Semantic Dementia as a Disorder of Memory

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A Brief History

- 1890s Arnold Pick: amnestic aphasia in patients with left temporal atrophy

- 1975 Warrington: “Selective loss of semantic memory”

- 1982 Mesulam “Primary progressive aphasia”

- 1989 Snowden et al “Semantic dementia”


Classification of FTD

(neary et al. 1998 Neurology 51, 1546-54)

- FTD
- Semantic dementia
- Prog. nonfluent aphasia
- Disinhibited variant
- Apathetic variant

Semantic dementia

(Neary et al. 1998)

- Insidious onset and gradual progression
- Language disorder characterised by
  - Fluent empty spontaneous speech
  - Loss of word meaning: impaired comprehension and naming
  - Semantic paraphasias
- Perceptual disorder characterised by
  - Prosopagnosia and/or associative agnosia
  - Preserved matching and drawing
  - Preserved single word reading

Semantic dementia: Our view

- Progressive loss of verbal and non-verbal semantic memory
**Semantic dementia**

- Progressive loss of verbal and non-verbal semantic memory
- Preservation of other cognitive domains (e.g., working memory, visuo-spatial ability, non-verbal problem solving ability, phonology & syntax)
- Good orientation and recall of recent events
- Atrophy to the infero-lateral temporal neocortex with relative preservation of the hippocampus early in the disease

**Three cases of semantic dementia**

- Case A: mild
- Case B: moderate
- Case C: severe

**Patient A**

- 50 year-old woman, university education
- 24 months word finding difficulty and “loss of memory for words”
- No impairment in conversational comprehension
- Intact everyday activities

**Patient A**

- Verbal fluency reduced for living and manmade items: 50% of normal
- Easy naming test: 92%
- Hard (Graded) naming test: 30%
- Semantic errors
**Patient A**

- Verbal fluency reduced for living and manmade items: 50% of normal
- Easy naming test: 92%
- Hard (Graded) naming test: 30% Semantic errors
- Word-picture matching and pyramids and palmtrees: 100%
- Visuo-spatial skills, problem solving, non-verbal memory: all normal

**Patient A: Is comprehension normal?**

- Synonym judgement impaired
  - **Rogue** scoundrel polka gasket
  - **Humour** whiff wit carbon
  - **Impetus** equity motivation misconception

**Patient A**

- MRI: anterior left TL atrophy

Diagnosis: Primary progressive aphasia: purely anomic?
**Mean effect of semantic distance on Word-to-Picture Matching**

- L0
- L1
- L2
- L3

**Patient A: Is comprehension normal?**
- Synonym judgement impaired
- Definitions of word meaning also impaired
- Word comprehension deficits are present if tested using harder tests
- Still PPA: fluent type?

**Patient B**
- 48 months word finding difficulty and “loss of memory for words”
- Spouse noted impairment in comprehension
- Intact everyday activities
- Becoming rigid and rather obsessional

**Patient B**
- Verbal fluency reduced for living and manmade items: 20% of normal
- Easy naming test: 41%
- Hard (Graded) naming test: 0%
Patient B

- Verbal fluency reduced for living and manmade items: 20% of normal
- Easy naming test: 41%
- Hard (Graded) naming test: 0%
- Word-picture matching: 80%
- Visuo-spatial skills, problem solving, non-verbal memory: all normal
- Normal use of objects in everyday life

Patient B

- Left anterior TL atrophy & FDG-PET
- Progressive aphasia with marked word comprehension deficit

Patient B: Is it just language?

- Impaired on pyramids and palmtrees (80%) and even more on Camel and cacti (60%)

Examples from Camel & Cacti Test

- Impaired on pyramids and palmtrees (80%) and even more on Camel and cacti (60%)
- Unusual objects battery: marked impairment in matching tasks and object usage
**Object Matching and Usage Battery**

- **Recipient**
- **Function**
- **Action**

**Object Matching Tests**

<table>
<thead>
<tr>
<th>Function</th>
<th>Recipient</th>
<th>Action</th>
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**Real Object Use**

<table>
<thead>
<tr>
<th>proportion</th>
<th>hold</th>
<th>movement</th>
<th>orientation</th>
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**Naming and Word-to-Picture Matching**

<table>
<thead>
<tr>
<th>Patients</th>
<th>control</th>
<th>mean patient</th>
<th>mean control</th>
</tr>
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<tbody>
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**Knowledge and Object Use**

<table>
<thead>
<tr>
<th>knowledge</th>
<th>object use</th>
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</table>

**Patient B: Is it just language?**

- Impaired on pyramids and palmtrees (80%) and even more on Camel and cacti (60%)
- Unusual objects battery: marked impairment in matching tasks and object usage
- Markedly impaired knowledge of object colour
Colouring line drawings...

