

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

*JSPS Fellowship 2013*  
*Bridge Fellowship 2015*

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## 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

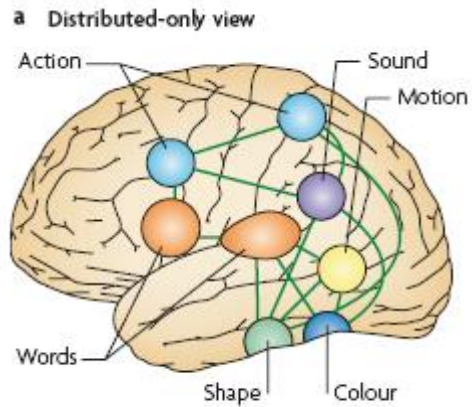
Semantic cognition is core to language and nonverbal skilled behaviours

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

How does the brain generate semantic cognition?

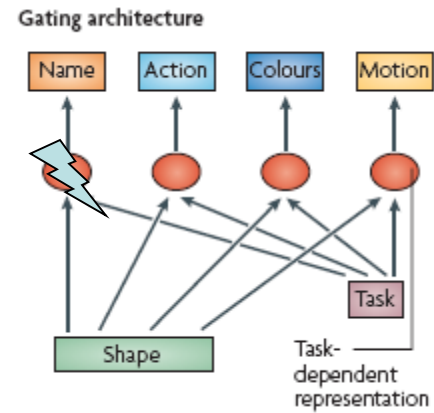
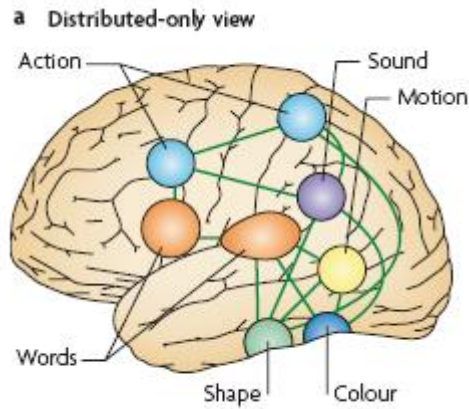
# Representations of semantic knowledge in the human brain

## Contemporary model



(Patterson et al., NRN, 2007)

# Representations of semantic knowledge in the human brain

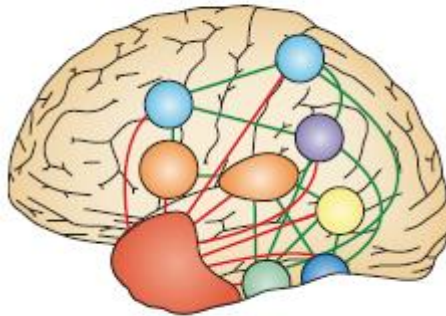


(Patterson et al., NRN, 2007)

# Representations of semantic knowledge in the human brain

## HUB + spoke model

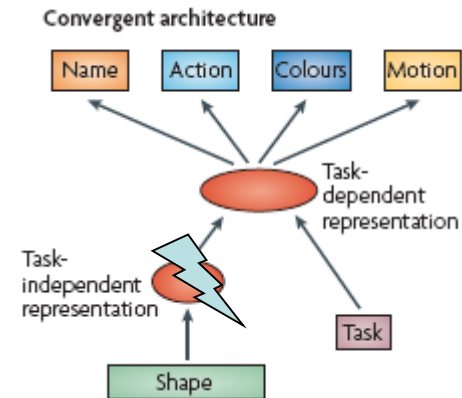
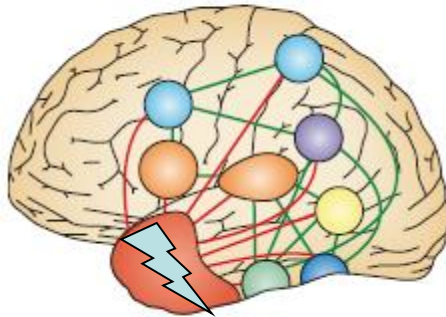
**b** Distributed-plus-hub view



(Patterson et al., NRN, 2007)

# Representations of semantic knowledge in the human brain

b Distributed-plus-hub view



(Patterson et al., NRN, 2007)

## Acquired disorder of semantic memory: Semantic dementia

Selective neuropsychological impairment:

