7th Annual Memory Clinical Conference
"Difficult to Diagnose Dementias"
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# Semantic dementia
## Characteristics, diagnosis and management


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# Semantic dementia

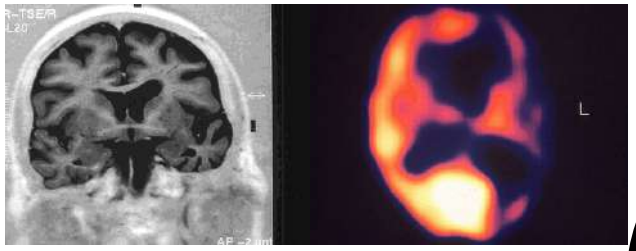
- Disorder of semantic memory / conceptual knowledge
- Associated with atrophy of temporal lobes, especially inferior and middle temporal gyri

- Semantic dementia ~ semantic variant primary progressive aphasia (svPPA)

# Frontotemporal dementias – FTLD pathology

Progressive non-fluent aphasia PNFA

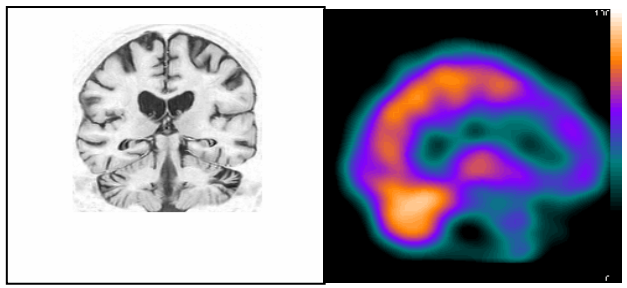
*Expressive Language*

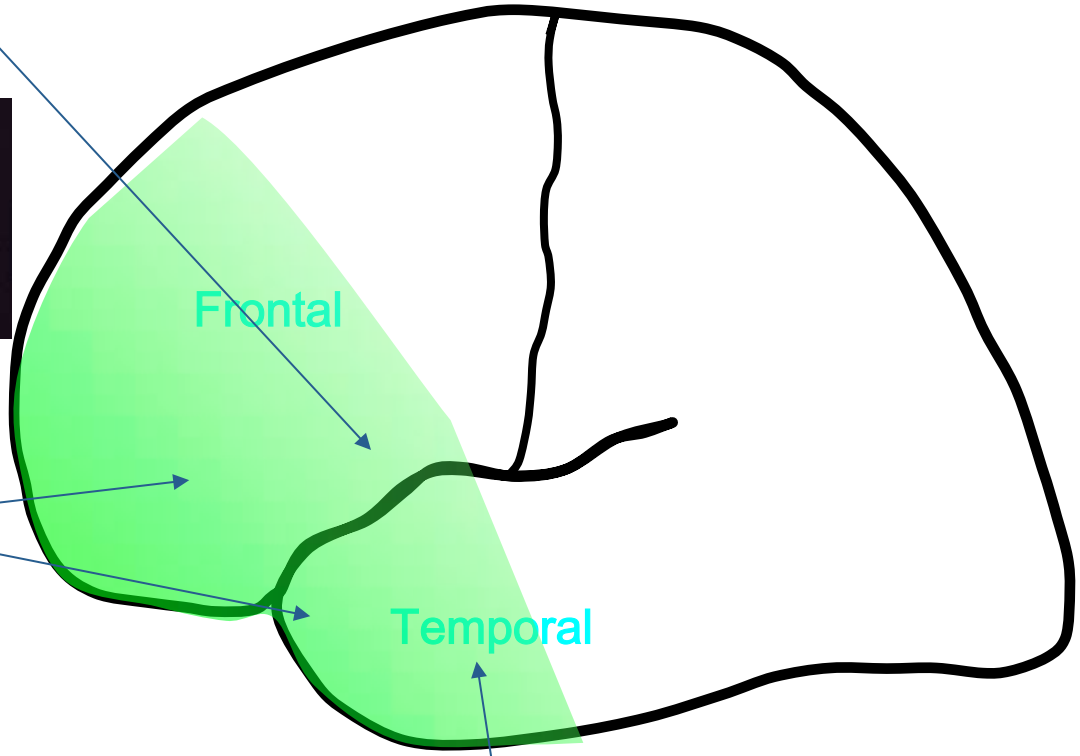


Frontotemporal dementia bv FTD

*Behaviour, Social skills*

*Reasoning and judgement*

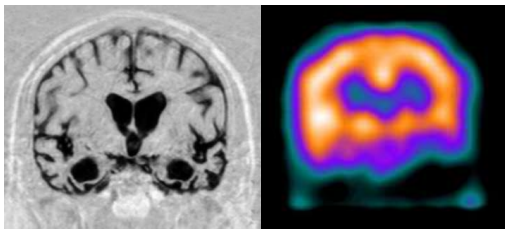





Semantic dementia SD

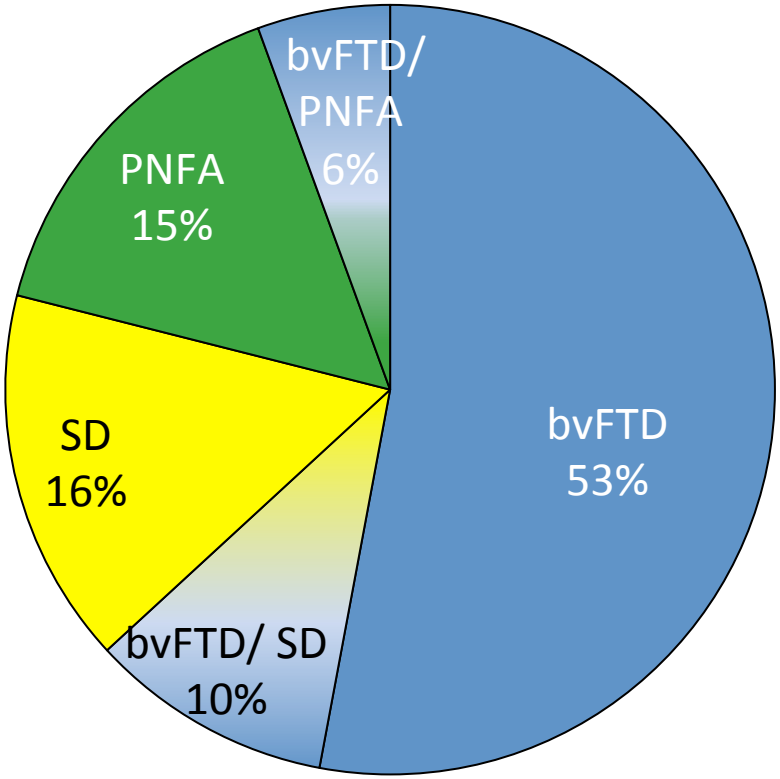
*Conceptual knowledge*

*(words, objects, faces)*



# Frequency of clinical phenotypes

## Cohort of 646 cases



# Semantic dementia Demographics

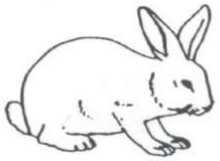
- Affects both men and women
- Onset around 60 years (range late 40s – 70s)
  (own series consistent with Hodges et al Brain 2010;133:300-6)
- Slightly older than bvFTD
  (own series bvFTD mean 57 years – statistical difference)
- Estimated survival ~ 12 years (own pathology series mean 10 years)
- Pure SD - low familial incidence compared to bvFTD
  (Hodges -estimated 2-7%)

But mixed bvFTD/SD strongly familial - associated with tau mutation

# Semantic dementia

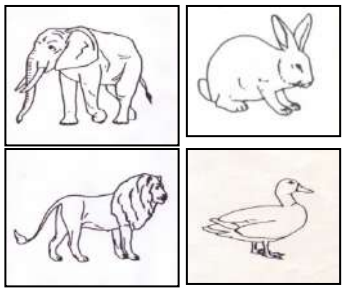
*Disorder of conceptual knowledge*

*Impaired* Naming and word comprehension

Naming What's this?  → "a little dog"

No effortful word search/tip-of-tongue effect/benefit from phonemic cues

Word comprehension Which is the rabbit?



← "this one"

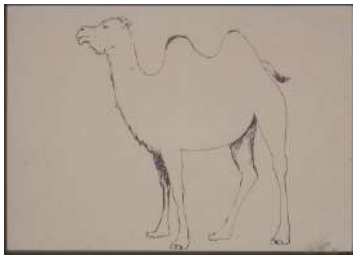
Asks for meaning of words

