Neural basis of conceptual knowledge: insights from non-invasive brain stimulation

JSPS Fellowship 2013
Bridge Fellowship 2015

Gorana Pobric

School of Psychological Sciences
University of Manchester
Semantic cognition

Semantic memory allows us to comprehend a multitude of different stimuli, such as words, pictures, objects, environmental sounds and faces.

Express knowledge in a wide variety of domains, both verbal (e.g., naming and verbal definitions) and non-verbal (e.g., drawing and object use).

Semantic representations allow us to generalise knowledge appropriately from one exemplar to another (Lambon Ralph & Patterson, 2008).
Semantic cognition

Semantic cognition is core to language and nonverbal skilled behaviours

When semantic cognition is impaired (brain damage), it results in significant disability

How does the brain generate semantic cognition?
Representations of semantic knowledge in the human brain

Contemporary model

(Patterson et al., NRN, 2007)
Representations of semantic knowledge in the human brain

(Patterson et al., NRN, 2007)
Representations of semantic knowledge in the human brain

HUB + spoke model

(Patterson et al., NRN, 2007)
Representations of semantic knowledge in the human brain

(Patterson et al., NRN, 2007)
Acquired disorder of semantic memory: Semantic dementia

Selective neuropsychological impairment:

- Central semantic impairment
  - × Anomia
  - ✓ Spared phonology and syntax
  - ✓ Spared nonverbal reasoning
  - ✓ Spared perceptual and spatial skills
  - Excellent memory for current events
Semantic Dementia

Circumscribed atrophy of anterolateral temporal lobes bilaterally but often asymmetric

(Ikeda et al., 2006)
Converging evidence for ATL semantic system

TMS - Task relevant neural signal – efficacy of that signal degraded – behavioural decrement

Interference technique: transient and reversible

Virtual lesion - advantage over patient studies: control over location, onset, spatio-temporal extent of interference
Effect of ATL rTMS

Synonym judgement vs. number judgement

<table>
<thead>
<tr>
<th>Lobster</th>
<th>Crayfish</th>
<th>Bracelet</th>
<th>Helmet</th>
<th>23</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>87</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>46</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>68</td>
</tr>
</tbody>
</table>

Pobric et al., *PNAS*, 2007
Effect of ATL rTMS

(Pobric et. al., *PNAS*, 2007)
<table>
<thead>
<tr>
<th></th>
<th>Semantic dementia (errors)</th>
<th>ATL rTMS (speed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comprehension</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Naming</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Multimodal effect</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Bilateral involvement</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>

JSPS Short Term Visiting Fellowship 2013

Enhancing semantic cognition in Japanese Kanji word comprehension
Strong electrical currents have been delivered to patients for the relief of headache and epilepsy for approximately two millennia.

In 1804, Aldini, Galvani’s nephew, was the first scientist in the modern era to report the use of electrical stimulation in the treatment of mental disorders.
Transcranial electric stimulation - TES

TES uses low level (1-2 mA) currents applied via scalp electrodes to specific brain regions. The effects of tDCS vary based upon polarity.

When applied in sessions of repeated stimulation, tDCS can lead to changes in neuronal excitability that outlast the stimulation itself. Such aftereffects are at the heart of the tDCS protocols for clinical application (Nitsche et al., 2011).

Promising results in therapy: migraines, dementia, stroke, schizophrenia, Parkinson’s disease.
AIM: to find the best and safest way of stimulating the brain in order to help brain damaged patients and the elderly who show signs of cognitive decline (e.g. difficulty in remembering words)
Synonym judgement

実験
(experiment)

研修
(job training)

研究
(research)
Number judgement

437

442  431
tDCS stimulation

- 20 healthy participants
- Between subject design

**TES:**

- anodal or sham stimulation (control)
- 1.5mA for 20 min – concurrently with the task
- Active electrode over ATL: size 25cm²
- Reference electrode - vertex: size 35cm²
Synonym judgement with two-alternative forced choices

The choices always share one Kanji character (in these examples, “研” and “強”)

実験

研究 研修

学習

屈強 勉強
Accuracy on kanji synonym judgment increased following tDCS stimulation.
The Bridge Fellowship - 2015

Understand stimulation mechanisms

In Manchester, we have already developed a novel scanning paradigm (dual-echo scanning) used to image temporal lobes of the brain (areas involved in semantic processing)

The Bridge Fellowship allowed me to:

1. implement the Manchester scanning paradigm with the Kyoto radiologists
2. pilot imaging experiment
3. pilot concurrent imaging and neurostimulation study

Combined fMRI-tDCS study in Kanji synonym judgment task
Teaching

The focus of this program is to respond to the challenges of an aging society and to develop new technologies and concepts that support fruitful longevity for all of us.

It is intended for non-medical graduate students who will gain medical knowledge for translational projects. This is a fantastic initiative and an amazing program.

I took part in delivery of English language lectures, debate classes and brain imaging curriculum.
Networking

Department of Psychiatry and Neuropathobiology at the Faculty of Life Sciences at Kumamoto University in Kumamoto.

Professor Ikeda and his group are world-leading experts for the early onset of dementia, intervention projects for depression in late life and suicide prevention.

Kumamoto data study: employ statistical analysis to uncover the main variables associated with language symptoms in dementia and Alzheimer’s disease.

Manchester data study: we will compare the results of Kumamoto project with language impairments as a result of stroke. This will inform our understanding of how different types of damage to specific brain areas leads to different types of language problems.

It might be possible to use brain scans from early after stroke or neurodegeneration as predictors of later language status and type of language problem. This information could then be used to tailor management and treatment strategies for patients.
The work supported by the JSPS enabled me to take part in a novel translational project and start a new collaboration with the colleagues in Kumamoto.

JSPS Alumni Association supported the continuation of both projects.

The fellowships gave me an opportunity to visit beautiful country, experience fascinating culture and make lasting friendships.
Special thanks to Prof. Mima, Dr Ishibashi, Prof. Lambon Ralph

Thank you