Central semantic impairment

× Anomia

✓ Spared phonology and syntax

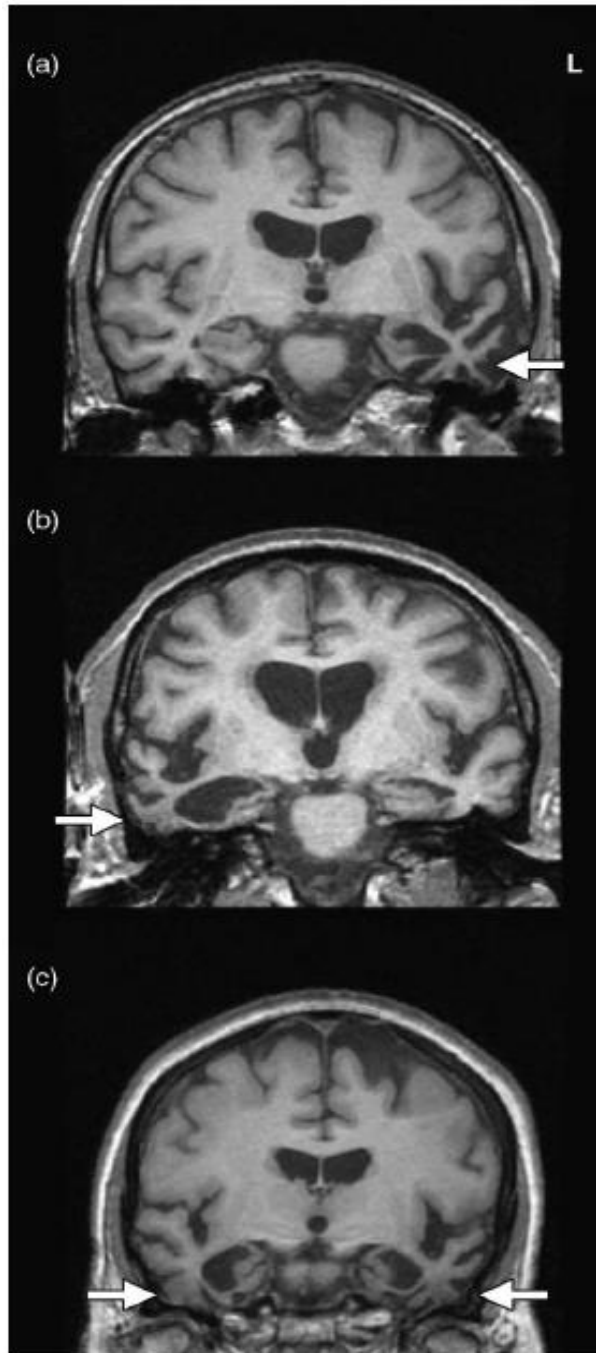
✓ Spared nonverbal reasoning

✓ Spared perceptual and spatial skills

Excellent memory for current events



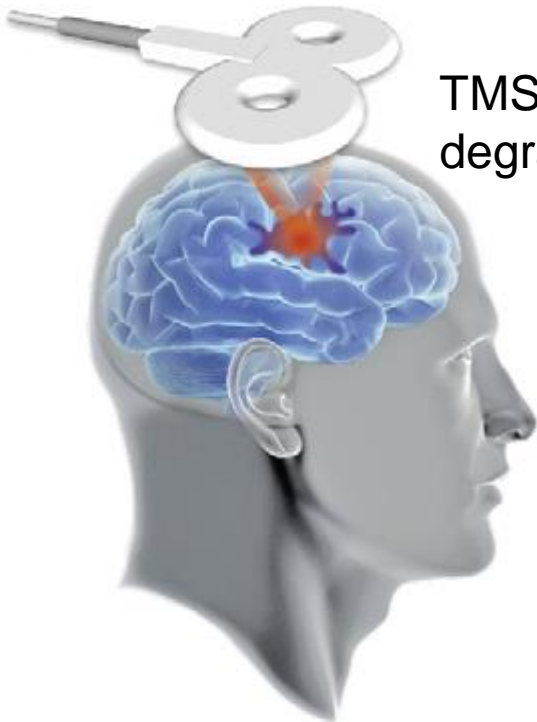