*Preserved* speech fluency, phonology, syntax

# Semantic loss - multimodal

***Impaired***

Recognition of:
faces, objects
nonverbal sounds
smells, tastes
tactile stimuli

***Preserved***

Perception of
sensory stimuli

# Painting by patient with semantic dementia

- No understanding of ‘church’
- No recognition of building

# Memory

Presenting symptom:

*Cannot remember things / does not know things*

Neuropsychological testing:

*Poor performance (e.g. list learning)*

Most common misdiagnosis:
Alzheimer's disease

# What to look out for

## Cognitive history

- "memory problems" → cannot remember people, words, things
- good day-to-day memory - keeps track of time, finds way, recalls events etc
- difficulty understanding words – asks what words mean
- use of wrong words

- Behavioural history…

# Behaviour in semantic dementia

- Self centred
- Narrowed behavioural repertoire (world view)
- Preoccupations
  - Personal hobby e.g. painting, dress making
  - Word and number games, jigsaws, Sudoku
- Preference for routine
  - Clockwatching, time bound

More obsessional than bvFTD

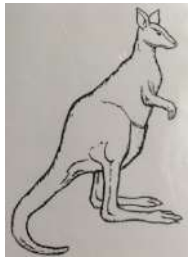
(*Snowden et al J Neurol Neurosurg Psychiatry 2001;70:323-32*)

# Neuropsychology crucial
## (elicits dissociations)

### Language assessment

Fluent (garrulous) conversational speech.  Yet…

•Profound naming disorder.



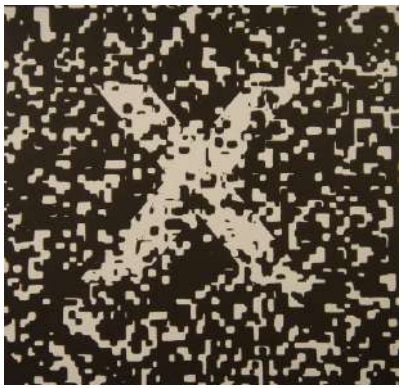
Graded naming test at referral (50 patients)
median score = 0, interquartile range 0-1

•Semantic errors in naming

• Word comprehension impairment

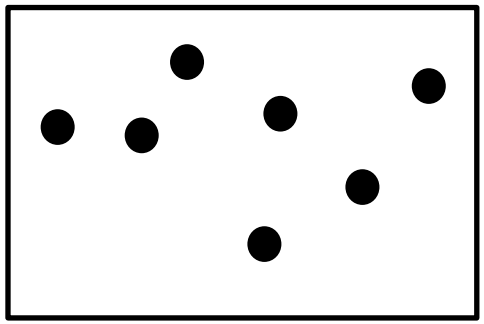
# Perceptual and spatial tests very helpful

Preserved provided that task does not require
*recognition of identity*

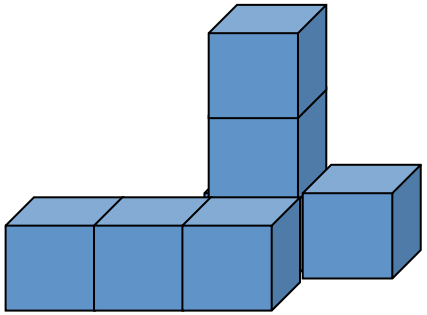


20/20

3/20



10/10



10/10

# Memory

Poor verbal memory performance

Preserved forced-choice visual recognition

*Which one did you see before?*

# Memory

## 10 Famous faces

At presentation:

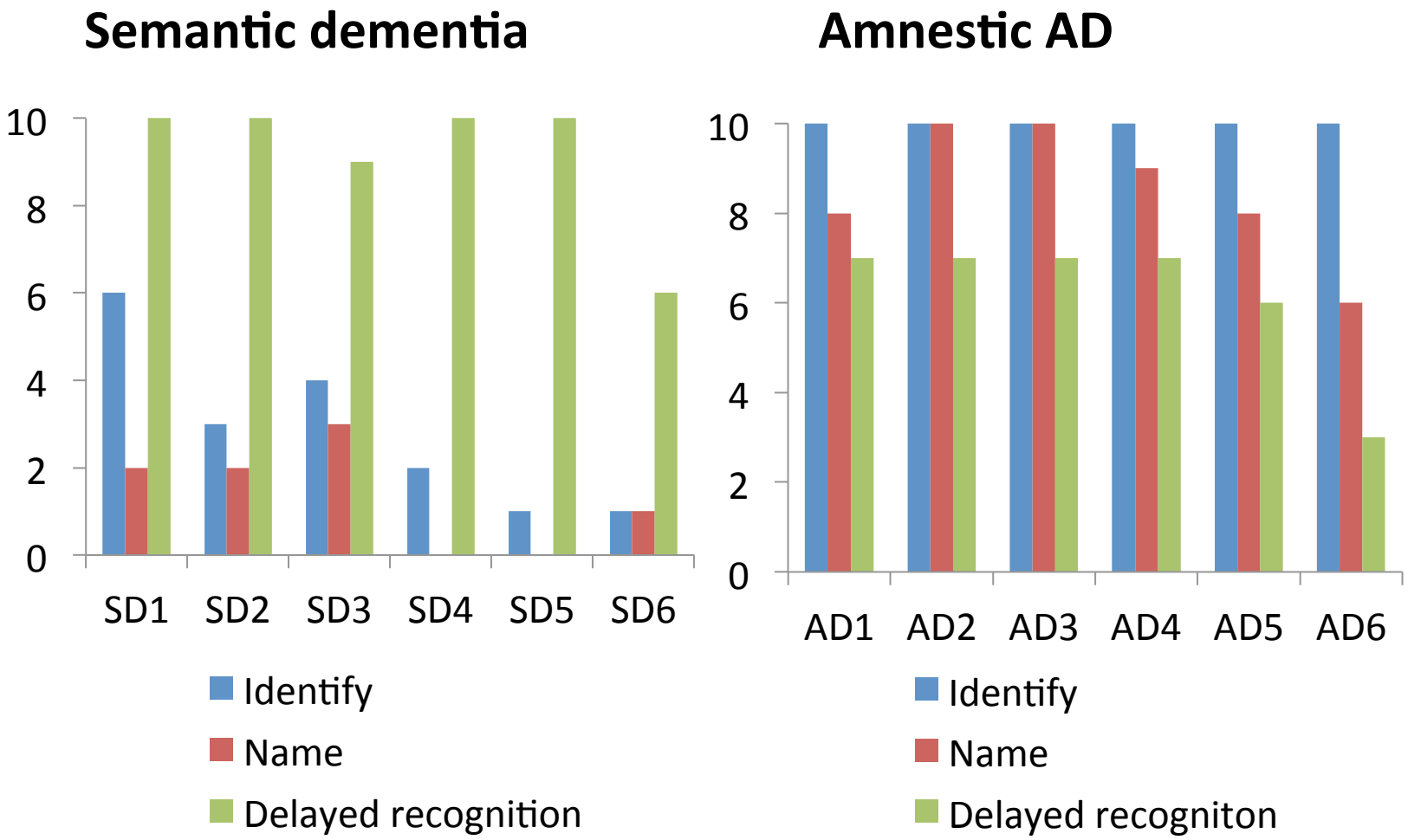
- Name
- Provide identifying information

# Forced-choice Recognition

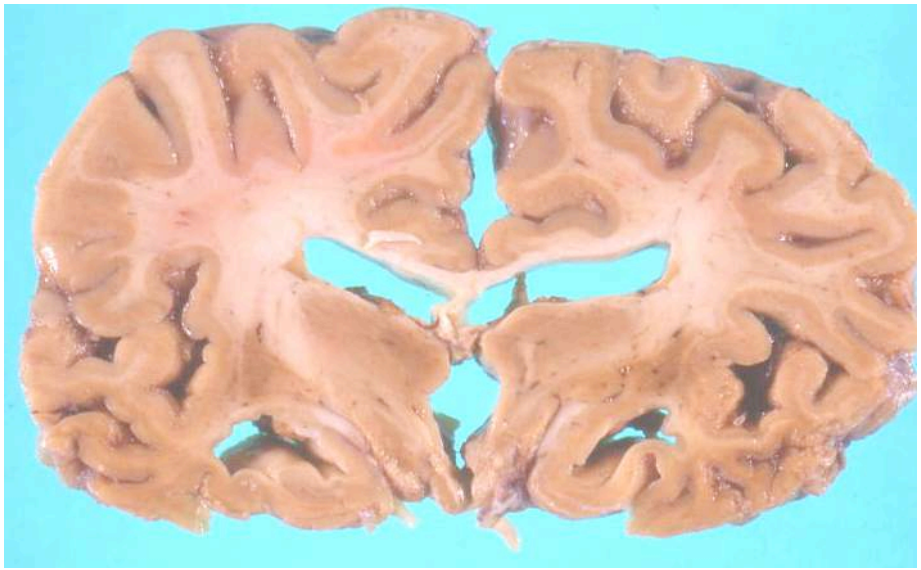
30 minute delay

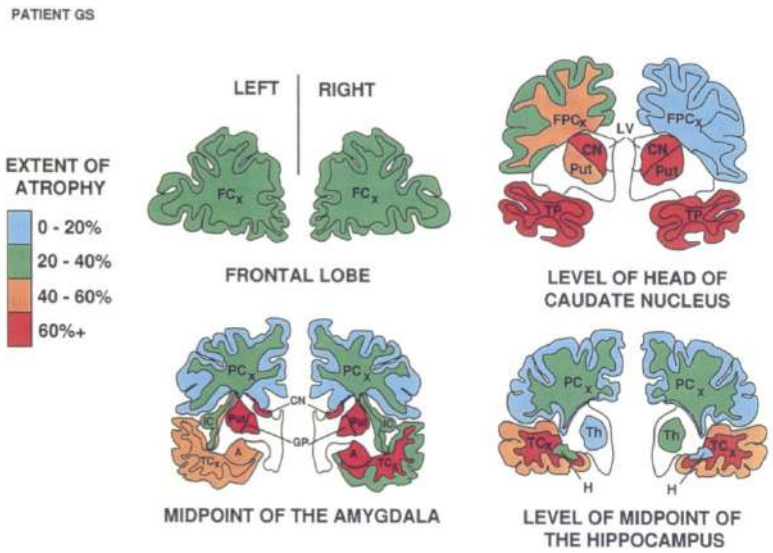
Which one did you see before?

