Semantic Dementia as a Disorder of Memory

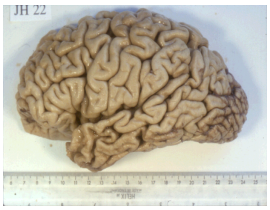
John R. Hodges

MRC-CBU Cambridge and University of Cambridge

MRC CBU

A Brief History

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

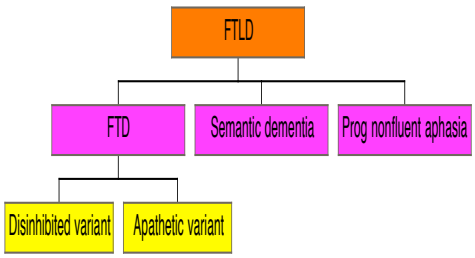


A Brief History

- **1975 Warrington: "Selective loss of semantic memory"**
- **1982 Mesulam "Primary progressive aphasia"**
- **1989 Snowden et al "Semantic dementia"**
- **1992 Hodges et al. "Semantic dementia: progressive fluent aphasia with left temporal lobe atrophy"**

Classification of FTD

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



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)

Semantic dementia

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- 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

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

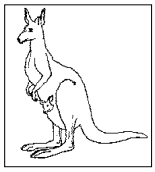
Patient A

- 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

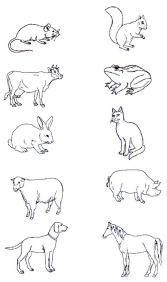
- Verbal fluency reduced for living and manmade items: 50% of normal
- Easy naming test: 92%
- Hard (Graded) naming test: 30% Semantic errors

Graded Naming Test **Semantic Battery**



Easy

Hard

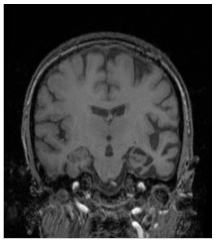


Patient A

- 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

- MRI: anterior left TL atrophy

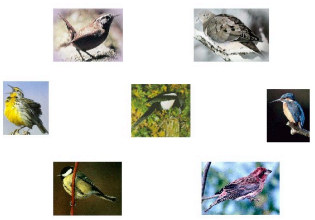


Diagnosis: Primary progressive aphasia: purely anomic?

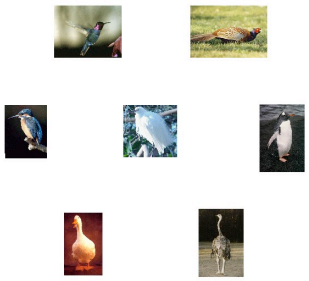
Patient A: Is comprehension normal?

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

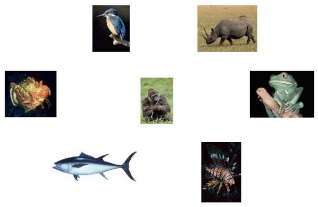
WP-Matching Level 0



WP-Matching Level 1

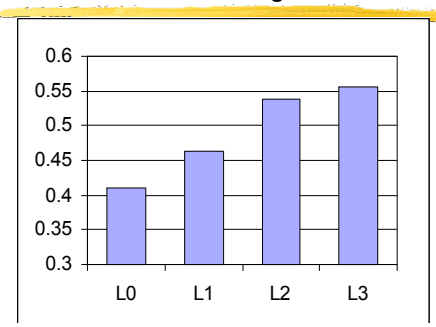


WP-Matching Level 2



WP-Matching Level 3

Mean effect of semantic distance on Word-to-Picture Matching



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

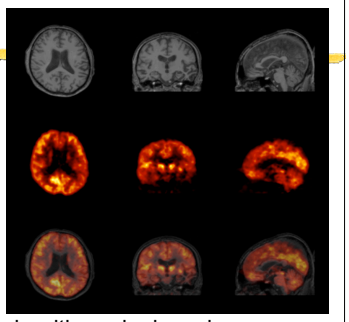
- Verbal fluency reduced for living and manmade items: 20% of normal
- Easy naming test: 41%
- Hard (Graded) naming test: 0%

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?

