

Clinical features of FTD

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**UNIVERSITY OF
CAMBRIDGE**

Pick's Disease

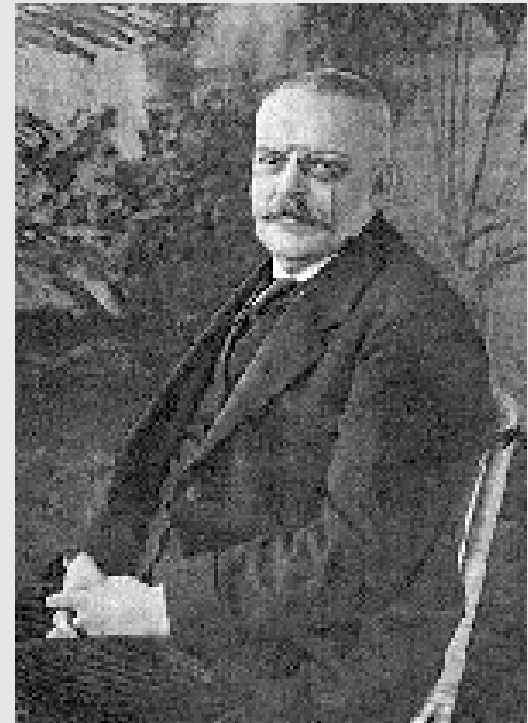
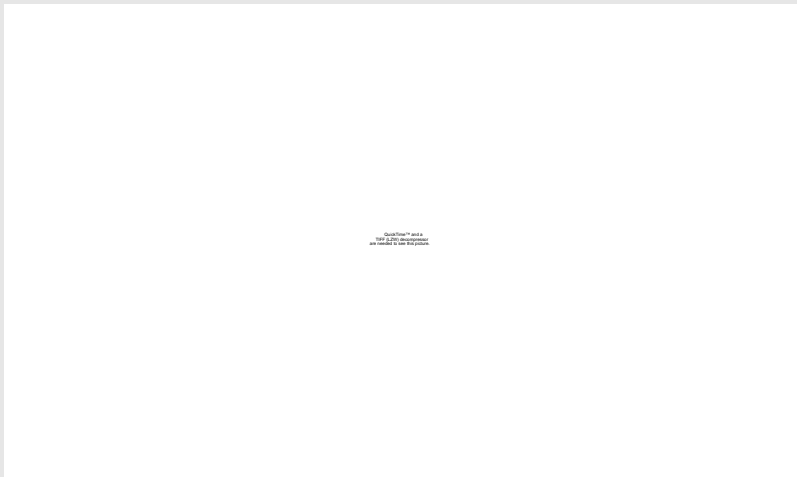
- Über die Beziehungen der senilen Hirnatrophie zur Aphasie, *Prager Medicinische Wochenschrift* (1892), 165-7
 - English translation see: *Girling & Berrios, History of Psychiatry Vol 5, 1994*



Arnold Pick 1854 -1924

Pathology

- 'Pick' bodies and cells
– 1911



Alois Alzheimer 1864-1915

‘There are no specific clinical features to separate Pick’s disease from Alzheimer’s, and the distinction is generally made at autopsy not in life.’

Oxford Textbook of Psychiatry, 1983

Prevalence of early-onset dementia

Clinical diagnosis	Age at appearance of symptoms <65 y, n = 108
AD	27 (25)
Frontotemporal dementia	17 (15.7)
Huntington's disease	21 (19.4)
Vascular dementia	17 (15.7)
Parkinsonian syndromes (PSP, PD, CBD, DLB, MSA, PPS)	12 (11.1)
Alcohol-related dementia	6 (5.6)
Secondary dementias	5 (4.6)
Undetermined	3 (2.8)

Frontotemporal lobar degeneration
(frontotemporal dementia)



Frontotemporal dementia
(frontal variant FTD)
(behavioural variant FTD)
Neuropsychiatric syndrome

Semantic dementia
(progressive fluent aphasia)

Progressive non-fluent aphasia

The modern era of progressive aphasia

- Mesulam (1982)
 - Described 6 cases of progressive language breakdown with relative preservation of other cognitive abilities.
- Mesulam and Weintraub (1992)
 - Progressive dissolution of language is the only salient deficit for at least two years.