# Face identification and memory



# Semantic dementia pathology

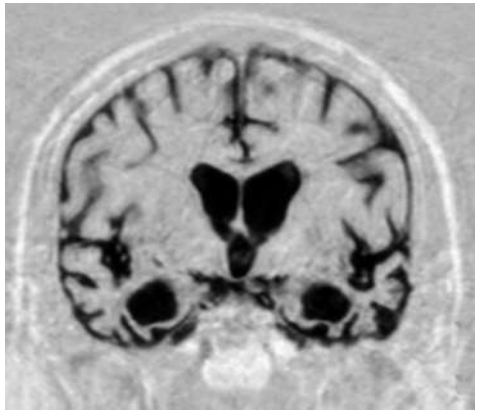


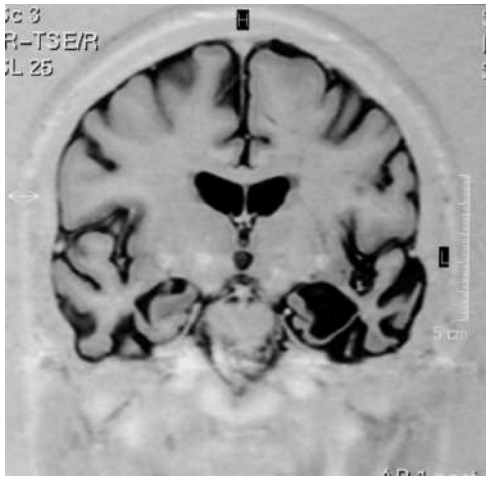



Bilateral temporal lobe atrophy

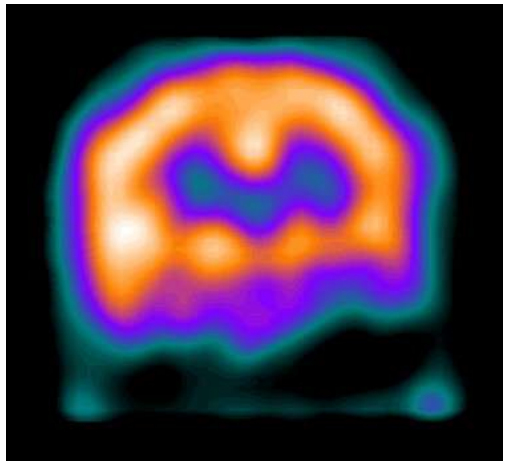
What is relationship between knowledge in different modalities?

# Temporal lobe atrophy and hypoperfusion in semantic dementia

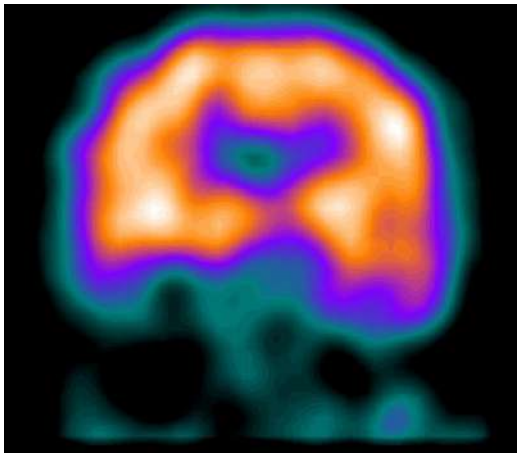




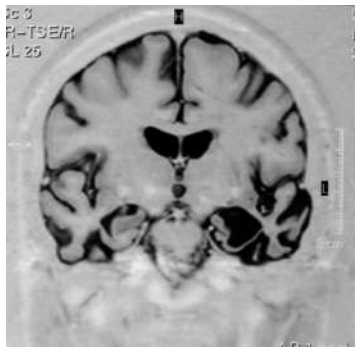
*Left > right*



*Right > left*



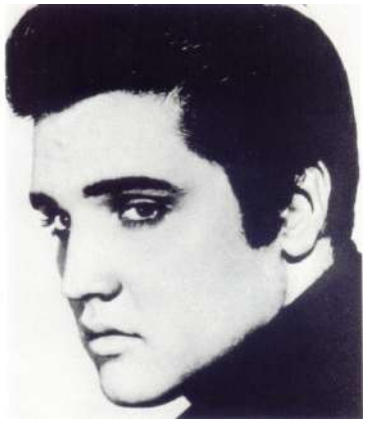
# Left versus right predominant semantic dementia



L>R Better recognition faces than names

Identity
Familiarity

R>L Better recognition names than faces



Margaret Thatcher

Elvis Presley

*Snowden et al. Brain 2004; 127: 860-72; Behav Neurol 2012;25: 35-44*

**SD case:** male, referred aged 69 years, 2 year history

Presenting complaints: difficulty recognising people and objects.

Cognitive profile of SD. Preserved elementary perception.

Imaging right > left temporal atrophy.

*Matched visual-verbal tasks*

- Famous faces and names/28: 4 choice familiarity judgement. Which is famous?