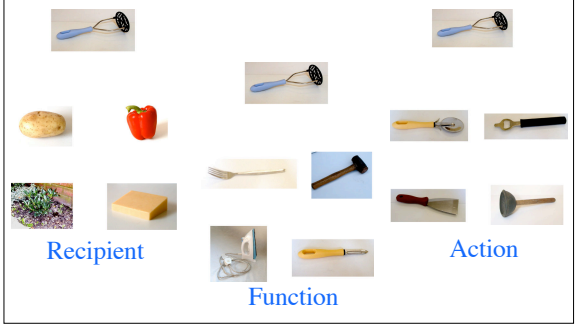
- Impaired on pyramids and palmtrees (80%) and even more on Camel and cacti (60%)

Examples from Camel & Cacti Test

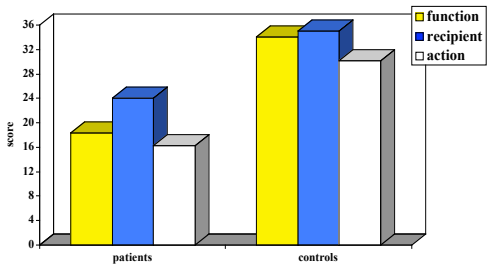
Patient B: Is it just language?

- 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

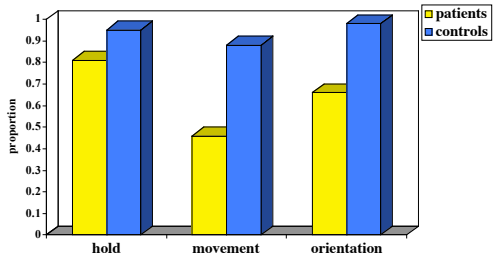
Object Matching and Usage Battery



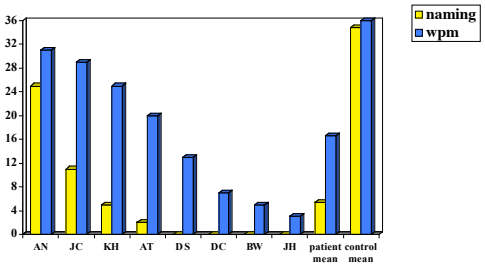
Object Matching Tests



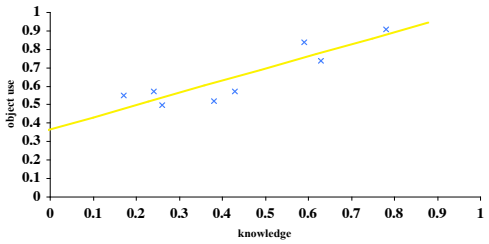
Real Object Use



Naming and Word-to-Picture Matching



Knowledge and Object Use

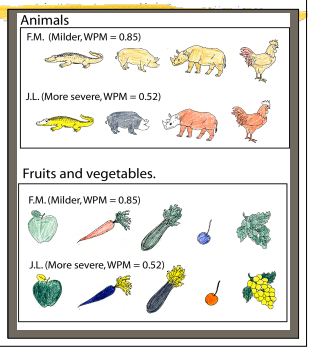


Patient B: Is it just language?

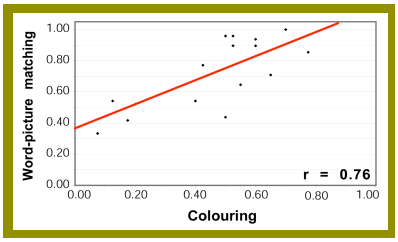
- Impaired on pyramids and palmtrees (80%) and even more on Camel and cacti (60%)
- Unusual objects battery: marked impairment in matching tasks and object usage
- Markedly impaired knowledge of object colour

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



Correlation with word-picture matching



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 palmtrees: very poor
- Preserved: digit span, visuospatial skills, recognition memory for pictures

Patients A, B and C are one!

