Aphasia Clinics – Part 2
Differential impairments of semantic cognition in progressive vs. stroke-related aphasias

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And many others
Semantic cognition

- Semantic cognition is a part of both verbal and nonverbal activities.
- At least three principal components:
  - Sensation ↔ meaning [agnosia/word deafness]
  - Semantic memory [degraded representations]
  - Semantic control [deregulated processing]
Introduction

• Semantic impairment found in:
  – Progressive disorders: e.g., semantic dementia
  – Stroke-related aphasia: 1/3 have measurable semantic impairment (Lambon Ralph et al., Aphasiology, 2002)
  – Other disorders (e.g., TLE, HSVE, head injury)

• Approach:
  – Direct, case-series comparisons – using same materials*
  – Embedded in same cognitive framework
  – Use other neuroscience methods* to confirm and extend patient findings, including neuroanatomy specificity
Semantic dementia

• Semantic dementia: temporal lobe variant of frontotemporal dementia

• Selective neuropsychological impairment:
  × Comprehension impairment
  × Anomia
  ✓ Spared phonology and syntax
  ✓ Spared nonverbal reasoning
  ✓ Spared perceptual and spatial skills
  ✓ Excellent memory for current events
Semantic dementia

- Atrophy & hypometabolism focused in anterolateral temporal lobes
- Bilaterally but often asymmetric

Structural MRI  Voxel-based morphometry  FDG PET

Mummery et al. (2000)

Nestor et al. (2005)
Summary of semantic impairment in SD

- Selective semantic impairment
- All domains affected: pictures, words, sounds, smells, tactile recognition, taste
- Receptive and expressive tasks
- Structured degradation of concepts

- ATL → basis for modality-invariant contribution to ‘coherent’ semantic representations
  
  [Lambon Ralph et al., PNAS 2010; Pobric et al., Curr. Biol. 2010]
Converging evidence for ATL contribution to semantic cognition

- Implications from SD questioned (e.g., Martin, 2007)
- Does not appear in classic neurological models of language
- If ATL is critical in producing impaired semantic memory – what about its normal functioning in intact people?
- Convergent evidence:
  - Repetitive transcranial magnetic stimulation (rTMS)
  - Functional neuroimaging
rTMS methods: equipment
Locating the temporal pole
Offline rTMS: “virtual lesion” method

- Repeated stimulation produces refractory period in underlying cortex:
  - 120% hand motor threshold
  - 1Hz for 10 minutes (600 pulses)
  - Refractory window ~ 15 minutes

- Use timed analogues of neuropsychological assessments for convergent evidence
rTMS: lateral ATL
Timed synonym judgement

Pobric et al., *PNAS*, 2007; Lambon Ralph et al., *Cerebral Cortex*, 2009
Functional neuroimaging and the anterior temporal lobe

Missing the meaning

- ATL notable by its absence in fMRI studies
- Absence of ATL self-reinforcing in fMRI-based studies
- ATL-semantics literature review (Visser et al., JoCN 2010):
  - PET > fMRI
  - Field of view
  - Control task: higher baseline > low level/rest
- Magnetic field distortion:
  - EPI gradient – signal split & shifted
ATL semantics across methods:
SD, rTMS & distortion-corrected fMRI

Binney et al., *Cerebral Cortex*, 2010

Pobric et al., *PNAS*, 2007
A very consistent fMRI-SD vATL story

Binney et al., *Cerebral Cortex*, 2010

Galton et al., *Neurology*, 2001
Graded variation of function across ATL
(Visser & Lambon Ralph, JoCN, in press)
Semantic impairments across diseases

- Semantic dementia: anterior temporal, bilateral
- HSVE: anterior temporal, bilateral
  
  (Lambon Ralph et al., *Brain*, 2007)

- Status of multi-modal semantics in CVA aphasia?
  
  (Jefferies & Lambon Ralph et al., *Brain*, 2006)
Transcortical Sensory Aphasia (TSA)

- Poor verbal comprehension, fluent speech and good repetition
- Status of non-verbal comprehension unclear
- How does this compare to SD given different location of damage?

(Berthier, 2001)
Multimodal semantic impairment: Semantic dementia vs. semantic aphasia
(Jefferies & Lambon Ralph, *Brain*, 2006)

- Ten chronic aphasic CVA patients
- All impaired on picture semantic association test (PPT/CCT)
  - Verbal + nonverbal impairment
  - Not just language comprehension deficit
- Compared to SD cases (matched overall)
  - Different neurology
  - Qualitatively different performance
## Selected patients with stroke aphasia

<table>
<thead>
<tr>
<th>Case</th>
<th>Aphasia</th>
<th>ATL lesion</th>
<th>LIPFC lesion</th>
<th>T-P lesion</th>
</tr>
</thead>
<tbody>
<tr>
<td>SC</td>
<td>Anomic/TSA</td>
<td>✗</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>ME</td>
<td>TSA</td>
<td>✗</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>JM</td>
<td>TSA</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>PG</td>
<td>TSA</td>
<td>✗</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>LS</td>
<td>TSA</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>NY</td>
<td>Mixed transcortical</td>
<td>✗</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>KH</td>
<td>Mixed transcortical</td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>BB</td>
<td>Mixed transcortical</td>
<td>✗</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>KA</td>
<td>Global</td>
<td>✗</td>
<td>✓</td>
<td>✗</td>
</tr>
<tr>
<td>MS</td>
<td>Global</td>
<td>✗</td>
<td>✓</td>
<td>✗</td>
</tr>
</tbody>
</table>
SD: Intra- & Inter-task comparisons

Within task

Between task
SA: Intra- & Inter-task comparisons

**Within task**

**Between task**

![Graph showing word PPT vs. picture PPT within task with a linear relationship.](image)