Progressive aphasia

- Alzheimer's disease
 - Commonest cause of progressive aphasia
 - Usually overshadowed by memory impairment and accompanied by other impairments (visuospatial, executive)
 - In 'typical AD' aphasia takes form of a fluent anomia giving rise to circumlocutions

Atypical AD

- Posterior cortical atrophy
- Primary progressive aphasia
 - Fluent
 - Non-fluent
 - Mixed
 - *Look for:*
 - *Subtle non-language deficits (esp. memory)*
 - *More global deficits with follow-up*
 - ***Absence of neuropsychiatric features***

Atypical AD

- Posterior cortical atrophy
- Primary progressive aphasia
 - Fluent
 - Non-fluent
 - Mixed
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Behavioural features of FTD (fvFTD)

- Insidious personality change
- Insightlessness
- **Stereotypic behaviours**
- **Change in food preference**
- Disinhibition
- Loss of empathy
- Rigidity
- Apathy
- Mood disturbance

Frontal variant FTD

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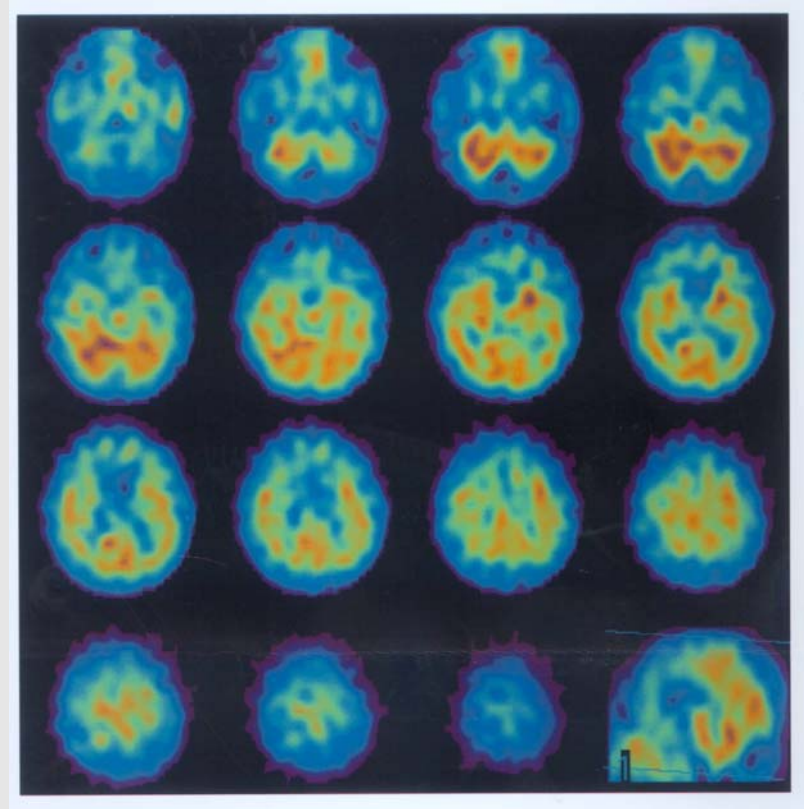
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fvFTD PET/SPECT

