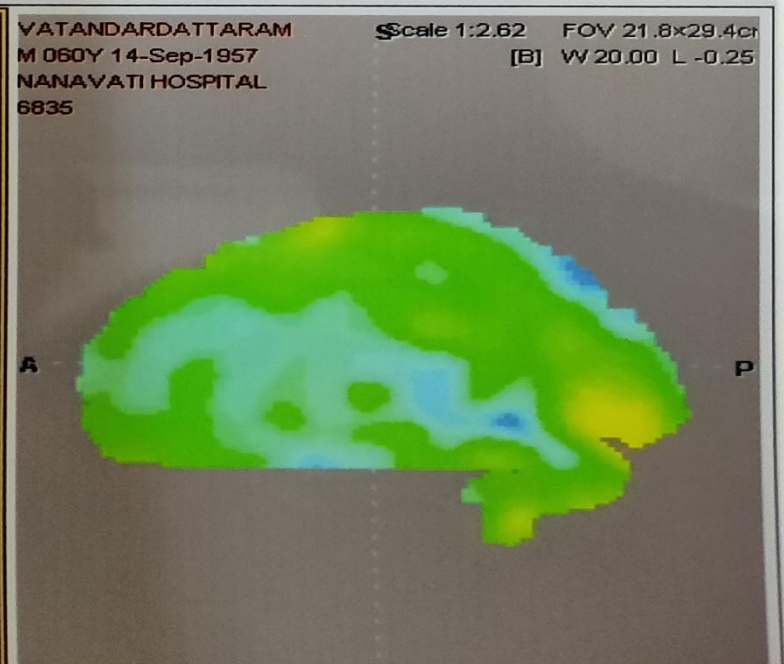
4 6 8

SUV	Mean # St...
6.26	-0.7
6.57	0.6
6.29	-0.9
6.42	-0.0
6.73	0.2
6.52	0.1
5.78	-1.2
5.51	-1.3
6.55	0.9
6.72	2.0
7.47	2.0
7.14	1.4
8.30	2.1
7.53	0.6
5.97	-0.4
6.59	0.3
4.31	-3.7
4.56	-2.3
5.72	-3.0
5.78	0.1

Statistics | Cortical Statistics | CT







Pointers towards FTD

- ✓Insidious onset
- ✓Gradual progression
- ✓Apathy
- ✓Loss of empathy
- ✓Change in personality
- ✓Decline in executive abilities
- ✓Sparing of Memory

Case 3

- Mrs C,67yr/F, married, BSc, telephone operator
- K/c/o paranoid Schizophrenia since 30yrs, on Tb Trifluperazine 10mg,Tb Trihexiphenidyl 4mg,Tb Amisulpride 100mg

- c/o worsening of abnormal behavior

  excessive eating since 1 ½ yrs

  repetitive actions (insidious, progressive)

  reduced self care

- Decreased interest in activities
- Difficulty in executive functions
- Repetitive activities
- Disinhibiton
- Dependant for ADL
- Reduced self care

- Shown to Pvt psychiatrist but no improvement
- Admitted- MRI done, diagnosed as FTD
- Tb Donepezil 10 mg,Tb Trifluperazine 1mg,Tb Clozapine 12.5mg

- Further deterioration of all symptoms with excessive eating food & drinking of water, continuous irrelevant talk, incontinence

MSE

- Conscious, minimally co-operative
- Attention : Active- arousable , ill sustained
  Passive - heightened
- ETEC : Initiated not maintained,
- Rapport : difficult to establish
- Mood : ok, shallow affect
- Speech: reduced spontaneous, poverty of content, no language impairment, occasional irrelevant
- Thought: No delusion
- No perceptual abnormality
- Immediate Memory : Reg- 3/3, Recall- 0/3
- Recent & remote memory : intact
- Orientation : Time/place/person present
- Judgment & concept : impaired
- Insight : absent

- Frontotemporal Dementia in case of Schizophrenia
- Stopped Donepezil, Trifluperazine,Clozapine
- Started on
  - Risperidone 2mg ➡ 4mg
  - Qutipin 100mg ➡ 400mg
  - Rivastigmine patch 4.5mg ➡ 9mg
- Improvement in behavioral problems

Pointers towards FTD

- Repetitive compulsive behaviors
- Hyperorality
- Disinhibition
- Impaired executive function

- Relative sparing of memory & visuospatial abilities

Summary

FTD and AD

- Detailed history
- In FTD:
  - Early age of onset
  - Relative sparing of memory
  - Stereotypical behaviours
  - Higher functional severity

FTD and Psychiatric disorders

Schizophrenia

- Symptoms similar to negative symptoms occur in FTD
- Positive symptoms less common in FTD
- Aphasia to be differentiated from irrelevant talk

Depression

- Apathy
- In FTD:
  - Lack of concern of symptoms
  - Normal mood
  - No feelings of guilt or thoughts of self-harm
  - No hopelessness or worthlessness

Treatment

- Cholinesterase inhibitors:
  - Rivastigmine – Improvement in behavioural and depressive symptoms (Moretti et al., in 2004)
  - Donepezil – Worsening of behavioural symptoms (Mendez et al., 2007; Kimura et al., 2013)
- NMDA receptor antagonist:
  - Memantine – Not effective (Boxer et al., 2013)

- SSRIs
  - Citalopram, Fluoxetine & Sertraline – Improvement in behavioural symptoms (Hermann et al., 2012; Anneser et al., 2007)

- Antipsychotics
  - Atypical
  - Quetiapine preferred
  - Watch for EPS, hypotension

- Others (? Benefit)
  - Syndopa
  - Pramipexole

Thank you