- Pyramids and Palm trees/52: 2-choice associative match of pictures and words

Pyramid

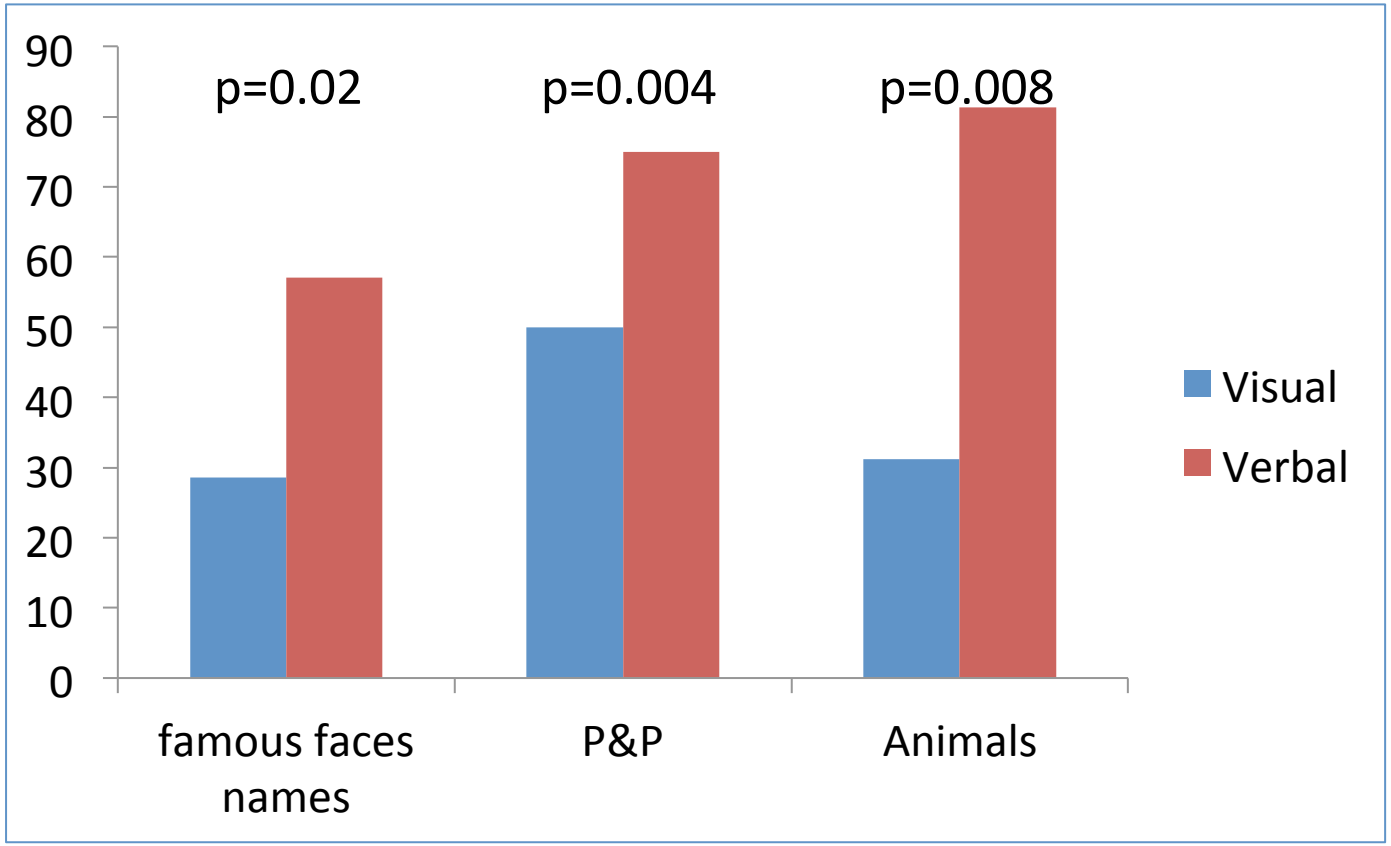
Palm tree

Pine tree

- Animals/20 Where would you find …?

frog

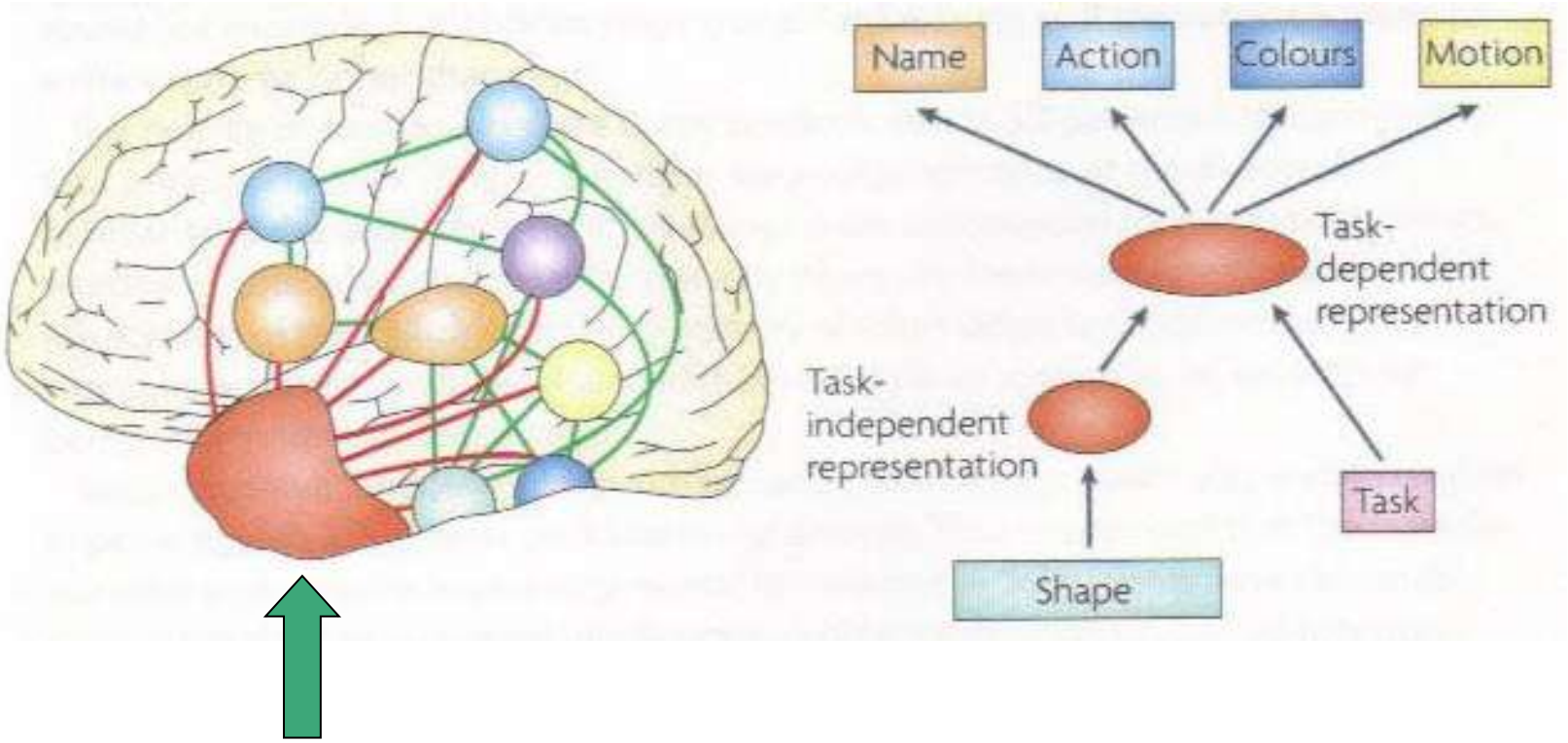
# SD patient: item-by-item comparison on matched visual/verbal tasks