## Semantic Dementia



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

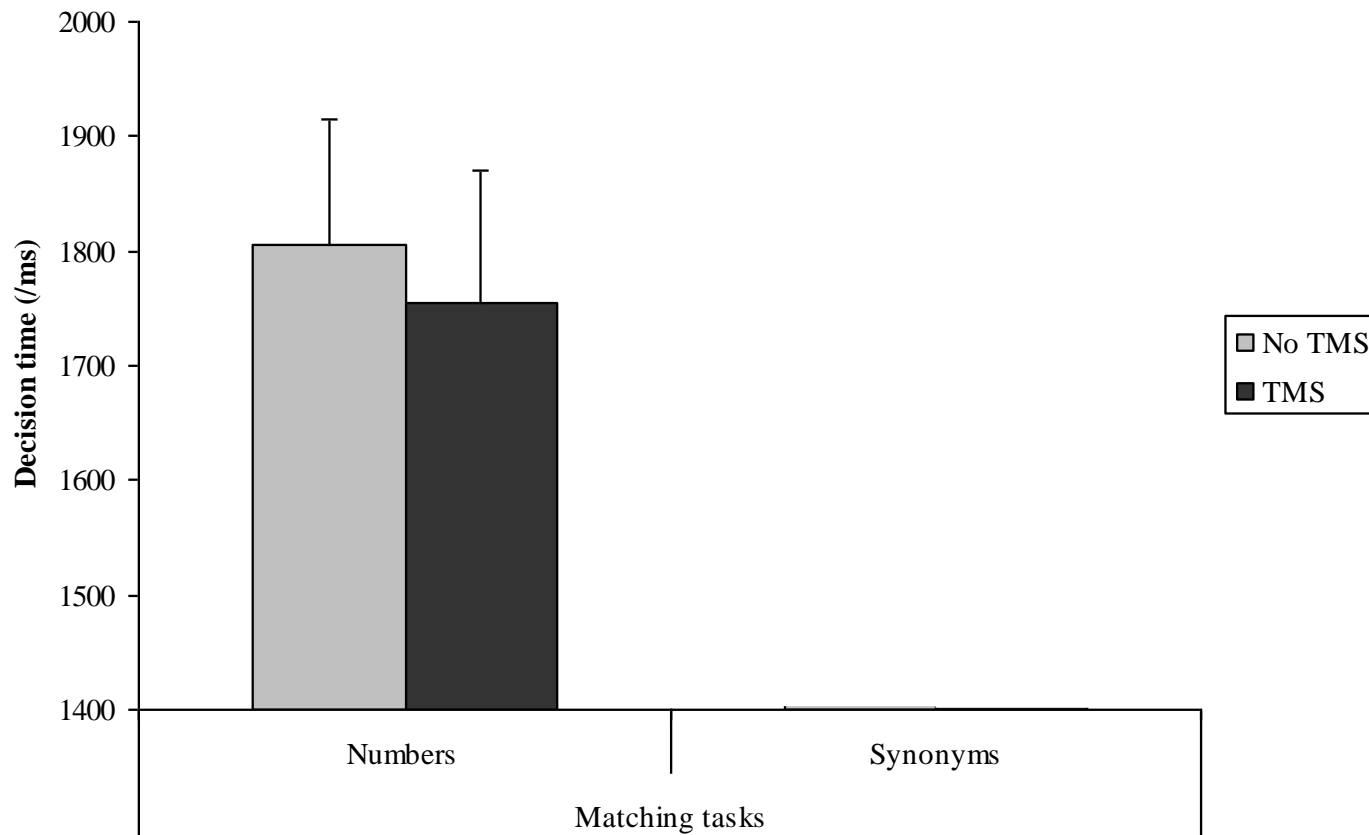
## Effect of ATL rTMS

*Synonym judgement* vs. *number judgement*

<b>Lobster</b>
<b>Crayfish</b> Bracelet Helmet

<b>23</b>
87 <b>46</b> 68

## Effect of ATL rTMS



(Pobric et. al., *PNAS*, 2007)

