Executive functions and the dysexecutive syndrome

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What are executive functions?

They're functions that are deployed when control needs to be exerted

- Typically described as 'supervisory' or 'controlling'
- Deployed when a situation is novel or difficult
- When you need to pay attention because there isn't an automatic / habitual response to the problem or the automatic response would be inappropriate

  Example: *If your friend's mobile phone rings on the table, you don't normally pick it up and answer it, although you might under certain circumstances*

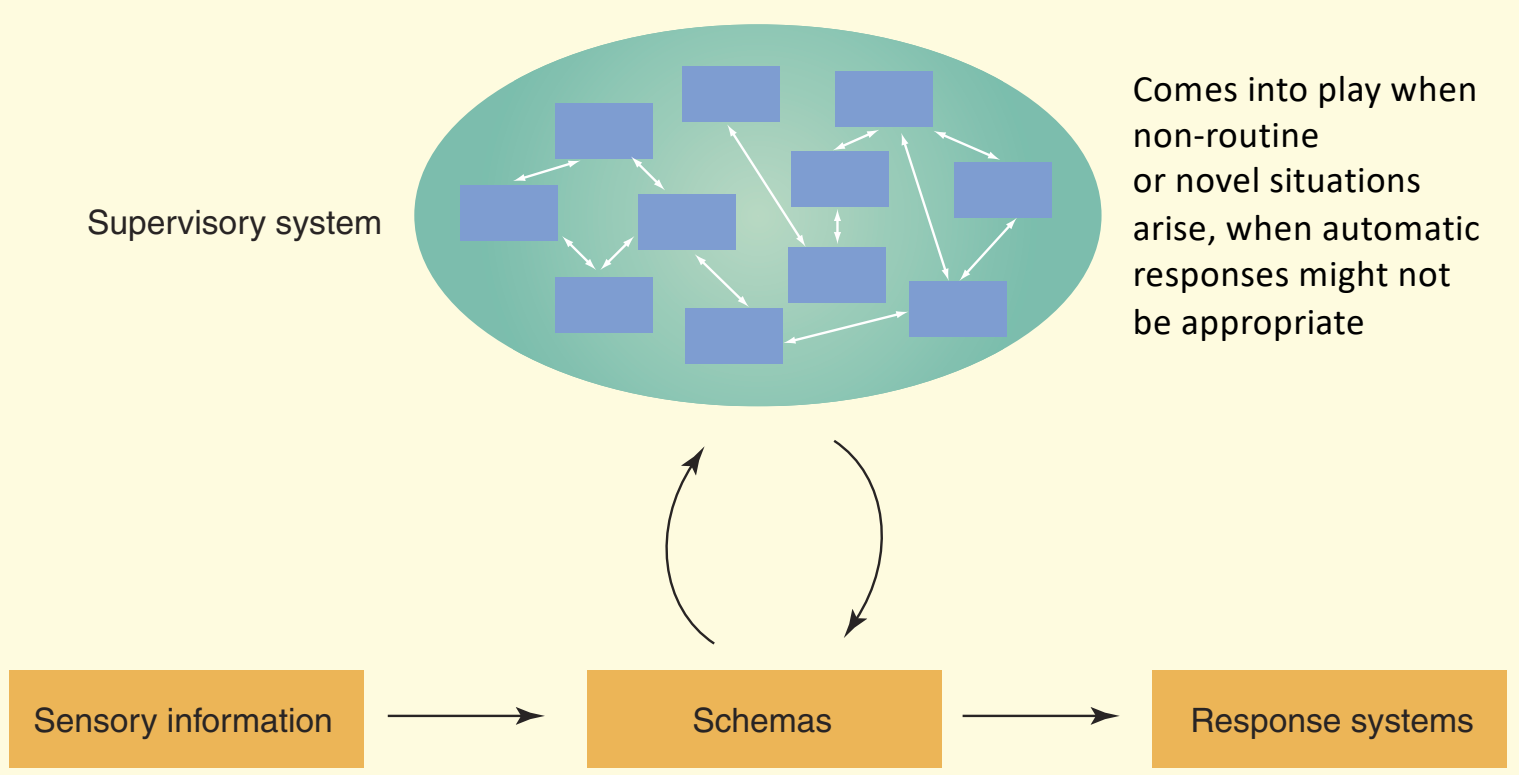
- When several cognitive processes need to be co-ordinated
- Or when you need to shift from one type of process to another





Supervisory attentional system model

A general model to explain executive functions | Norman and Shallice



Orchestration of behaviour

They're functions deployed when control needs to be exerted

- Initiate
- Maintain / Sustain / Invigorate / Energize
- Stop ongoing action / Inhibit prepotent response
- Monitor consequences of behaviour / error monitoring
- Switch to a different behavioural set / set shifting / mental flexibility
- Working memory: manipulation of items in short term memory
- Planning and prioritization
- Multi-tasking
- Social / emotional regulation
- Strategic retrieval and selection of information from episodic memory

When executive function breaks down

Executive function	Associated executive dysfunction	Clinical presentation / Behavioural disorder
Task initiation and energization	Reduced self-generated behaviours Procrastination	Akinetic mutism, abulia, apathy. Reduced fluency
Sustain attention / maintain actions	Poor ability to stay on task or sustain attention	Distractible
Response inhibition	Difficulty inhibiting behaviours Acting 'without thinking'	Disinhibited