# Where would you find ?

| | | | |
|---|---|---|---|
| **Frog** | In water |  | Don’t know |
| **Cow** | On a farm |  | In the house. It’s a dog. |
| **Duck** | On ponds. I also see them on the river when I go out walking. |  | Outside the house. There are lots of them. |
| **Squirrel** | In the woods, in the country. They’re wild. |  | In water. It’s got a bushy tail so it’s good at swimming. |
| **Monkey** | In trees, in Africa |  | In the house. It’s somebody’s son. |

# *Semantic hub model of semantic memory*




Amodal hub

*Patterson et al. Nature Reviews Neuroscience 2007;8: 976-88.*

Performance influenced by distribution of temporal lobe atrophy in right and left hemisphere

Consistent with ‘multimodal’ account of semantic memory

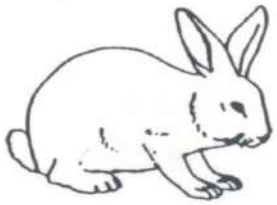
Challenge for ‘amodal’ account

# Factors influencing what is known/not known?

- Frequency, familiarity, typicality

e.g. Woollams et al. Neuropsychologia 2008;46: 2503-14

Animal fluency: *"cat, dog, horse"*

Naming:  *"A dog"*

- Personal familiarity

Graded Naming test performance = 0/30

SD 1 *"I help Reverend Jones prepare the chalice for the Eucharist. Afterwards, I put the chalice back in the vestry"*

SD 2 *"When I was in Connecticut I attended the inauguration of President Reagan"*

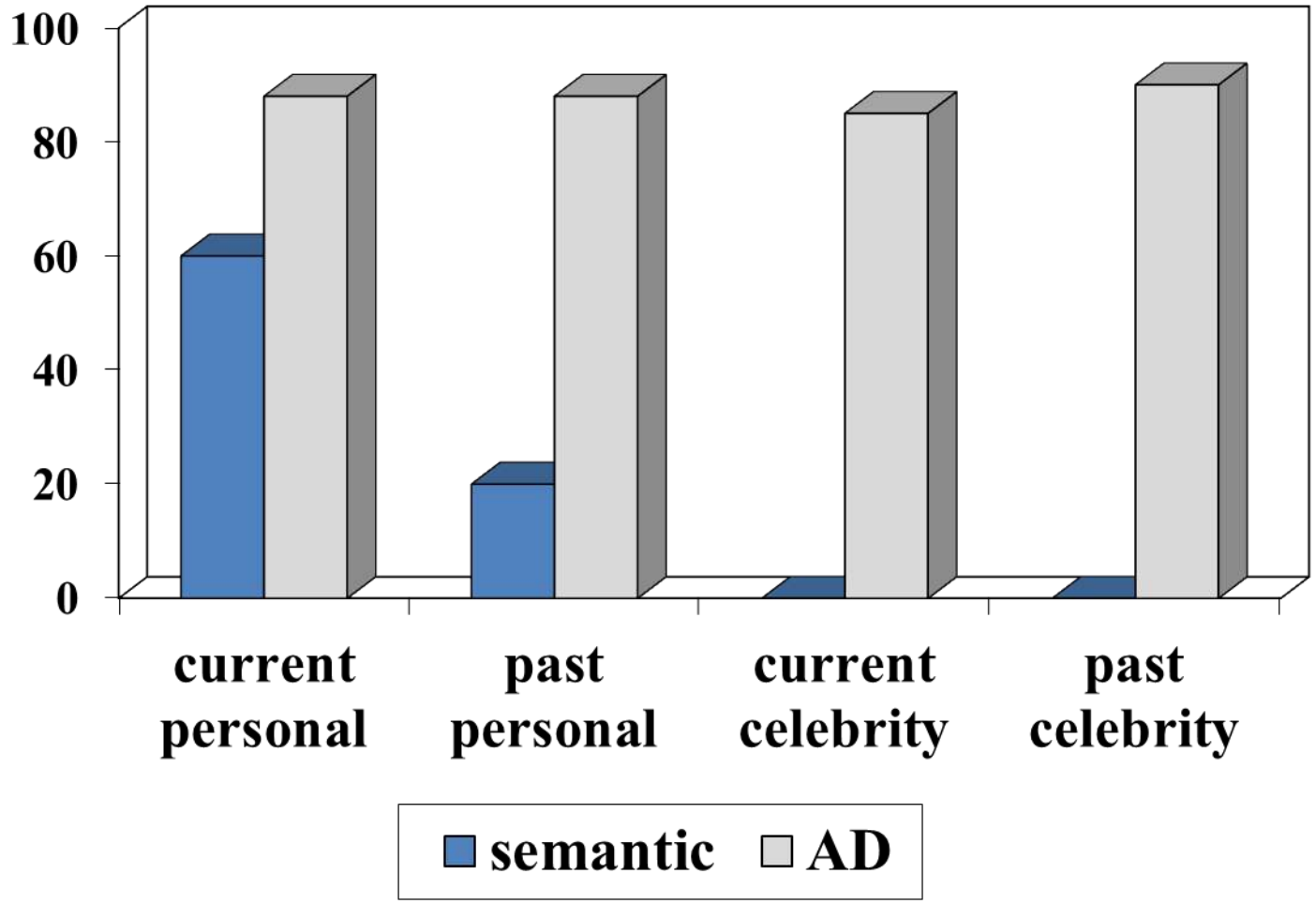
Autobiographical Influence ?

