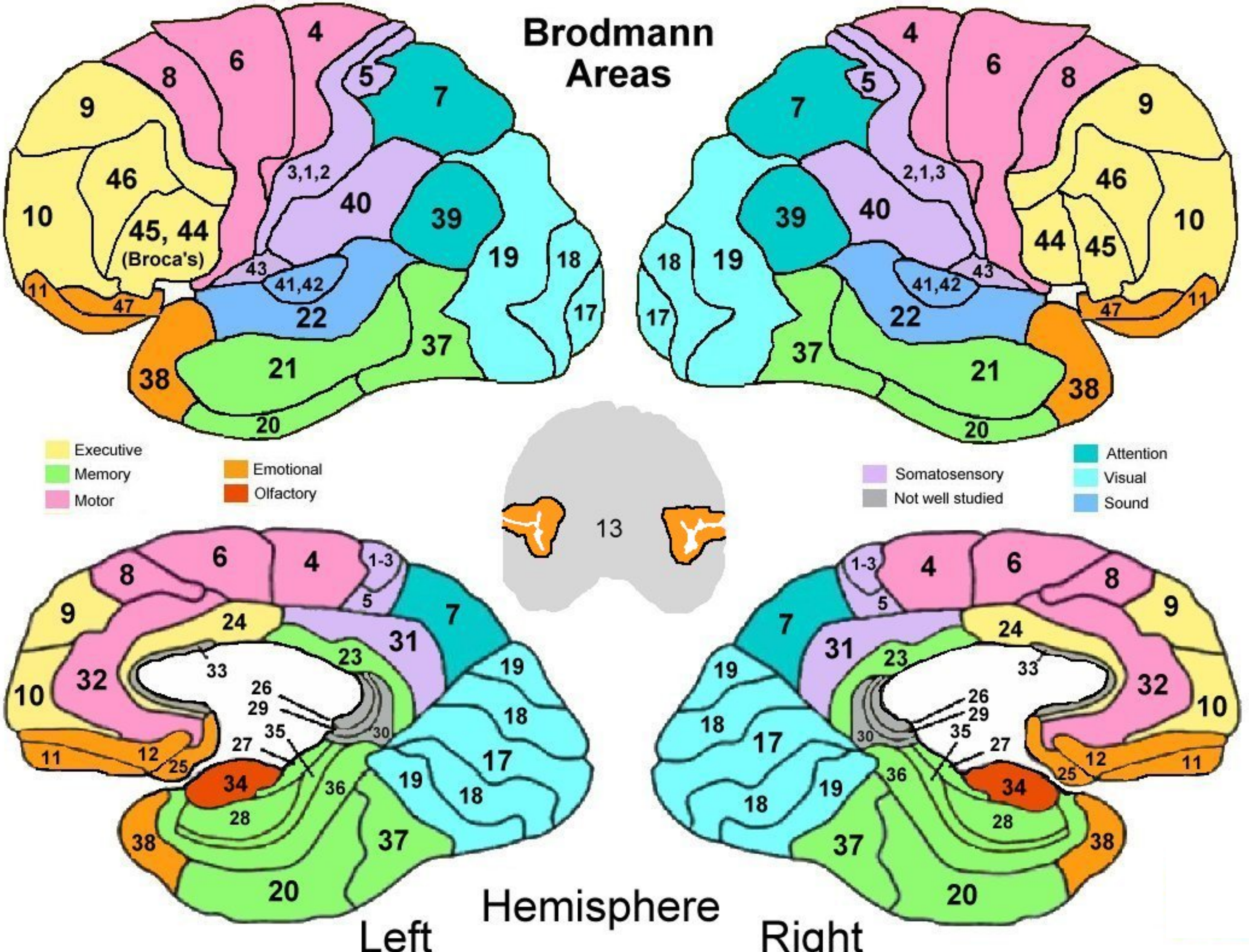
# Plasticité cérébrale et cognition

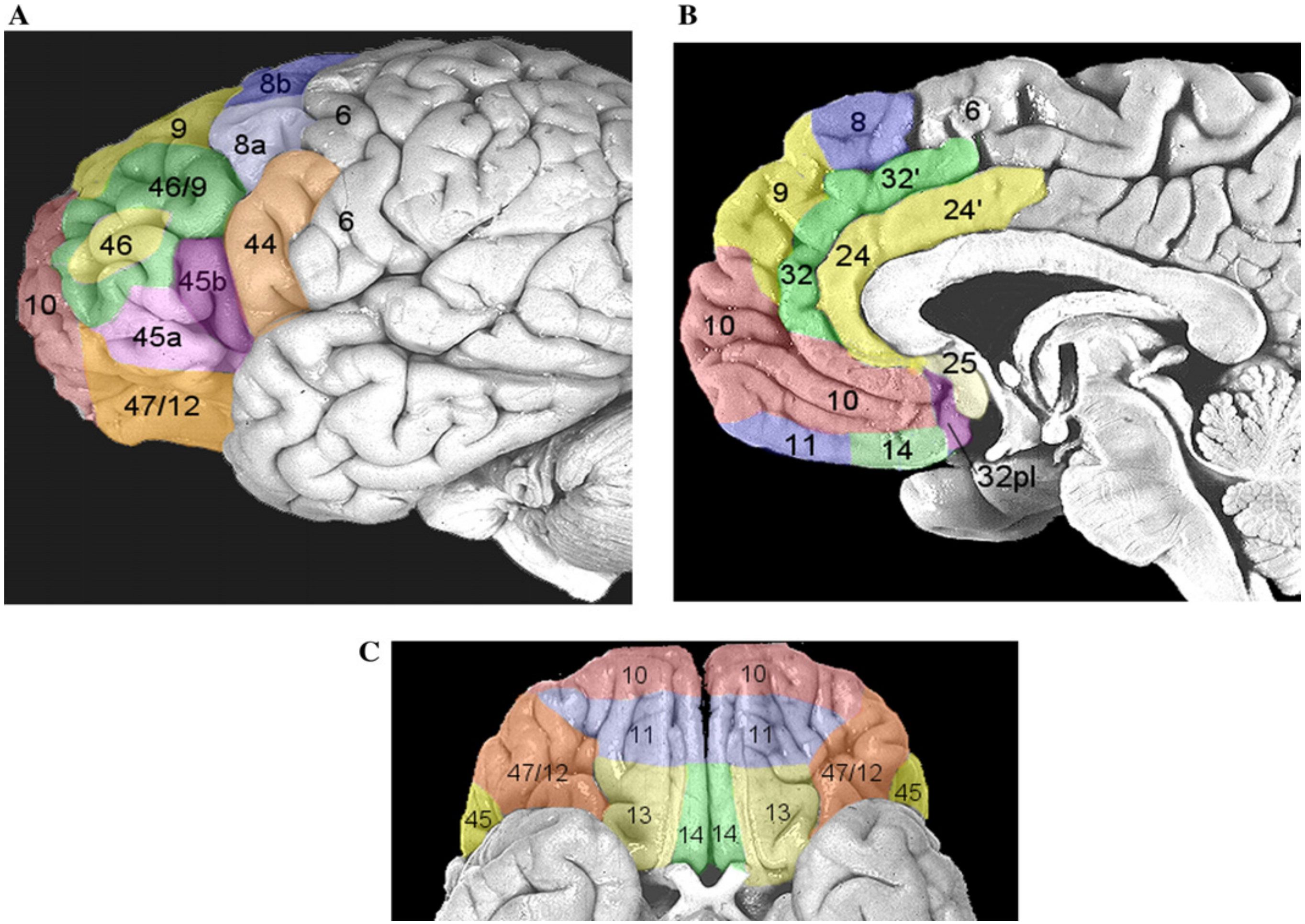
Gilles Lafargue
mars 2016

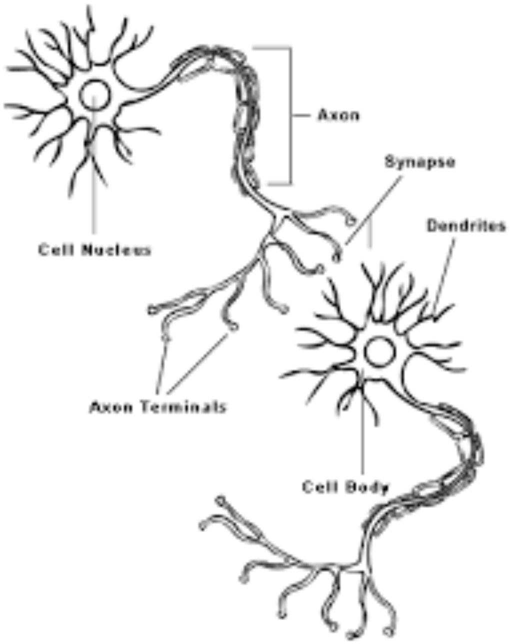
gilles.lafargue@gmail.com

**Vision localisationniste des fonctions cérébrales**

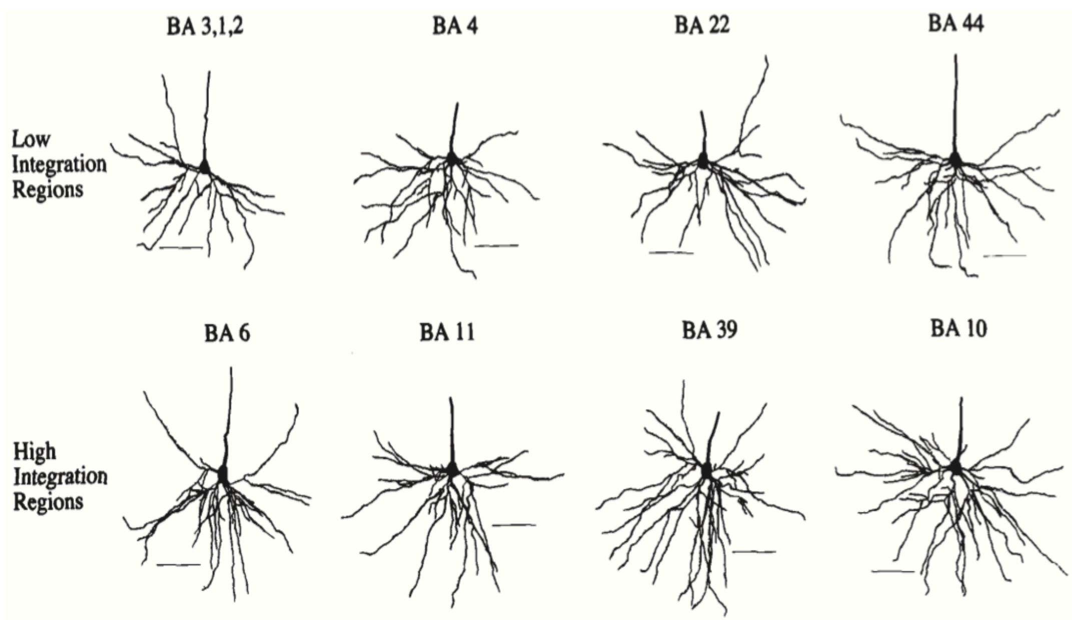