Executive function tests

Executive function	Cognitive measure	Example of test
Task initiation and energization	Verbal fluency Non-verbal (e.g. design) fluency	Words beginning with F; designs joining four dots on a grid in a minute
Sustain attention / maintain actions	Sustained attention	Continuous performance test
Response inhibition	Inhibition of pre-potent response	Go / No Go; Stroop; Hayling tests

Executive function tests

Stroop task

Congruent condition	Incongruent condition
GREEN	BLUE
BLUE	RED
RED	GREEN
BROWN	BLUE

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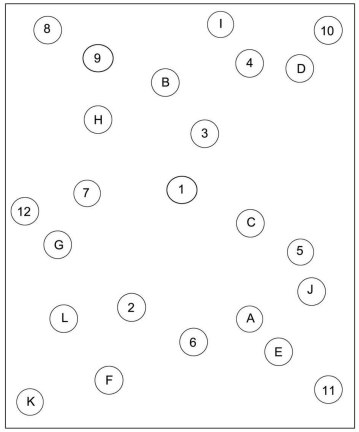
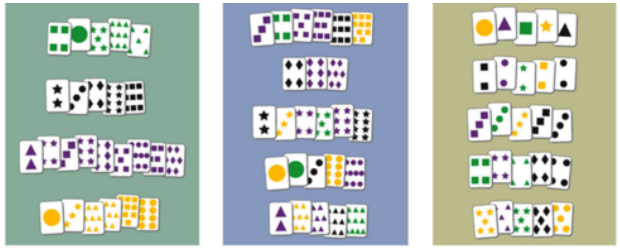
Trail making test B



Wisconsin Card Sorting Test



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Working memory	Verbal working memory forwards and backwards Visuospatial working memory forwards and backwards	Digit span (forwards and reverse) Corsi blocks (forwards and reverse)
Multi-tasking	Optimal allocation of time	Multiple errands; six elements tests
Planning and prioritization	Planning and problem solving	Tower of London / Tower of Hanoi tests

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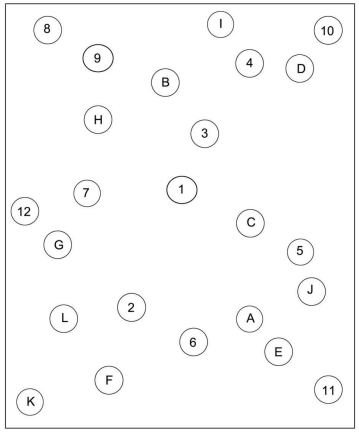

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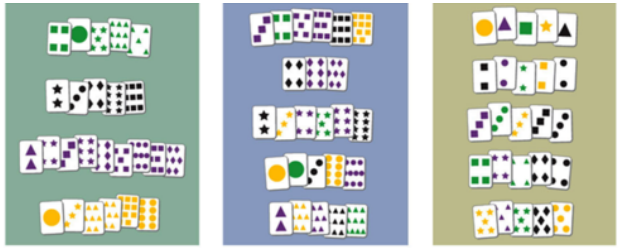

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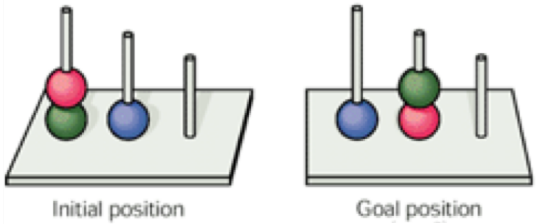
Tower of London



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Social / Emotion regulation	Ability to infer the thoughts of others	Tests of theory of mind

Theory of mind

Assessed for example using the Faux pas (breach of etiquette) test

Example:

Jill had just moved into a new apartment. Jill went shopping and bought some new curtains for her bedroom. When she had just finished decorating her apartment, her best friend, Lisa, came over. Jill gave her a tour of the apartment and asked, "How do you like my bedroom?"

"Those curtains are horrible" Lisa said, "I hope you are going to get some new ones!"

Q1 Did Lisa know the curtains were new?

Q2 Did someone say something they shouldn't have?

For example of findings in patients with frontal lobe dysfunction, see Torralva *et al* (2009) *Brain*

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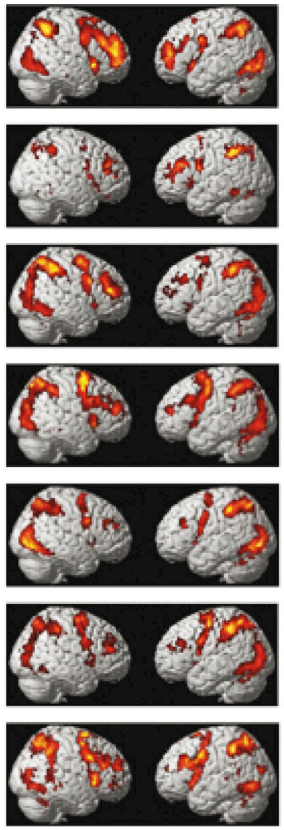
Strategic retrieval from episodic memory	Recall and recognition	Word list learning; source memory tests; autobiographical memory

Executive functions are not just ‘frontal’