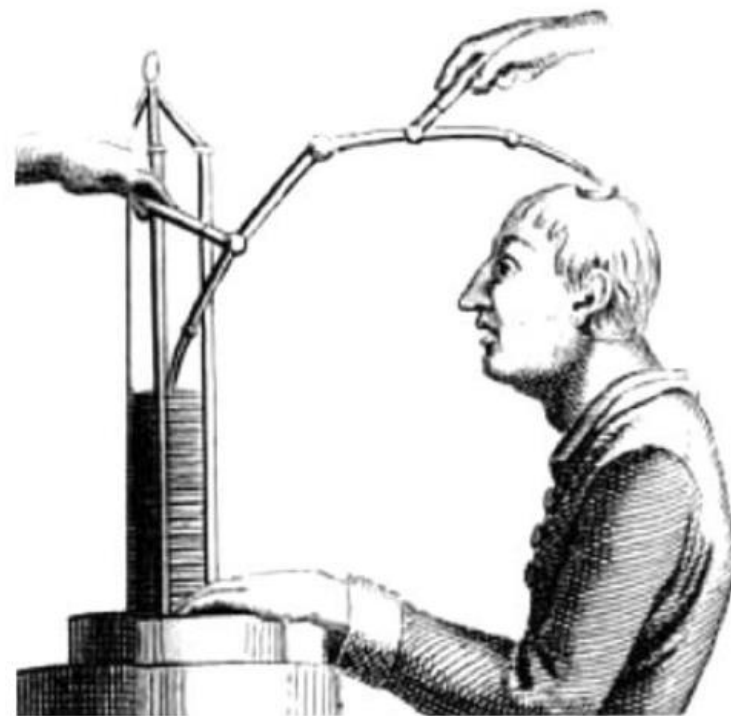
	<u>Semantic dementia</u> (errors)	<u>ATL rTMS</u> (speed)
Comprehension	✓	✓
Naming	✓	✓
Multimodal effect	✓	✓
Bilateral involvement	✓	✓

## JSPS Short Term Visiting Fellowship 2013

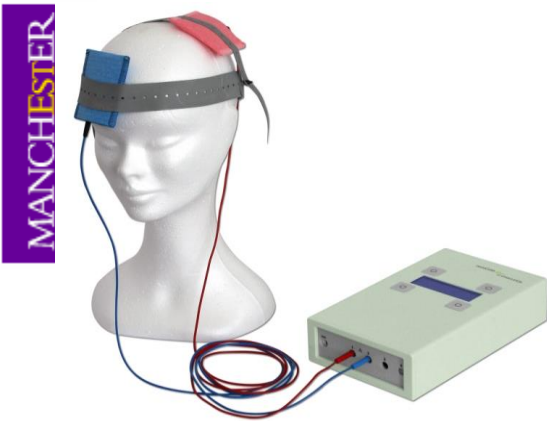
Enhancing semantic cognition in Japanese Kanji word comprehension

Strong electrical currents have been delivered to patients for the relief of headache and epilepsy for approximately two millennia

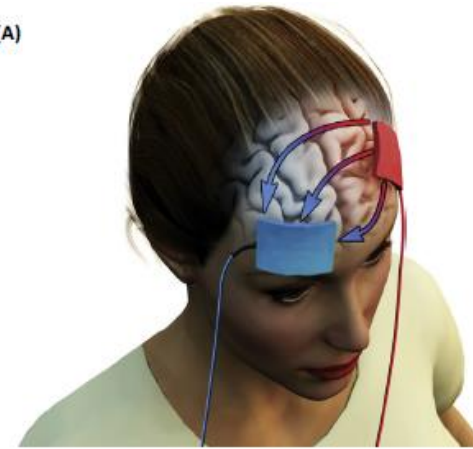
In 1804, Aldini, Galvani's nephew, was the first scientist in the modern era to report the use of electrical stimulation in the treatment of mental disorders



## Transcranial electric stimulation - TES



(A)



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)

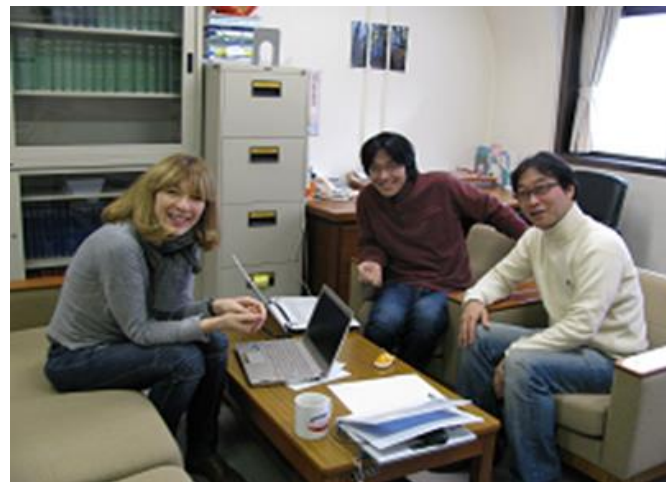
Promising results in therapy: migraines, dementia, stroke, schizophrenia, Parkinson's disease