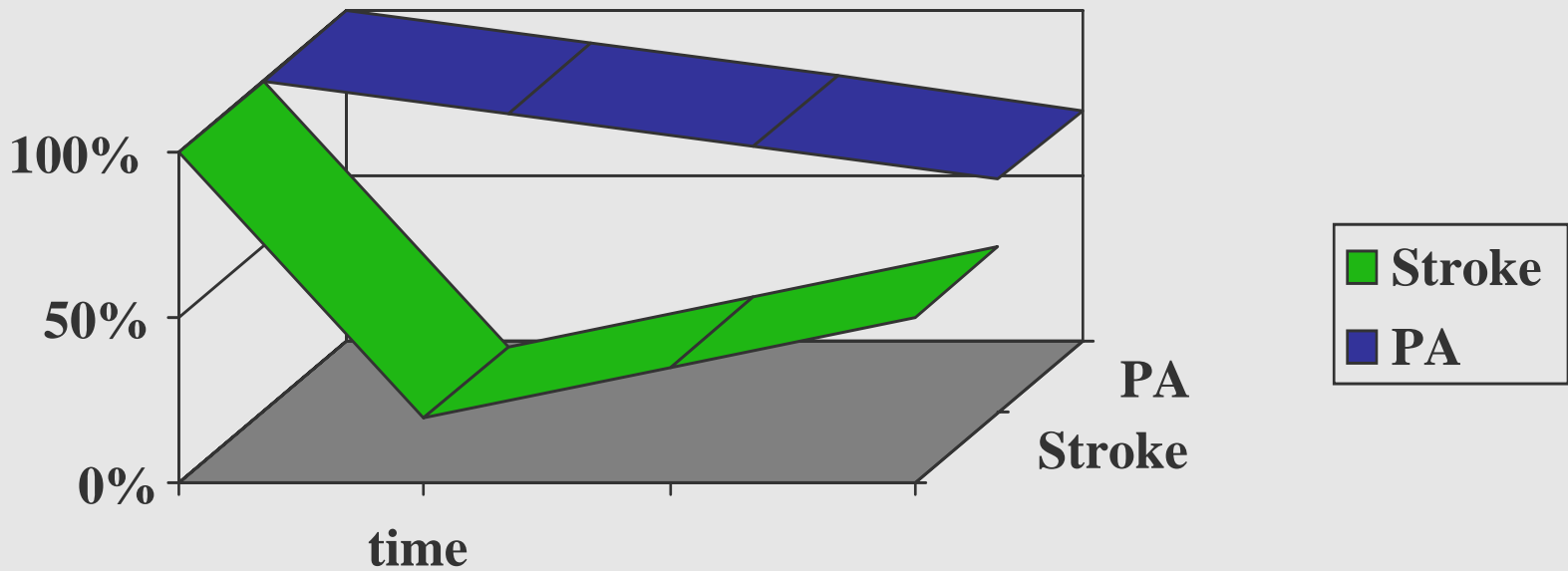
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Neurological examination

- Primitive reflexes
 - Grasp/pout/glabellar tap/palmo-mental
- Motor neuron disease
- Parkinsonism

Insidious versus Acute Aphasia



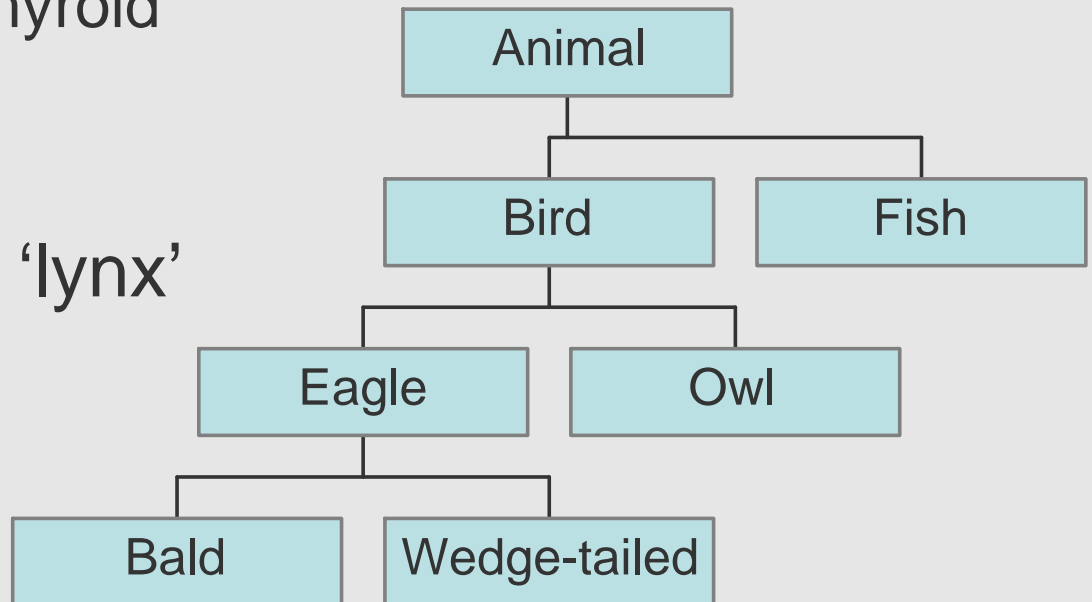
Dissolution of language in progressive fluent aphasia (semantic dementia)

Age of acquisition

- 'cat' versus 'thyroid'

Word frequency

- 'cat' versus 'lynx'