Frontoparietal system – ‘Mulitple demand’ system – identified across studies

1



Hard vs easy contrasts

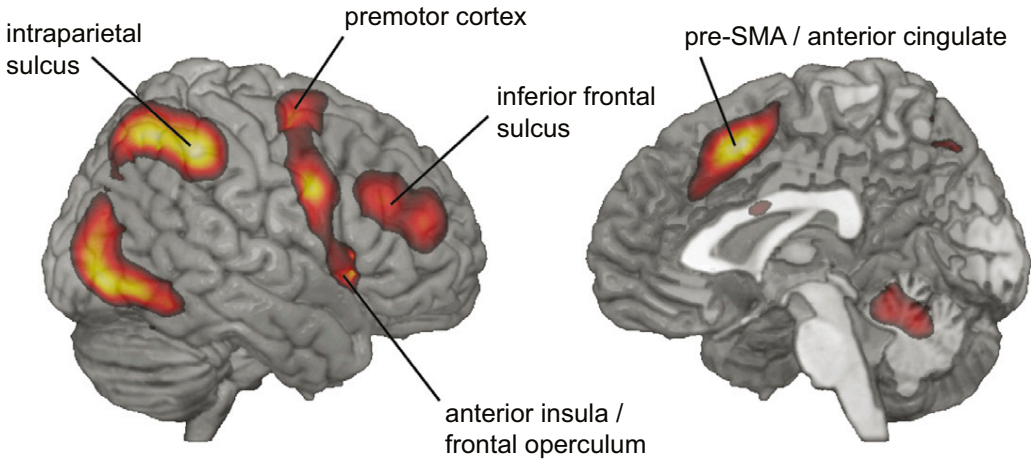
Remembering words / non-words

Arithmetic

Spatial working memory

Verbal working memory

Three different ‘conflict tasks’

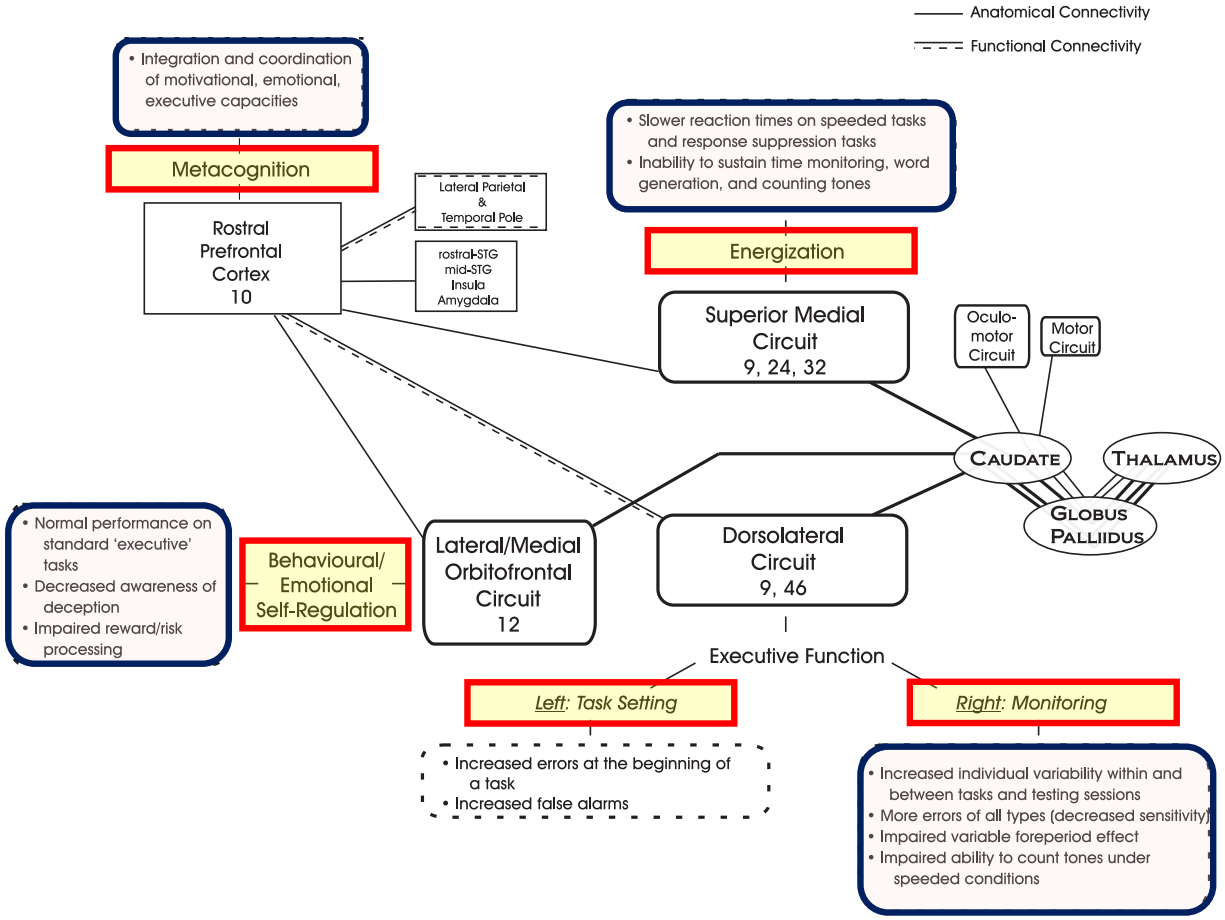


Duncan (2013) *Neuron*

Fractionation of the 'dysexecutive syndrome'