京都大学 医学研究科 附属  
脳機能総合研究センター

Human Brain Research Center  
Kyoto University Graduate School of Medicine



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

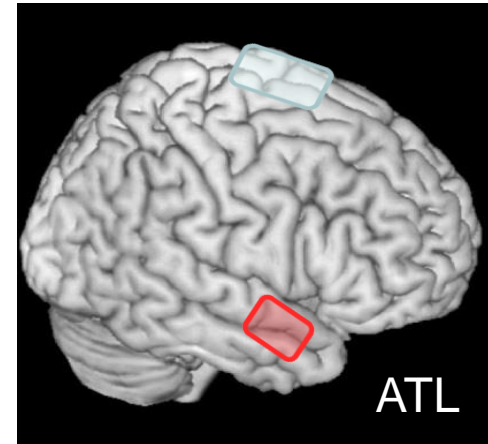
431

## tDCS stimulation

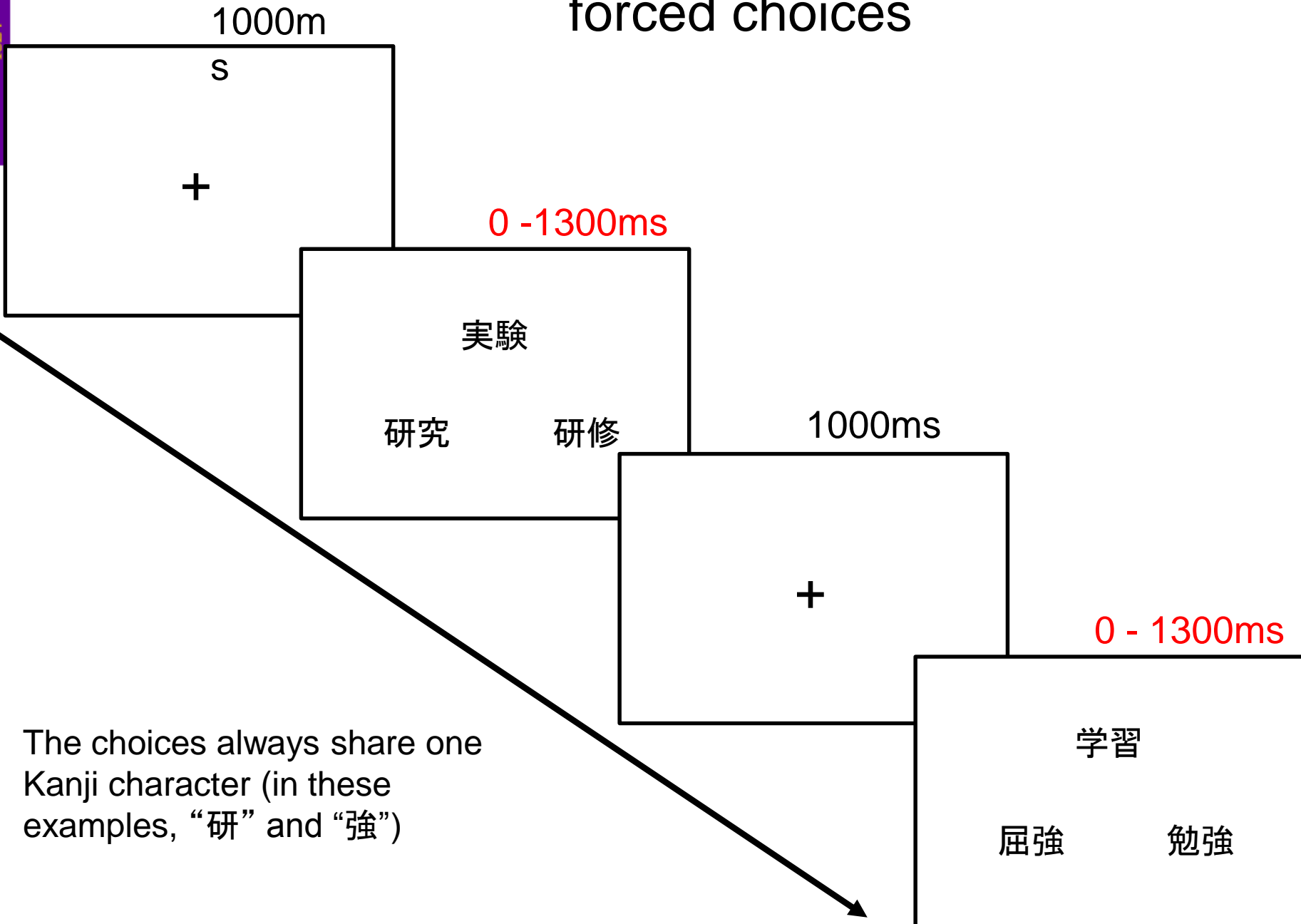
- 20 healthy participants
- Between subject design