WP-Matching Level 0



WP-Matching Level 1



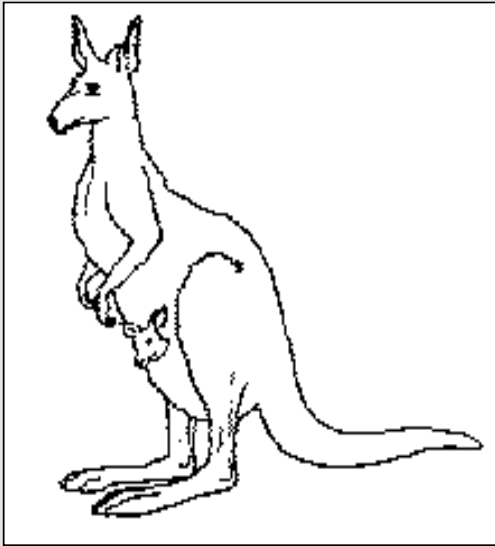
WP-Matching Level 2



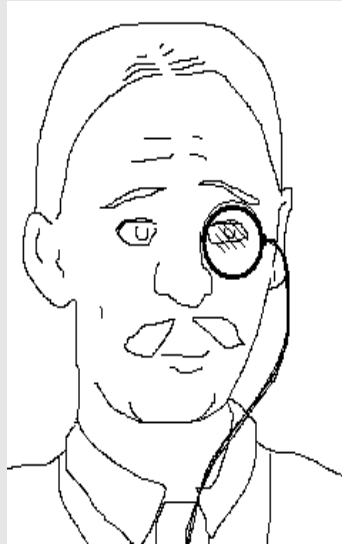
WP-Matching Level 3



Graded Naming Test

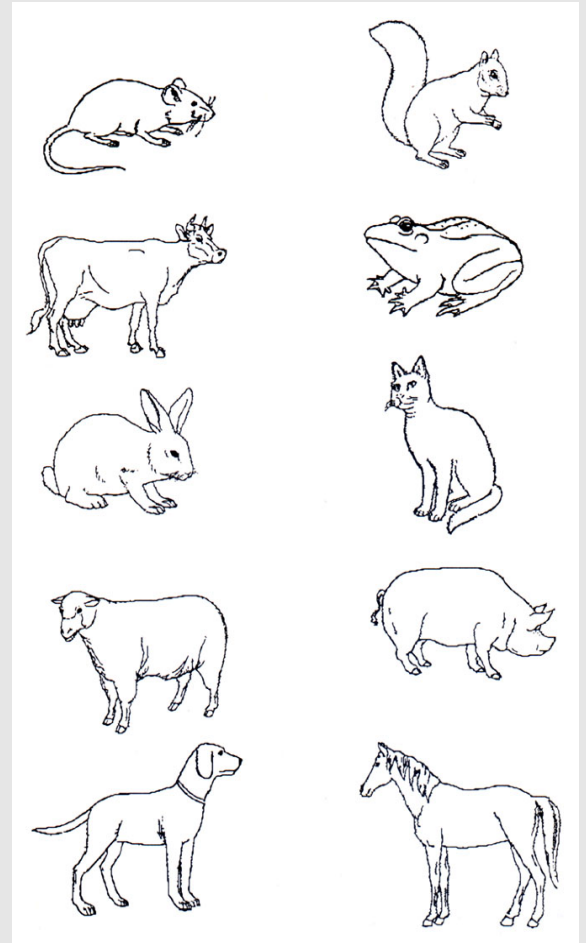


Easy

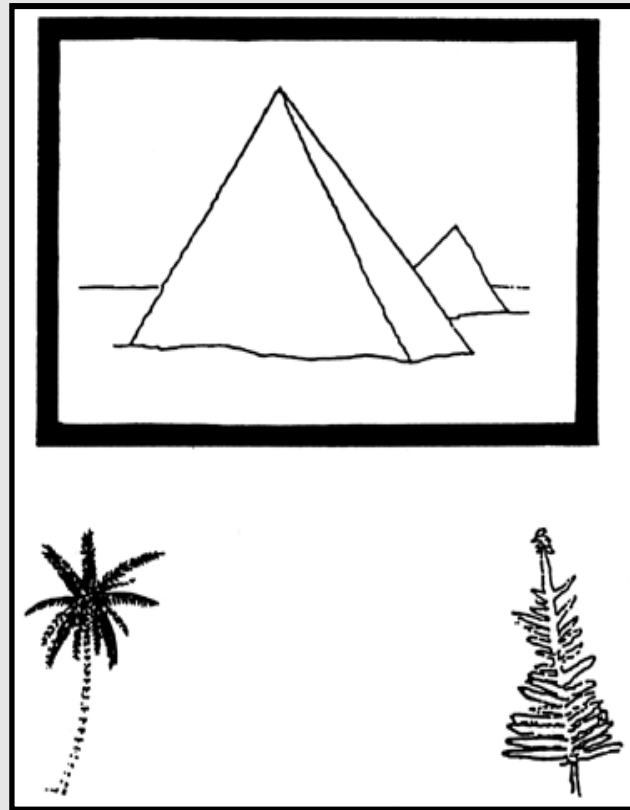


Hard

Word-picture matching



Pyramids and Palm Trees

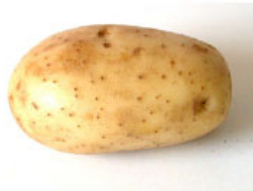


Object Matching and Usage Battery

Object

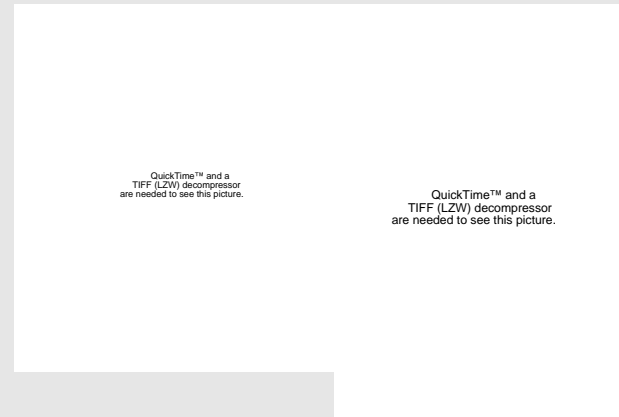
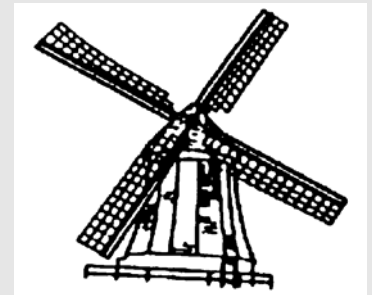
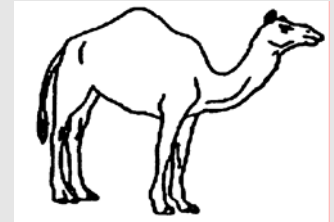


Recipient



Bedside testing for semantic dementia

- Semantic knowledge loss
 - Category fluency
 - Naming:
 - pictures
 - to description
 - famous faces
 - Definitions
 - Surface dyslexia



Bedside testing for semantic dementia

- Definitions

- What is an ‘accordion’, an ‘aubergine’, a ‘hippopotamus’.
- What do you call a large, grey animal with a trunk?
- Point to an artificial source of illumination.
- *(C.f. Point to the table, then the door but first point to the window.)*

ADDENBROOKE'S COGNITIVE EXAMINATION (ACE)

ADDENBROOKE'S / NORFOLK & NORWICH DEPARTMENTS OF NEUROLOGY

Name :	
Date of birth :	1947 F
Hospital no. :	

Age at leaving education : _____
(school/college etc.)

Date of testing : 12/6/02

Tester's name : P. Nestor

ORIENTATION

a) What is the

	Year	✓
	Season	✓
	Date ±2	✓
<i>Record errors.</i>	Day	✓
	Month	✓

[Score 0 - 5]

5

b) Where are we

	Country	✓
	County	X
	Town	X
<i>Record errors.</i>	Hospital/building	X
	Floor Allow if almost correct.	✓

[Score 0 - 5]

2

ORIENTATION

a) What is the

	Year	<u>03</u>
	Season	✓
	Date ±2	X
<i>Record errors.</i>	Day	✓
	Month	<u>Jan</u>

[Score 0 - 5]

4

b) Where are we

	Country	
	County	
	Town	
<i>Record errors.</i>	Hospital/building	<u>ok on floor</u>
	Floor Allow if almost correct.	