2

Different cognitive deficits associated with different frontal lesions

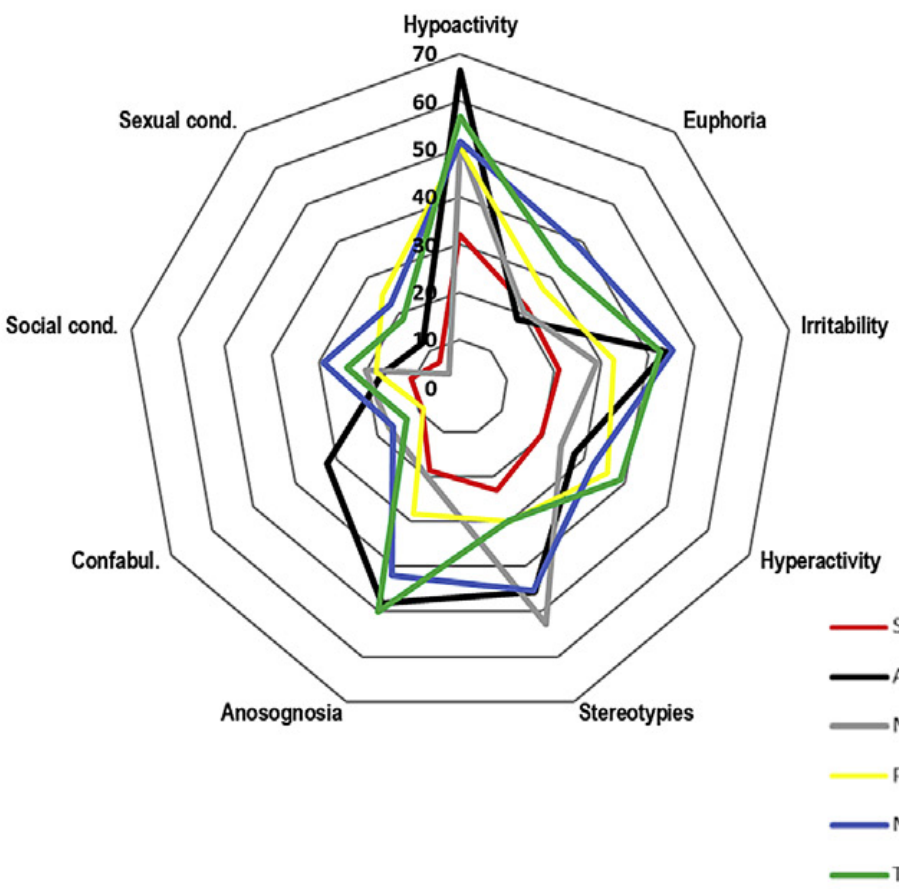


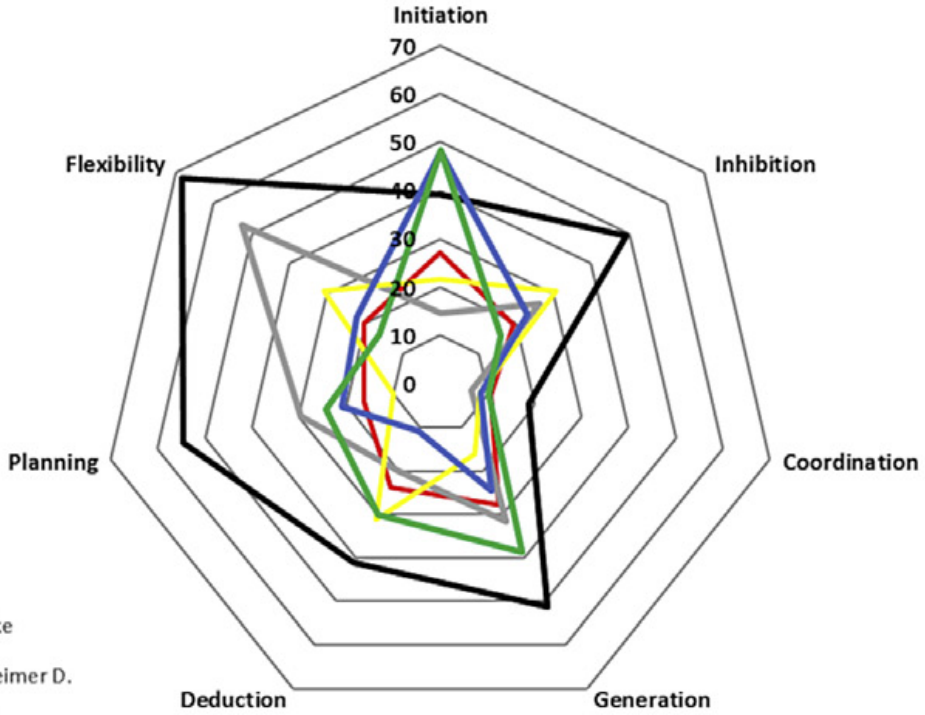
Stuss (2011) *J Int Neuropsyhcological Soc*

Fractionation of the 'dysexecutive syndrome'

2

Both behavioural and cognitive changes occur but not uniformly | Data from 828 patients





Godefroy *et al* (2018) *Cortex*

Behavioral variant frontotemporal dementia (bvFTD)

3

Associated with behavioural change and bilateral frontal atrophy

Possible bvFTD

Three of the features (A–F) must be present; symptoms should occur repeatedly, not just as a single instance:

A Early (3 years) behavioural disinhibition
B Early (3 years) apathy or inertia
C Early (3 years) loss of sympathy or empathy
D Early (3 years) perseverative, stereotyped, or compulsive/ritualistic behaviour
E Hyperorality and dietary changes
F Neuropsychological profile: executive function deficits with relative sparing of memory and visuospatial functions

Probable bvFTD

All the following criteria must be present to meet diagnosis:

A Meets criteria for possible bvFTD
B Significant functional decline
C Imaging results consistent with bvFTD (frontal and/or anterior temporal atrophy on CT or MRI or frontal hypoperfusion or hypometabolism on SPECT or PET)

Definite bvFTD

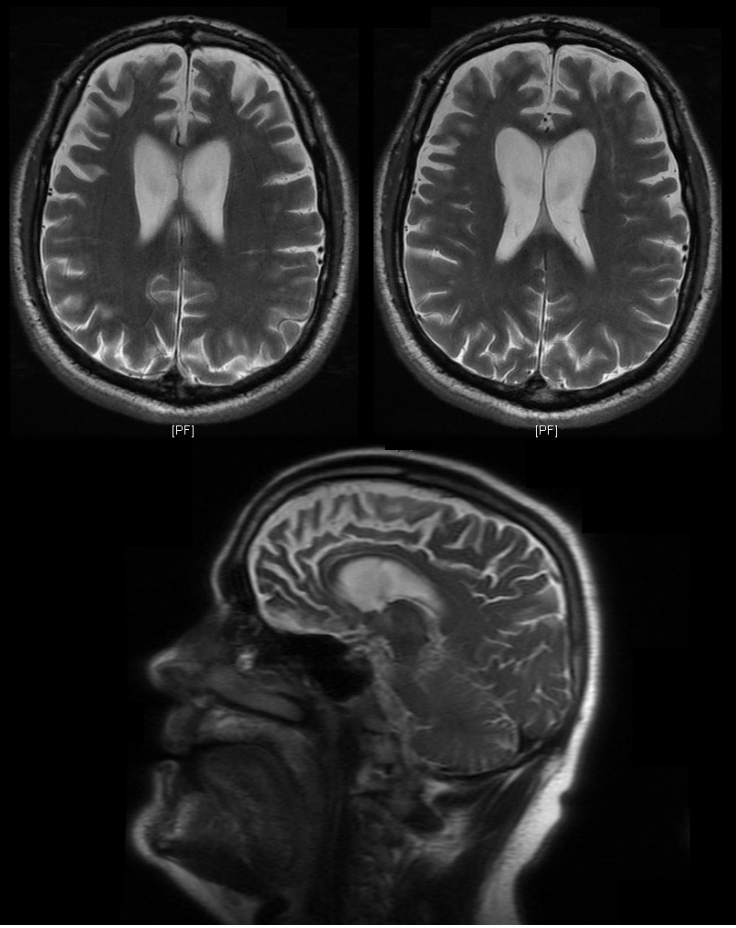
Criteria A and either B or C must be present to meet diagnosis:

A Meets criteria for possible or probable bvFTD
B Histopathological evidence of FTLD on biopsy at post mortem
C Presence of a known pathogenic mutation

Exclusion criteria for bvFTD

Criteria A and B must both be answered negatively; criterion C can be positive for possible bvFTD but must be negative for probable bvFTD:

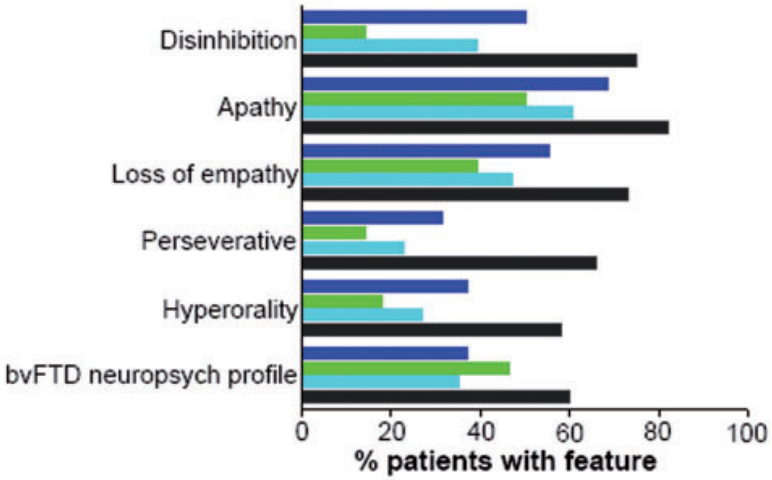
A Pattern of deficits is better accounted for by other non-degenerative nervous system or medical disorders
B Behavioural disturbance is better accounted for by a psychiatric diagnosis
C Biomarkers strongly indicative of Alzheimer's disease or other neurodegenerative process



Increasingly recognized that there are behavioural or dysexecutive presentations in Alzheimer's disease too