*Snowden et al Cog Neuropsychol 1994;11:265-88; Memory 1995; 3: 225-46; Cog Neuropsychol 1996; 8: 1101-37*

*Also: Westmacott et al, Neuropsychologia 2004; 42; 25-48*
*Péron et al. Front Human Neuroscience 2015; 9: No625*

# Name identification

## personally relevant versus famous names



# Autobiographical influence

## People

- Recognises names and faces of personal acquaintances better than those of famous people

## Names of places (towns/countries/regions)

- Recognises (as meaning a 'place') place names that have autobiographical significance better than impersonal place names
  - Auvergne: "it's in France by the Dordogne. We used to go there in the caravanette"
  - Portugal: "What's Portugal? I've never heard of Portgual"

## Word comprehension

- Partial understanding – linked to own experience

# Autobiographical influence

## Object recognition

- Identifies own objects better than alternative exemplars

*"It's for telling the time. It's twenty-four minutes past two"*

*"I don't know what that is"*

- Identifies object better in usual location
  - e.g. recognises kettle in kitchen better than in bedroom

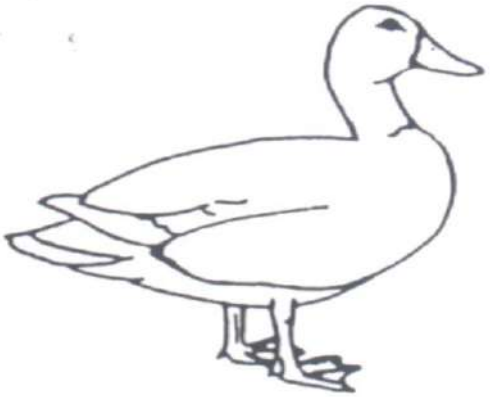
- Identifies object according to own usage
  - Water jug as vase
  - Clothes peg as cereal packet fastener

# Is re-learning of lost words possible?

Yes.

Better learning/retention if:

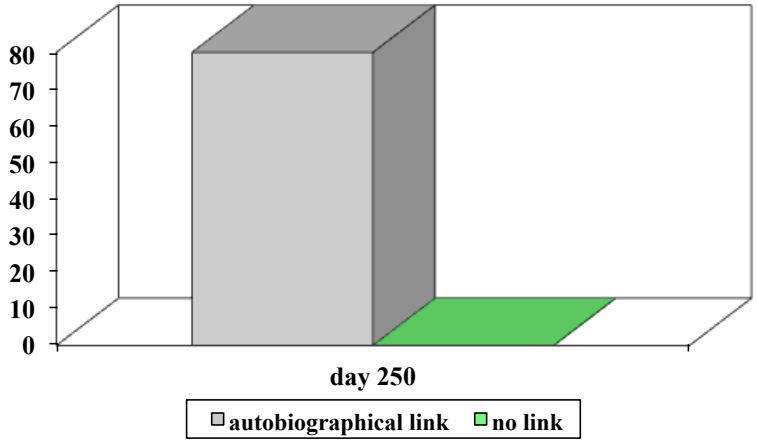
- Recognises object
- Spatial context is same
- Temporal context is same
- Linked to daily experience



**duck**

*"You see this on the lake when you go for a walk in the park".*

Learning of object names and retention over time better if autobiographically linked



# Management implications

Importance of :

- context
- experiential associations
- routine – time and place
- maintaining experiential links

# Dealing with comprehension problems

- Use same words / names
- Place words in context (sentence, experiential)

- Keep objects in same place
- Remove irrelevant objects

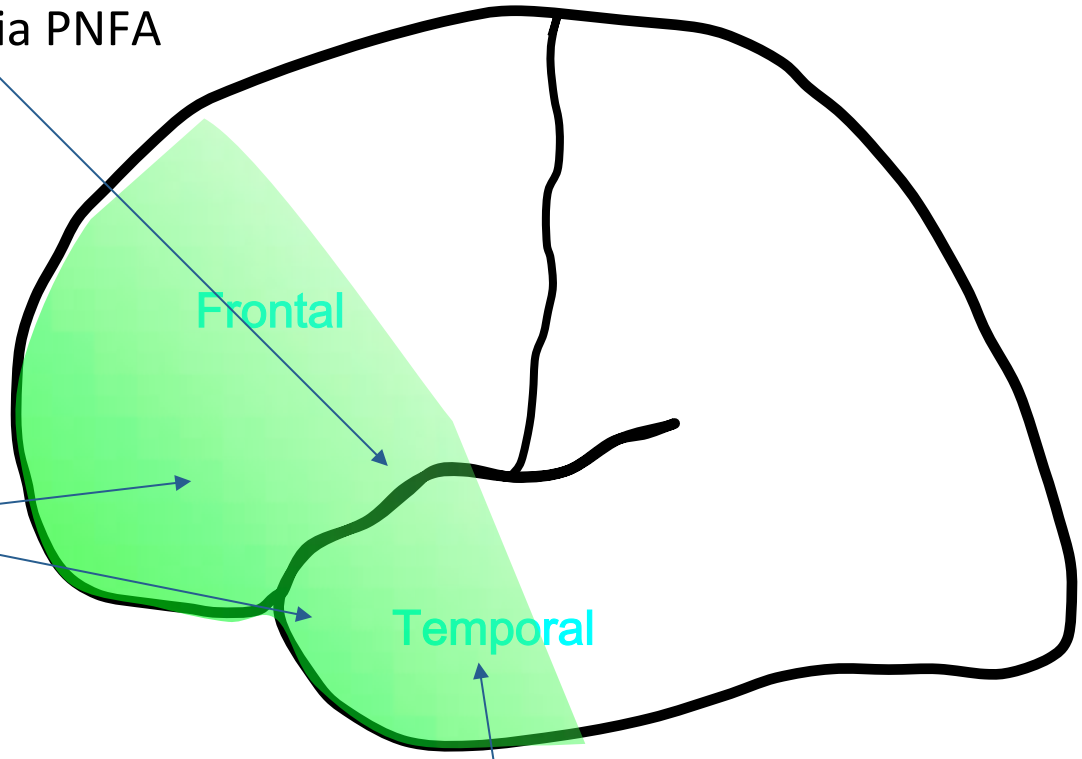
- Maintain routines

→ Change slowly (e.g. driving, residence)