### TES:

- anodal or sham stimulation (control)
- 1.5mA for 20 min – concurrently with the task
- Active electrode over ATL: size 25cm<sup>2</sup>
- Reference electrode - vertex: size 35cm<sup>2</sup>

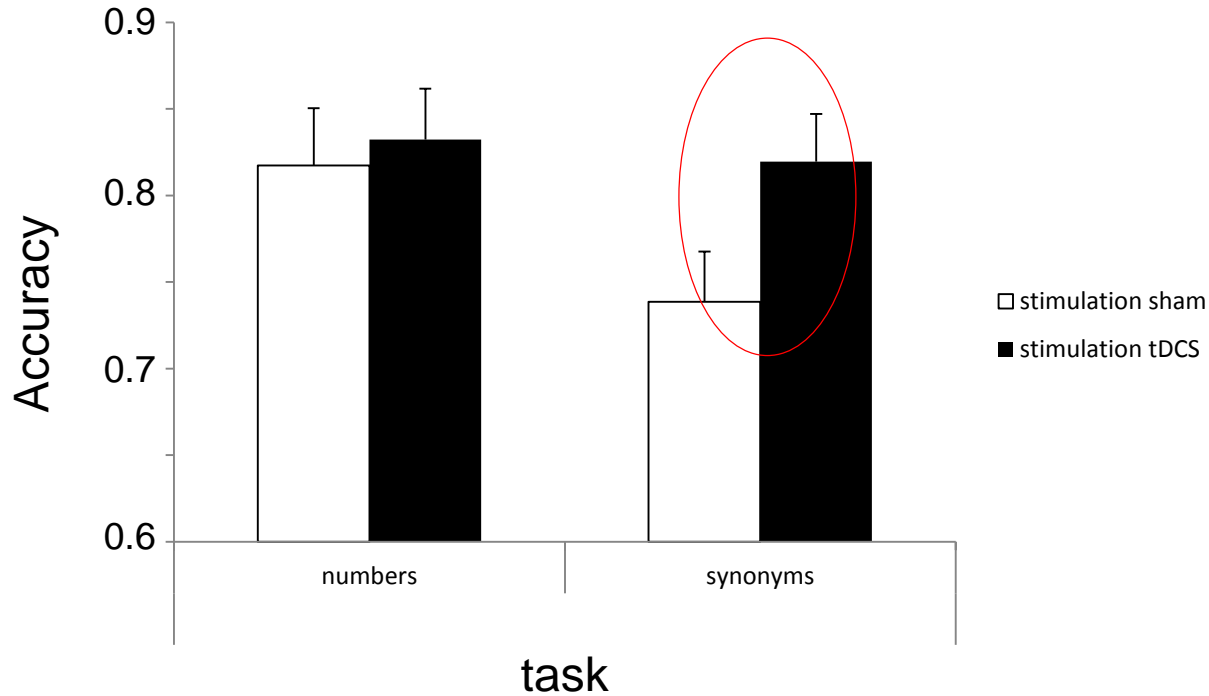


# Synonym judgement with two-alternative forced choices



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

## Results



Accuracy on kanji synonym judgment increased following tDCS stimulation

## The Bridge Fellowship - 2015

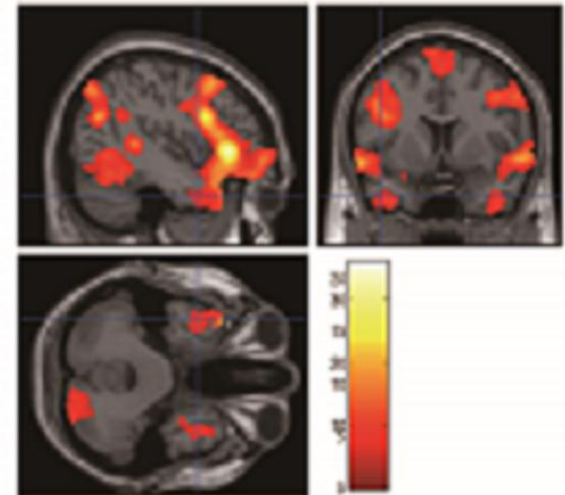
### Understand stimulation mechanisms

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



充実した健康長寿社会を築く

総合医療開発リーダー育成プログラム

Training Program of Leaders for Integrated Medical System

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



日本学術振興会  
Japan Society for the Promotion of Science

JSPS ALUMNI ASSOCIATION  
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**Thank you**