4

	Behavioural/ dysexecutive variant Alzheimer's disease	Behavioural presentation Alzheimer's disease	Dysexecutive presentation Alzheimer's disease
N	75	55*	29*
Age[a]	65.8 ± 8.5	64.7 ± 8.8	69.2 ± 8.5
Sex (% male)	68.0	72.7	60.7
Education (years)[b]	15.5 ± 3.1	15.7 ± 2.3	15.7 ± 2.7
MMSE[c]	22.7 ± 5.6	22.5 ± 5.4	24.6 ± 3.3
CDR[d]	0.9 ± 0.6	0.9 ± 0.4	0.8 ± 0.3
GDS[e]	3.4 ± 2.9	3.2 ± 2.8	3.7 ± 3.2
NPI[f]	14.3 ± 16.8	15.4 ± 17.6	12.3 ± 18.1
% *APOE* ε4 carriers[g]	51.7	59.5	40.0
APOE $\varepsilon 4^{++/+-/--}$[g]	6/25/29	6/19/17	2/8/15
TIV (l)	1.60 ± 0.17	1.60 ± 0.15	1.61 ± 0.19
Autopsy-confirmed	24	17	12
PET/CSF biomarkers	41/22	28/18	15/10



Behavioural presentation Alzheimer's disease
Dysexecutive presentation Alzheimer's disease
Combined behavioural/dysexecutive Alzheimer's disease
bvFTD (adapted from Rasckovsky et al.)

Ossenkoppele *et al* (2015) *Brain*

Progressive dysexecutive syndrome

Proposed recent criteria

5

- Persistent, predominant and progressive decline >6 months in core executive function (working memory, cognitive flexibility and/or inhibition)
- Absence of predominant behavioural features (does not meet criteria for behavioural variant frontotemporal dementia)
- Evidence of impaired executive functions from patient and/or informat reports in conjunction with cognitive assessment

Progressive dysexecutive syndrome with possible Alzheimer's disease

- Decreased CSF $A\beta_{41\text{-}42}$ or $A\beta_{42}/A\beta_{40}$ ratio or abnormal amyloid PET

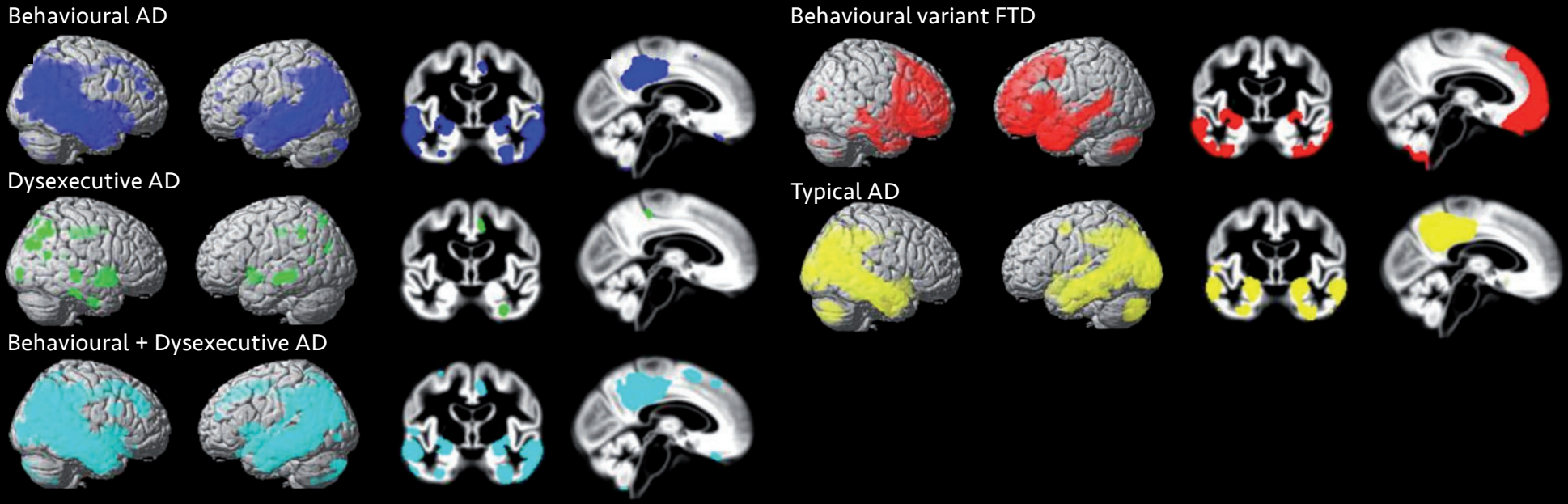
Progressive dysexecutive syndrome with definite Alzheimer's disease

- Meets criteria for possible AD plus one of: increase CSF P-tau, abnormal tau PET, autosomal dominant familial AD mutation, post mortem confirmation of AD pathology