# Relationship between semantic dementia and other frontotemporal dementias?

Progressive non-fluent aphasia PNFA

*Expressive Language*




Frontotemporal dementia

bvFTD

*Behaviour, Social skills*

*Reasoning and judgement*

Semantic dementia SD

*Conceptual knowledge*

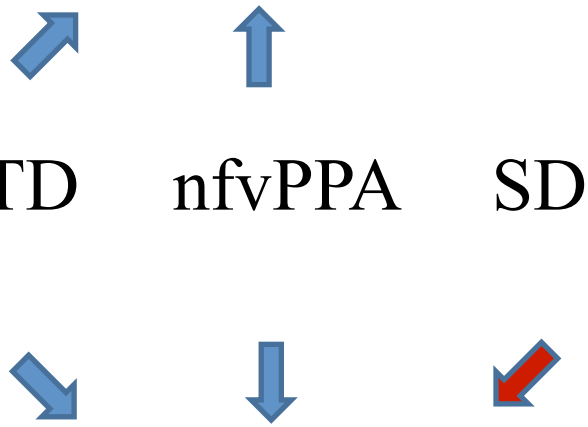
*(words, objects, faces)*

# Frontotemporal lobar degeneration

2 main pathologies

*Abnormal protein*

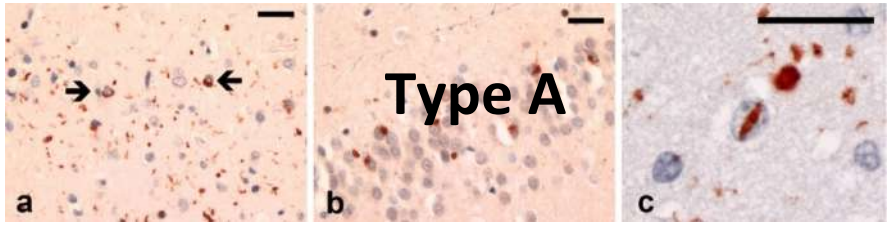
**Tau**



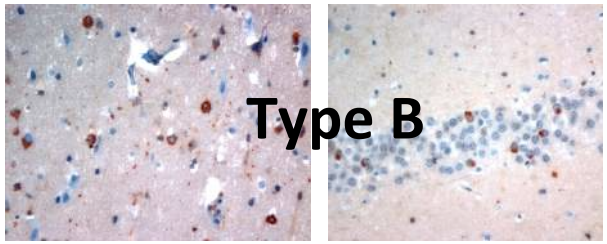
bvFTD nfvPPA SD

**TDP-43**

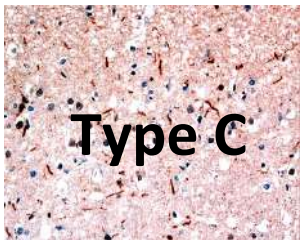
# TDP-43 subtype and clinical phenotype




cytoplasmic inclusions intranuclear inclusions

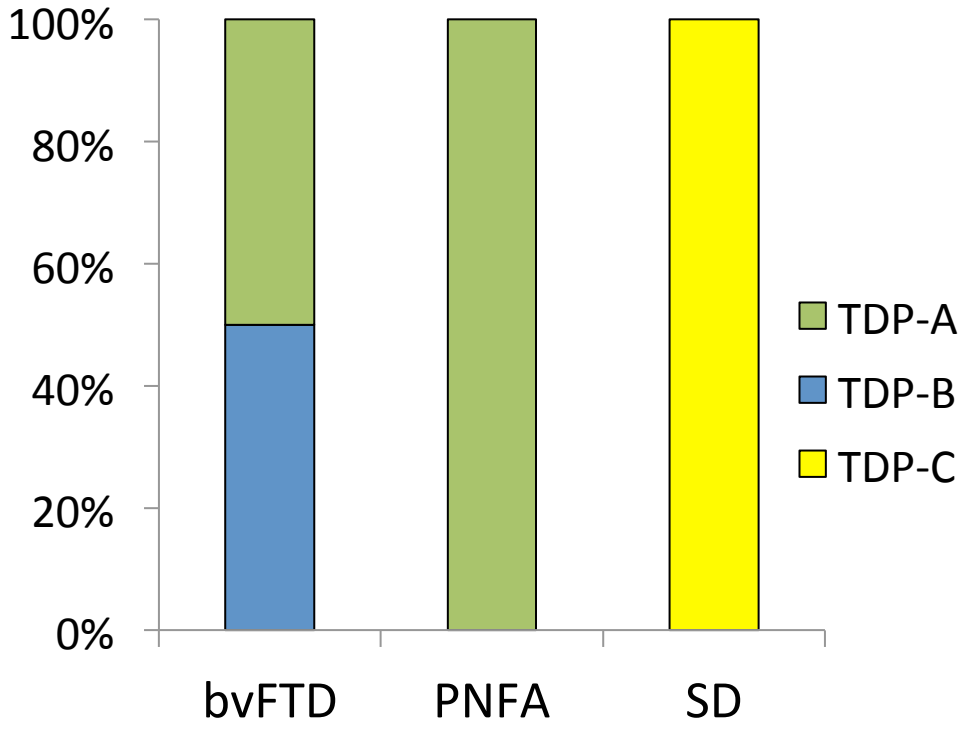



cytoplasmic inclusions




dystrophic neurites

*Mackenzie et al. Acta Neuropathol 2011; 122: 111-3*




*Saxon et al. J Neurol Neurosurg Psychiatry 2017 in press*

# Conclusions

- Distinctive clinical syndrome (loss of associations/connections)
- Confused with Alzheimer's disease because of:
  - history of memory complaints
  - fluent speech output so semantic disorder may not be apparent at interview
- Need for careful clinical history. Importance of cognitive assessment
- **Diagnosis crucial for effective clinical management**

# Acknowledgements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