[Score 0 - 5]

0

Bedside testing for semantic dementia

- Surface dyslexia*†
 - ‘Hint’, ‘Rint’ (*Phonological route*)
 - ‘Pint’ (*semantic route*)

 - ‘Yacht’ ‘Yot’
 - ‘Dough’ → ‘dowff’

**Particularly salient in English*

†surface dysgraphia occurs for the same reason

Profile of SD

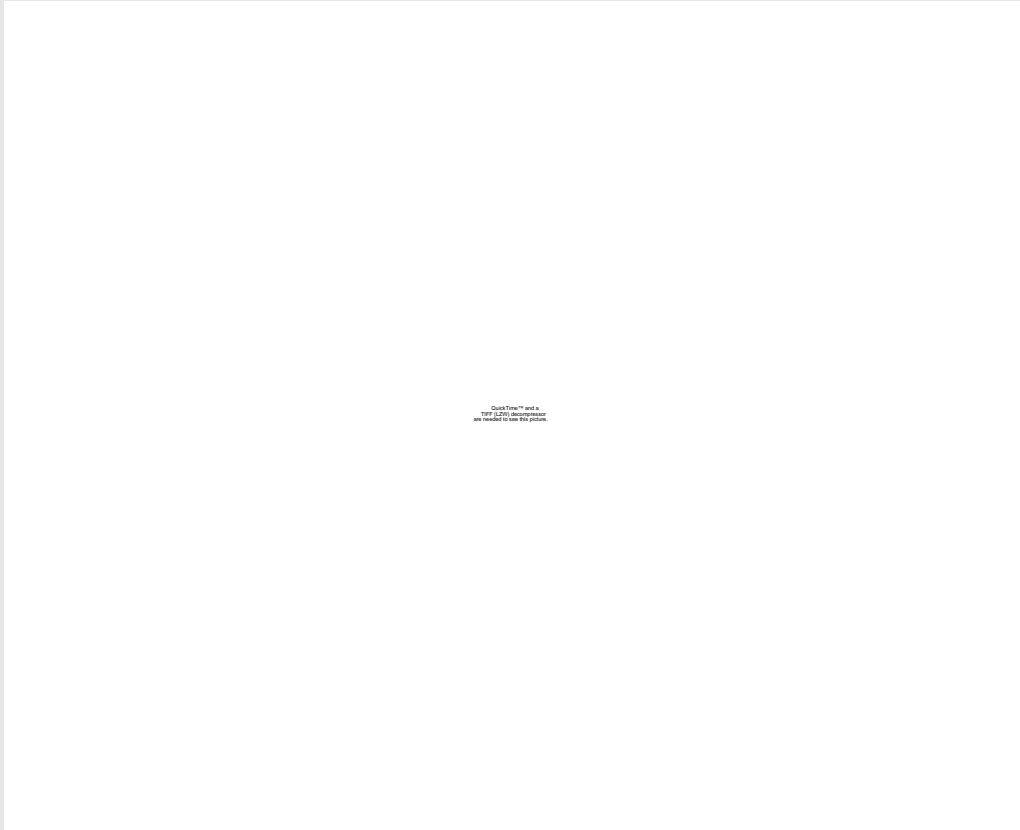
- Fluent speech with relative preservation of syntax and phonology.
- Loss of word meanings/object and fact knowledge (i.e. semantic memory) giving rise to:
 - Vacuous, circumlocutive output
 - Use of generic or superordinate rather than specific terms ('animal' {or 'big dog, small dog etc.'}, 'thing')
- Relative preservation of episodic memory and visuospatial skills

SD overlap with frontal dementia

- May not be present initially, but SD cases usually develop the neuropsychiatric syndrome of FTD.
 - Change in food preference
 - Stereotypic behaviours
 - Impulsivity
 - Disinhibition etc.

 - Puzzles!

Neural associations of semantic dementia



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Pathology in SD

- FTD variants
 - Classic Pick's
 - Tau positive
 - DLDH
 - **Tau negative, ubiquitin positive**

*Rossor et al. Brain,
2000, Davies et al.
Brain, 2005*

Dissolution of language in non-fluent progressive aphasia

- Loss of fluency in spontaneous speech
- Phonological errors
- Progressive agrammatism

- PNFA cases exhibit good single word comprehension.

Loss of fluency is often noticed by the patient well before the relatives

- Hesitations and phonological errors occur, to some extent, in normal speech.
- Wide normal variation in speech production rates.