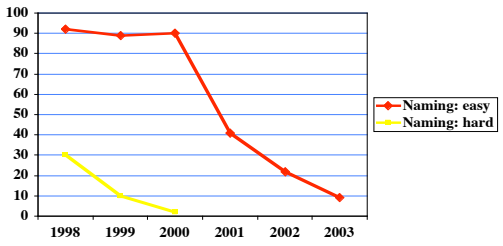
- Patient A = W.M in 1998
- Patient B = W.M. in 2001
- Patient C = W.M in 2003

- Typical longitudinal course in semantic dementia

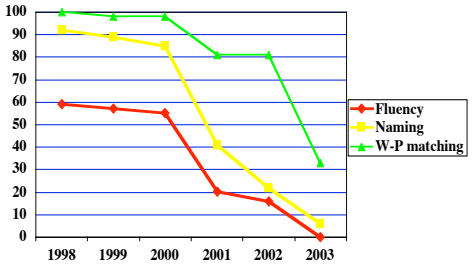
Change in naming errors

	1998	2001	2003
dog	+	+	+
horse	+	+	creature
zebra	+	horse	creature
kangaroo	koala	australian	creature
eagle	pigeon	bird	d.k.

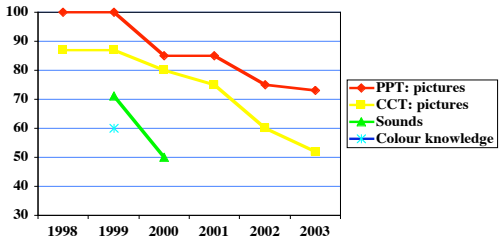
Naming in SD: effects of difficulty in patient W.M.



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



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



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
  - Loss of word meaning: impaired comprehension and naming
  - Semantic paraphasias
- Perceptual disorder characterised by
  - Prosopagnosia and/or
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- Preserved matching and drawing
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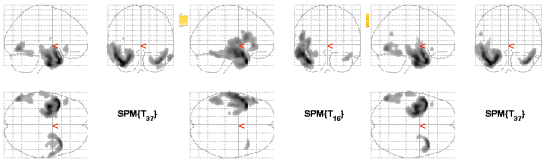
Longitudinal MRIs in W.M.

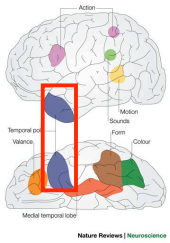


16-12-99

18-08-00
+246 days

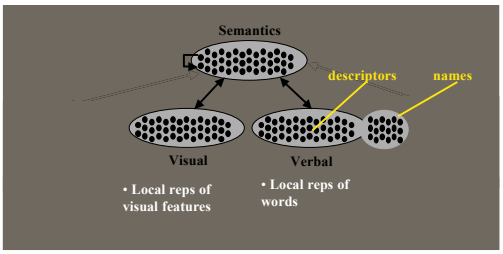
27-06-01
+559 days

Neural basis of concept knowledge?



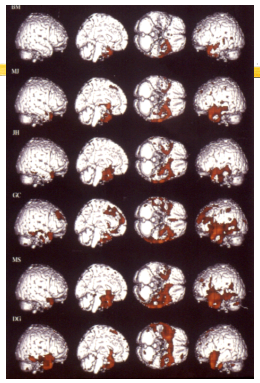
From McClelland and Rogers (2003)