![Graph showing word PPT vs. word-picture matching between tasks without a clear relationship.](image)
Effect of external constraint: phonemic cueing (BNT)
Control of semantic activation: Types of semantic naming error

- **Coordinate**
  - Orange → “apple”
  - Squirrel → “cat”

- **Superordinate**
  - Orange → “fruit”
  - Squirrel → “animal”

- **Associative**
  - Orange → “juice”
  - Squirrel → “nuts”
Semantic control impairment

- LIPFC & angular gyrus: cognitive & semantic control
- Areas damage in SA
- Semantic control (Noonan et al., *JCN*, 2010):
  - Inflexible semantic access
  - Poor inhibition of semantic competitors
  - Improved with external constraint

  e.g.,
  - Understanding of dominant > subordinate meaning (e.g., BANK)
  - Performance on subordinate equalised with sentence context
Semantic control: Convergence of patients & rTMS

(Hoffman et al, J. Neurosci, 2010)
Semantic control: Convergence of patients & imaging

Noonan et al. (submitted): ALE meta-analysis of 53 imaging studies of semantic control

(Berthier, 2001)
Semantic control:
Convergence of patients & rTMS

(Whitney et al, Cereb. Cortex, in press)
Semantic control: Convergence of patients & rTMS

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(Whitney et al, Cereb. Cortex, in press)
Semantic control: Convergence of patients & rTMS

(Whitney et al, Cereb. Cortex, in press)
## Semantic aphasia vs. semantic dementia

<table>
<thead>
<tr>
<th></th>
<th>SD</th>
<th>SA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multimodal comprehension impairment</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>ATL damage</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>PFC and/or temporoparietal</td>
<td>✗</td>
<td>✔</td>
</tr>
<tr>
<td>Correlation of performance across different tasks</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>Item familiarity + word frequency</td>
<td>✔</td>
<td>✗</td>
</tr>
<tr>
<td>Item consistency</td>
<td>✔</td>
<td>~</td>
</tr>
<tr>
<td>Correlation with ‘executive’ assessments</td>
<td>✗</td>
<td>✔</td>
</tr>
<tr>
<td>Improvement with cueing (verbal and nonverbal)</td>
<td>✗</td>
<td>✔</td>
</tr>
</tbody>
</table>

Where does Wernicke’s Aphasia fit in?

- SA selected for SD comparison (cf. Chertkow et al, 1999)
- No WA patients in SA group
- WA – the classical comprehension impairment in neurology
- WA – associated with pSTG and pMTG damage
Wernicke’s Aphasia participants

- 9 Wernicke’s aphasia participants (3 female), mean age 74
- “Classical” chronic WA = impaired auditory comprehension + jargon (BDAE: Goodglass et al., 2003)

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Time post-onset at testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>AB</td>
<td>85</td>
<td>F</td>
<td>6-12 months</td>
</tr>
<tr>
<td>LB</td>
<td>78</td>
<td>F</td>
<td>6 years</td>
</tr>
<tr>
<td>EL</td>
<td>60</td>
<td>M</td>
<td>4-6 months</td>
</tr>
<tr>
<td>MR</td>
<td>64</td>
<td>M</td>
<td>5-7 months</td>
</tr>
<tr>
<td>DH</td>
<td>74</td>
<td>M</td>
<td>5-7 months</td>
</tr>
<tr>
<td>DM</td>
<td>86</td>
<td>M</td>
<td>5-7 months</td>
</tr>
<tr>
<td>RD</td>
<td>86</td>
<td>M</td>
<td>12 – 14 months</td>
</tr>
<tr>
<td>AC</td>
<td>53</td>
<td>M</td>
<td>5-9 months</td>
</tr>
<tr>
<td>HS</td>
<td>81</td>
<td>F</td>
<td>6-8 months</td>
</tr>
</tbody>
</table>

- Comparison Groups: SA n=10, SD n=10
Comparative temporal lobe lesion distributions

A. Wernicke’s aphasia
B. Semantic dementia
C. Semantic aphasia
Comparative patient results

Environmental Sounds Test

Cambridge Semantic Battery

Robson et al. (submitted)
Comparative patient results

Environmental Sounds Test

Cambridge Semantic Battery

Robson et al. (submitted)
### Three-way comparison

<table>
<thead>
<tr>
<th></th>
<th>SD</th>
<th>SA</th>
<th>WA</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Multimodal impairment</strong></td>
<td>✓</td>
<td>✓</td>
<td>~✓</td>
</tr>
<tr>
<td><strong>Acoustic-phonological deficit</strong></td>
<td>✗</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td><strong>ATL damage</strong></td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td><strong>PFC or temporoparietal</strong></td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Item familiarity</strong></td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td><strong>Item consistency</strong></td>
<td>✓</td>
<td>~</td>
<td>~</td>
</tr>
<tr>
<td><strong>Correlation with ‘executive’ assessments</strong></td>
<td>✗</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

Robson et al. (*submitted*)
WA vs. SA

The diagram shows a scatter plot with two axes:

- **Cognitive-Semantic Factor** (x-axis)
- **Phonological Factor** (y-axis)

The plot includes two groups labeled WA and SA, represented by different markers.

The vertical line at the right side of the plot represents the control cut-off for cognitive-normal limits.
Summary and conclusions

• Clear patterns revealed by comparative, case-series approach:
  – Intra-group consistency; inter-group differences
• SD: progressive degradation of modality-invariant, basal ATL representations leading to pan-modal receptive and expressive semantic impairment.
• SA: multi-modal semantic impairment reflects damaged semantic/cognitive control [prefrontal and/or pMTG-AG region]
• WA: combination of acoustic-phonological impairment and semantic control deficit [key extension to pSTG/iSMG]
The End

For further information and papers:
www.psych-sci.manchester.ac.uk/naru/