Phonological errors

- Listen carefully to conversational speech
- Word length effect
 - Test with long words
 - Catastrophe
 - Asparagus
 - Accordion

Target	Response
Behind	be'hond
Words	wads
Constructed	con'stracted
Spoonerism	'spoozerism
Trumpet*	'trambet
Cucumber*	'cufedent
Volcano*	vol'kako
Skeleton*	'skelekon
Pagoda*	pa'golo
Sextant*	'santinet
Snail*	'eskarto

Grammatical errors*

- Impaired use of complex syntax
 - Function words
 - Verb conjugations
 - Etc.
- Agrammatism not restricted to output:
 - *The lion was eaten by the tiger...who survived?*
 - (c.f. *The tiger ate the lion.*)
 - *The rug, the table is on, is brown...what is brown?*
 - (c.f. *The table is on the brown rug.*)

* *Poor correlation between agrammatism and fluency*

Other features

- The neuropsychiatric syndrome of FTD is often not present.
- Variably present
 - Buccofacial apraxia
 - Repetition deficits

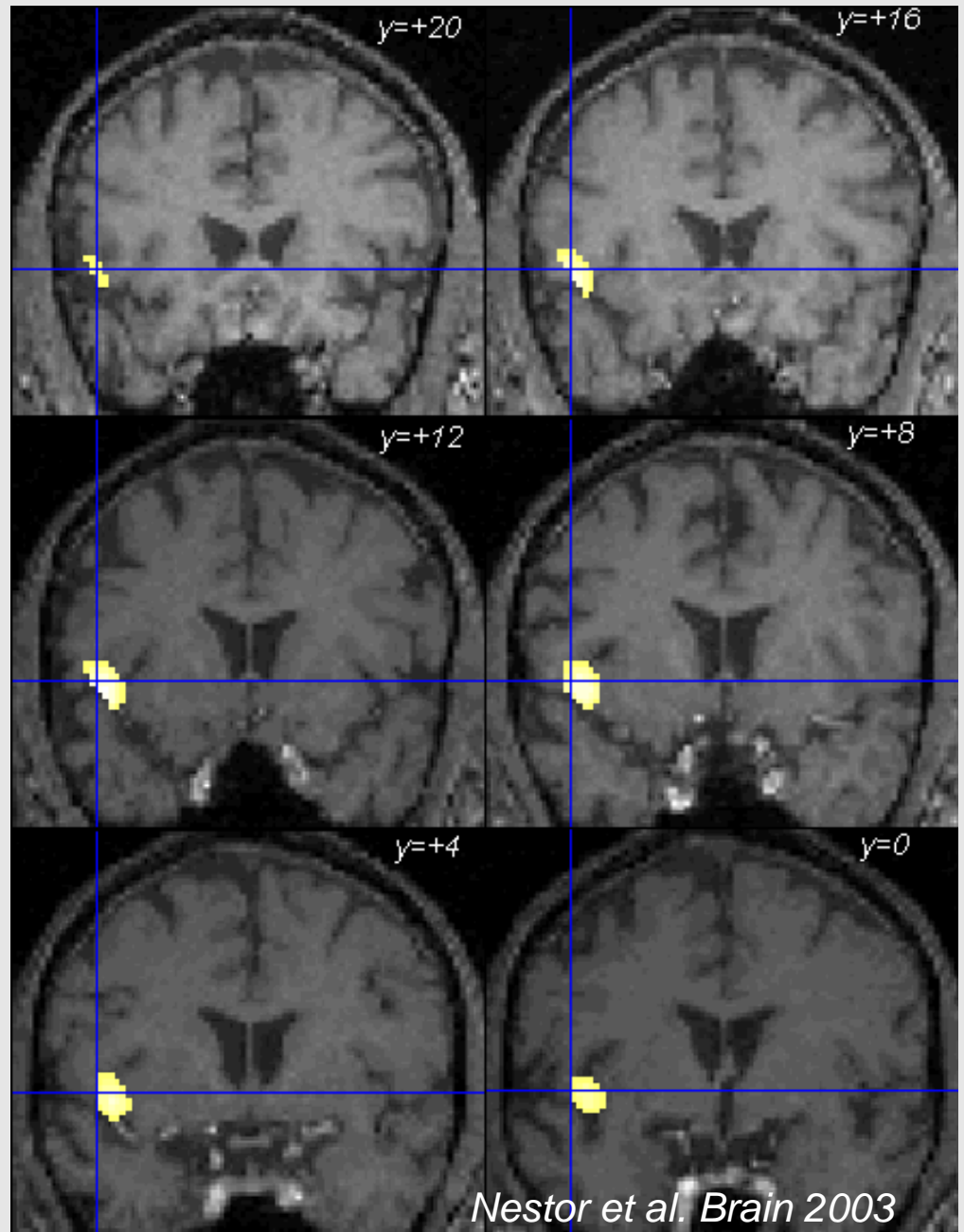
Neuroimaging

- Single case findings are far more heterogeneous than in SD
 - Left peri-Sylvian atrophy often reported but cases vary from normal through to global atrophy