- 15 SD patients asked to colour 40 line drawings of common objects
- Objects included animals, fruits and vegetables, body parts, and artifacts with conventional colours
- 2 patients coloured all objects, the rest pointed to the colours they would use

Patient C

- 60 months word finding difficulty and “loss of memory for word”
- Marked impairment in comprehension
- Restricted everyday abilities, good with numbers, able to cook, still driving!
- Strange habits

Patient C: Spontaneous Speech

JH: What kind of job did you do?
Patient: I did things, you know... In the house
JH: Do you have any hobbies?
Patient: Hobbies, what are they? *That’s just my problem I don’t know words*
JH: Things you like to do.
Patient: Oh, I like to play golf.

Patient C: Is she demented?

- Fluency: “what’s an animal”
- Naming: zero
- Word-picture matching: chance
- Pyramids and palm trees: very poor
- Preserved: digit span, visuospatial skills, recognition memory for pictures

Patients A, B and C are one!

- Patient A = W.M in 1998
- Patient B = W.M. in 2001
- Patient C = W.M in 2003

- Typical longitudinal course in semantic dementia
### Change in naming errors

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<tr>
<th></th>
<th>1998</th>
<th>2001</th>
<th>2003</th>
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<tr>
<td>dog</td>
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<td>+</td>
<td>+</td>
</tr>
<tr>
<td>horse</td>
<td>+</td>
<td>+</td>
<td>creature</td>
</tr>
<tr>
<td>zebra</td>
<td>+</td>
<td>horse</td>
<td>creature</td>
</tr>
<tr>
<td>kangaroo</td>
<td>koala</td>
<td>australian</td>
<td>creature</td>
</tr>
<tr>
<td>eagle</td>
<td>pigeon</td>
<td>bird</td>
<td>d.k.</td>
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### Naming in SD: effects of difficulty in patient W.M.

- **Naming: easy**
- **Naming: hard**

### Fluency, naming and comprehension in SD: patient W.M.

- **Fluency**
- **Naming**
- **W-P matching**

### Comprehension in SD: effects of stimuli in patient W.M.

- **PPT:** pictures
- **CCT:** pictures
- **Sounds**
- **Colour knowledge**

### Progression in semantic dementia

- Fluency and naming low freq and atypical exemplars. Word definition tests.
- Impairment on comprehension tests requiring specific "low level" knowledge
- Particular problems where the mapping of stimulus to meaning is arbitrary
  - Words -> sounds -> pictures -> objects

### What is semantic dementia?

- Insidious onset and gradual progression
- Language disorder characterised by
  - Fluent empty spontaneous speech
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- Perceptual disorder characterised by
  - Prosopagnosia and/or
  - Associative agnosia
- Preserved matching and drawing
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Longitudinal MRIs in W.M.

16-12-99  18-08-00  27-06-01
+246 days  +559 days

Neural basis of concept knowledge?

From McClelland and Rogers (2003)

A computational implementation

Voxel Based Morphometry in Semantic dementia
Mummery et al. 2000

VBM Correlation with semantic loss in FTD/SD series

Semantic and Episodic Memory

Semantic Memory task

Episodic Memory task
**Performance of SD Patients**

![Graph showing Performance of SD Patients]

**Performance of AD Patients**

![Graph showing Performance of AD Patients]

**Temporal source memory test**

**Study Phase 1**

**Study Phase 2**

*Simons et al. Brain 2002*

**Test Phase**

*“Did you see the picture in Set 1, Set 2, or not at all?”*
Source discrimination: SD cases ranked by severity

CANTAB PAL task
- Visuospatial associative memory; subjects must learn location of novel visual stimuli
- Difficulty increases from 1-2-3-6-8 stimuli
- Subjects have 10 chances to learn each problem

Errors at 6 pattern stage of the PAL (Lee et al., 2003)

The circuit of Papez

Method
- Regions of interest traced onto 3T volumetric MRI.
- FDG-PET co-registered onto MRI
- CMRglc calculated
- Normalised to cerebellum
- 3-compartment partial volume correction

FDG-PET findings in AD and MCI
Early PET changes in MCI/AD

Mammillary bodies and thalamus

FDG-PET changes in MCI/AD

Hippocampal complex in AD and SD

* P<0.05 v Controls
† P<0.01 v Controls

FDG-PET Findings in series of SD cases

* SPM P(corr)=0.05

Posterior Cingulate in AD and SD

Mamillary bodies in AD and SD

Summary of metabolic changes

<table>
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<tr>
<th>AD</th>
<th>SD</th>
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<tr>
<td>HC</td>
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<tr>
<td>MB</td>
<td>MB</td>
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<tr>
<td>Thalamus</td>
<td>Thalamus</td>
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<tr>
<td>PC</td>
<td>PC</td>
</tr>
<tr>
<td>Amygdala</td>
<td>Amygdala</td>
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Kim Graham
Karalyn Patterson
Jon Simons
Peter Nestor
Rhys Davies
Clare Galton
Mieke Verfaeille
Tim Rogers
Andy Lee