A computational implementation

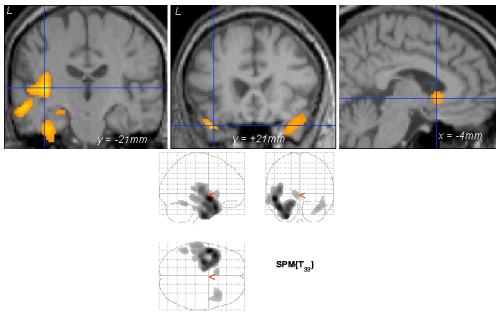


Voxel Based Morphometry in Semantic dementia

Mummery et al. 2000

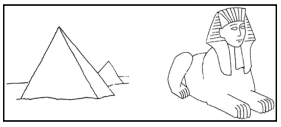


VBM Correlation with semantic loss in FTD/SD series



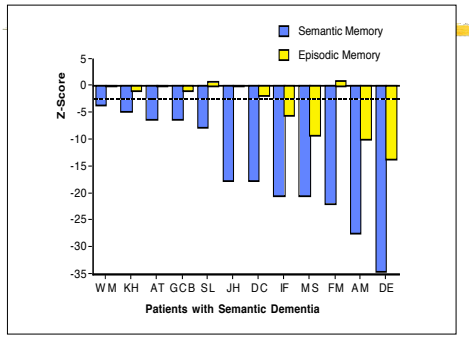
Semantic and Episodic Memory

Semantic Memory task

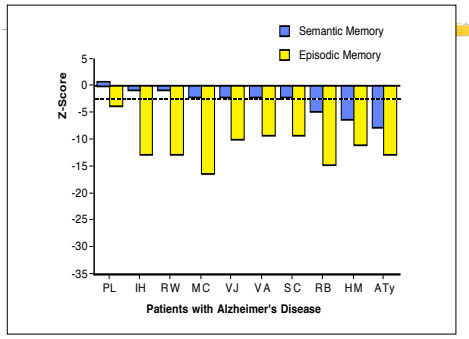


Episodic Memory task

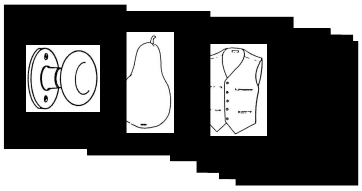
Performance of SD Patients



Performance of AD Patients

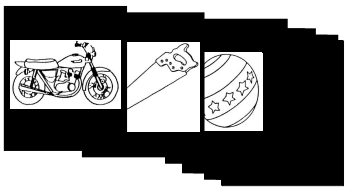


Temporal source memory test
Study Phase 1

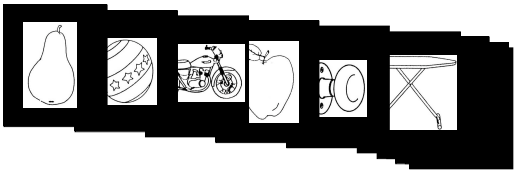


Simons et al. Brain 2002

Study Phase 2

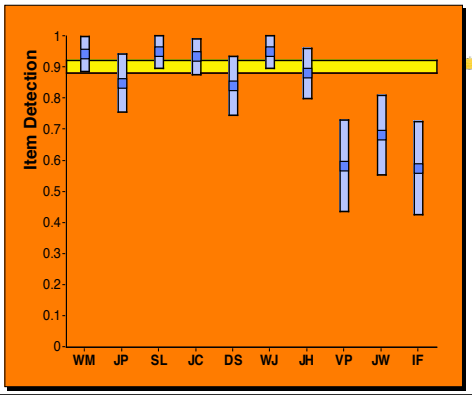


Test Phase

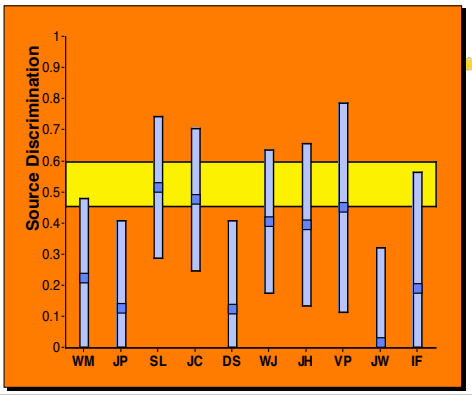


"Did you see the picture in Set 1, Set 2, or not at all?"

Item Detection: SD cases ranked by severity

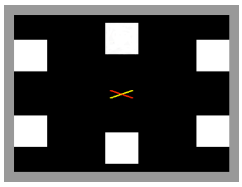


Source discrimination: SD cases ranked by severity

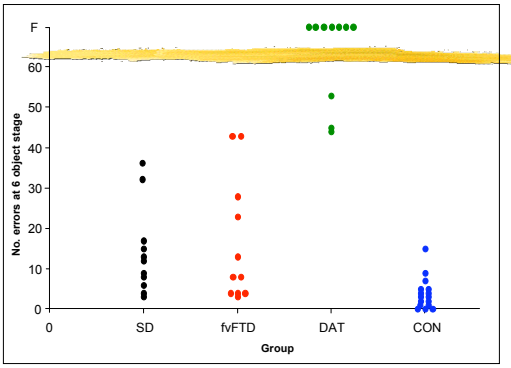


CANTAB PAL task

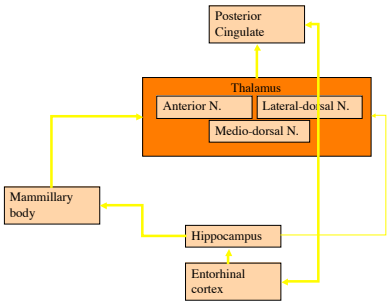
- Visuospatial Associative memory; subjects must learn location of novel visual stimuli
- Difficulty increases from 1-2-3-6-8 stimuli
- Subjects have 10 chances to learn each problem