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PNFA:
hypometabolism
centred on left
anterior insula
extending into
frontal operculum

*FDG-PET in 10 PNFA
cases compared to 10
AD cases with normal
fluency*



Nestor et al. Brain 2003

Pathology

- Although classified as a syndrome of FTD the pathology is more heterogeneous than in SD:
 - FTD variants (inc. MND overlap)
 - Alzheimer's disease
 - Global decline over time
 - Corticobasal degeneration
 - Dyspraxic right hand, etc.

Summary

- Progressive aphasia divided clinically into fluent (SD) and non-fluent types.
- SD → FTD pathology
- PNFA → Heterogeneous pathology
- Early language deficits are subtle and clinician needs examination that stresses system to expose deficits.

Behavioural features of FTD (fvFTD)

- Insidious personality change
- Insightlessness
- Stereotypic behaviours
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- Rigidity
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Case history

- 59 year old female
- Presented with 12 months progressive personality and behavioural changes
 - No family history
 - Past history: diabetes

Initial symptoms

- Gross over-eating of chocolates at Christmas time
 - including stealing chocolates from grandchildren
 - Weight gain of 2 stone

Other features...

- Appeared unaffected by death of father
- Restless and pacing
 - E.g. outdoors at night looking at ‘Mr Moon’
- Disinhibition, giggly, repetitive phrases
- Poor table manners
- Clock-watching, rigid
- Aggressive
- Insightless

Cognitive exam.

- Disorganised and very unreliable when tested but appeared relatively intact on:
 - Memory, language, visuospatial abilities

Frontal variant FTD

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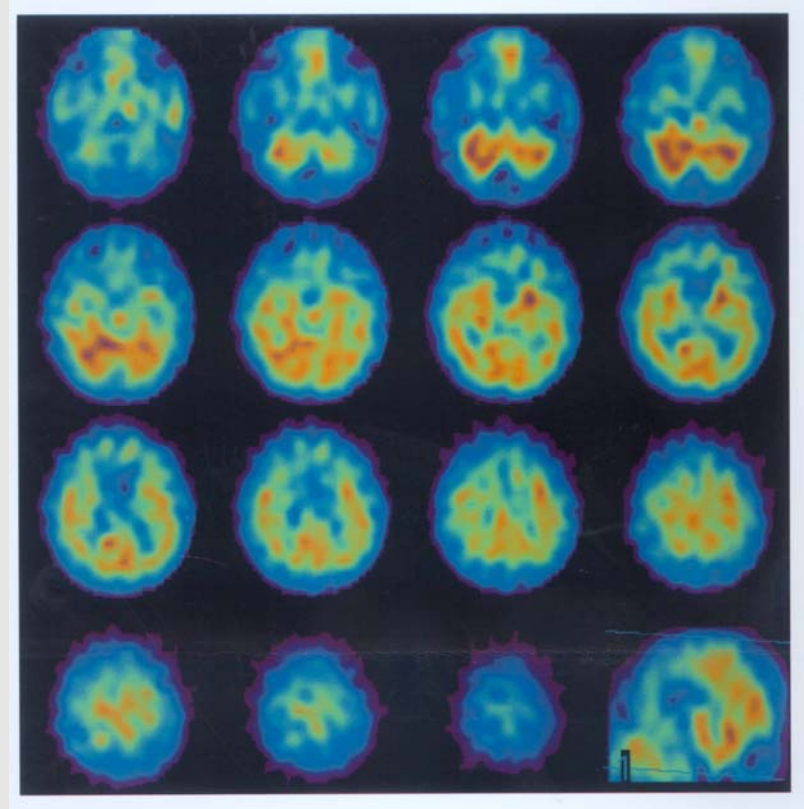
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