Townley *et al* (2020) *Brain Communications*

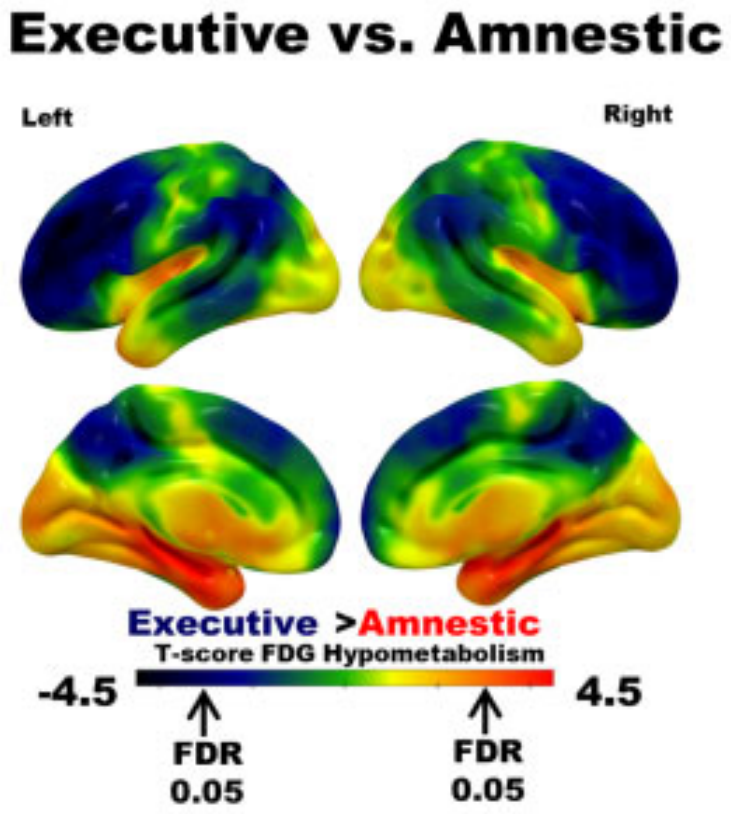
Frontal atrophy in behavioural or dysexecutive Alzheimer's can be fairly subtle

6



Ossenkoppele *et al* (2015) *Brain*

FDG PET in progressive dysexecutive syndrome

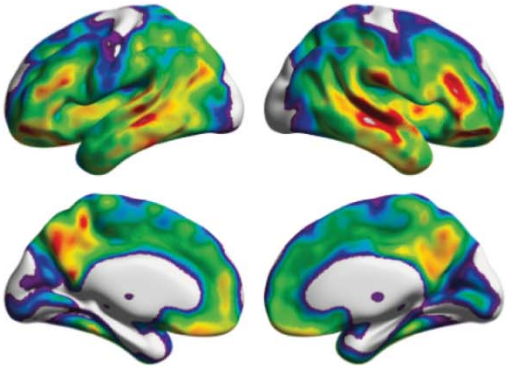


Townley *et al* (2020) *Brain Communications*

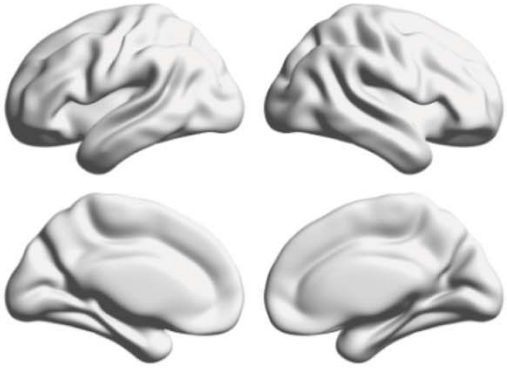
Tau PET in progressive dysexecutive syndrome

Amyloid PET [18F]AZD4694

B. b/d AD > CU elderly



D. b/d AD > Amnestic AD



Tau PET [18F]MK6240

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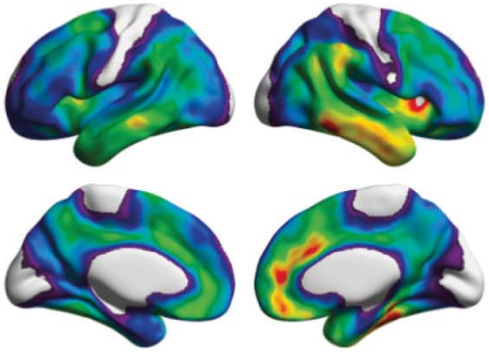

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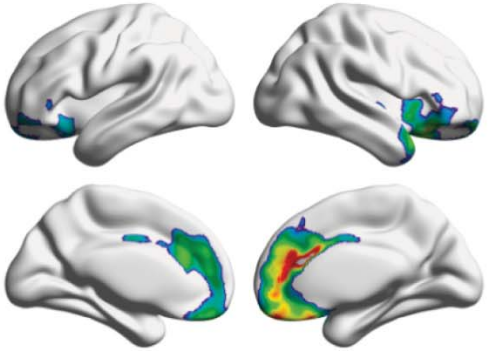