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

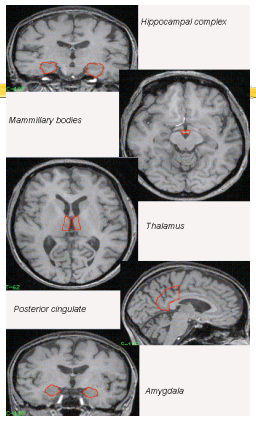


The circuit of Papez

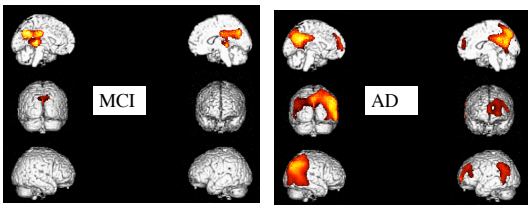


Method

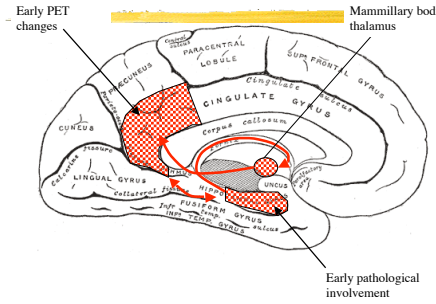
- Regions of interest traced onto 3T volumetric MRI.
- FDG-PET co-registered onto MRI
- CMRglc calculated
- Normalised to cerebellum
- 3-compartment partial volume correction



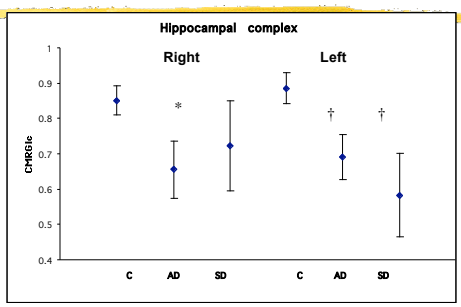
FDG-PET findings in AD and MCI



FDG-PET changes in MCI/AD

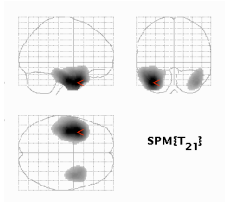


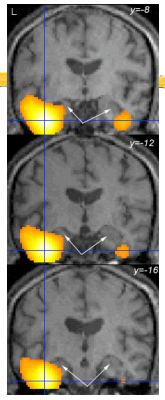
Hippocampal complex in AD and SD



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

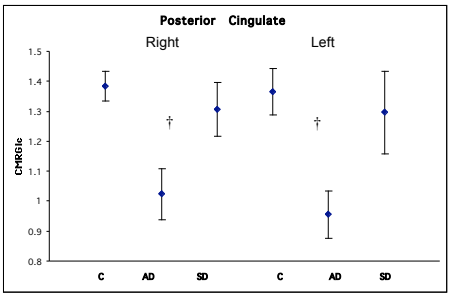
FDG-PET Findings In series of SD cases



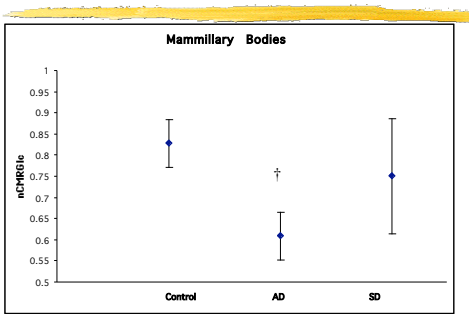


* *SPM P(corr)=0.05*

Posterior Cingulate in AD and SD



Mamillary bodies in AD and SD



Summary of metabolic changes

AD	*SD*
HC	HC
MB	MB
Thalamus	Thalamus
PC	PC
Amygdala	Amygdala

Kim Graham
Karalyn Patterson

Jon Simons
Peter Nestor
Rhys Davies
Clare Galton
Mieke Verfaeille
Tim Rogers
Andy lee