Therriault *et al* (2021) *Neurology*

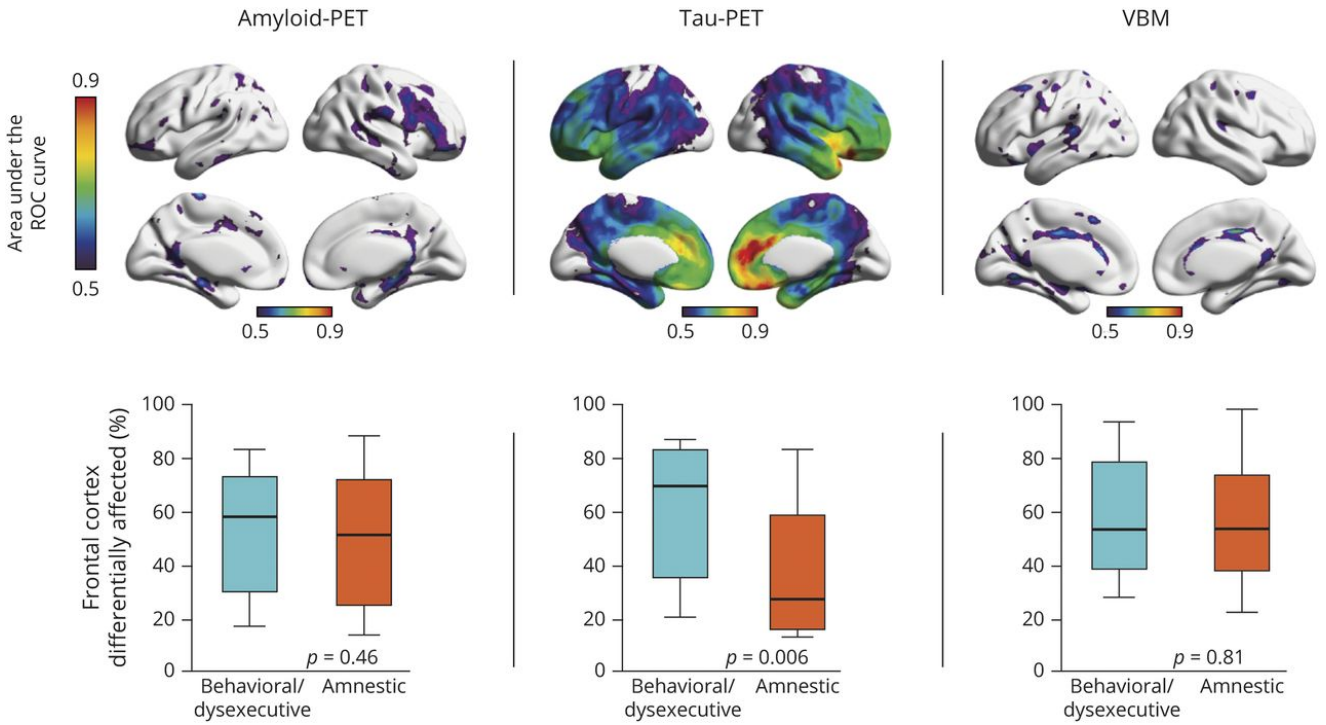
Summary

Executive function and dysexecutive syndrome

- Overview of executive functions and their breakdown to lead to cognitive deficits and behavioural change
- Not just ‘frontal’: importance of frontal networks connecting to other brain regions
- Fractionation of the dysexecutive syndrome
- Contribution to behavioural variant frontotemporal dementia (bvFTD)
- Emerging interest and study of patients with a progressive dysexecutive syndrome associated with Alzheimer’s disease

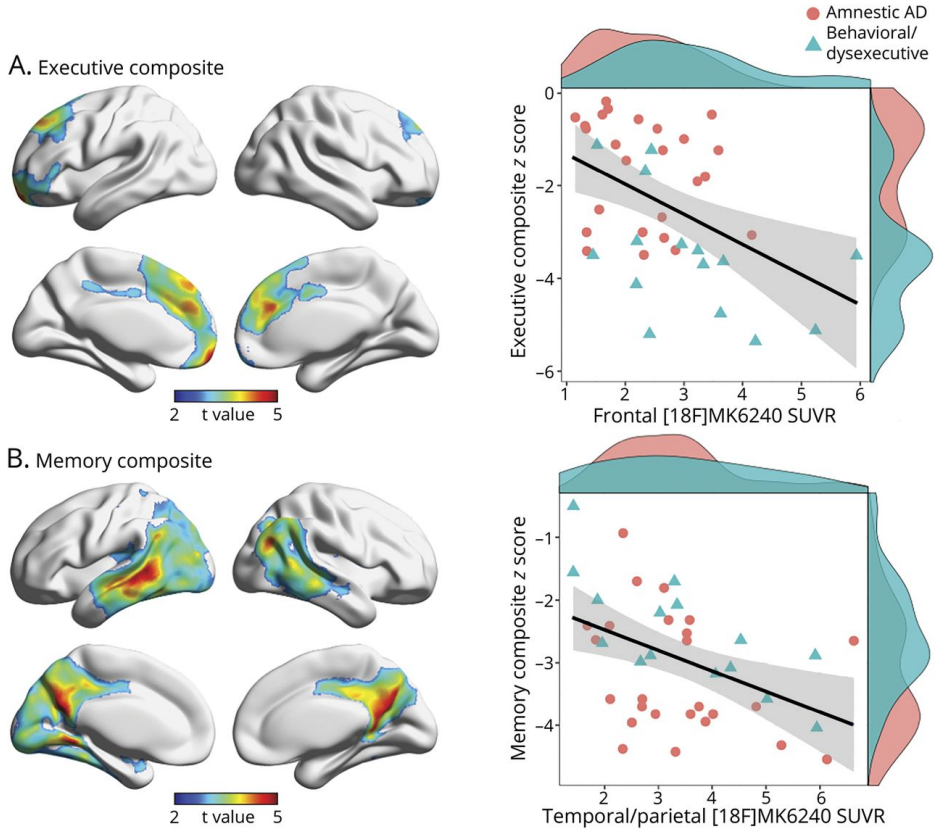
PDF of talk under Lectures tab at masudhusain.org

Figure 5 Accuracy of Imaging Biomarkers for Discriminating Behavioral/Dysexecutive (b/d) Alzheimer Disease (AD) From Amnestic AD



Joseph Therriault et al. Neurology 2021;96:e81-e92

Figure 6 Association of Frontal Tau-PET Uptake With Executive Dysfunction in Alzheimer Disease (AD)



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