sur la bases de données histologiques, neuropsychologiques, de neuroimagerie,..


Brodmann
Areas
45, 44
(Broca's)
Executive
Memory
Motor
Emotional
Olfactory
Somatosensory
Not well studied
Attention
Visual
Sound
13
Hemisphere
Left
Right


A
8b
9
6
8a
46/9
46
44
6
45b
10
45a
47/12
B
8
6
32'
9
24'
24
32
10
25
10
11
14
32pl
C
10
10
11
11
47/12
47/12
45
45
13
13
14
14



Axon
Synapse
Dendrites
Cell Nucleus
Axon Terminals
Cell Body

BA 3,1,2
BA 4
BA 22
BA 44
Low Integration Regions
BA 6
BA 11
BA 39
BA 10
High Integration Regions

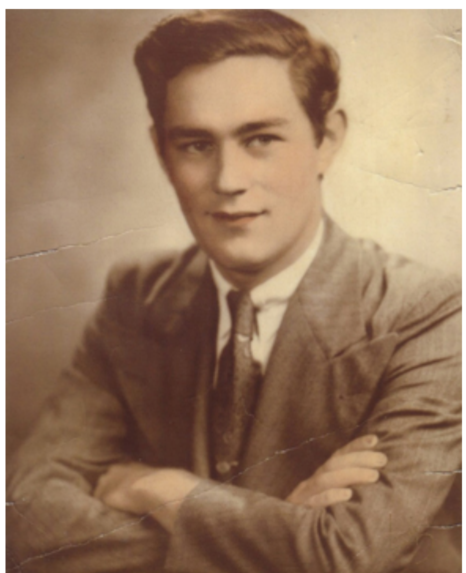
*J. Neurol. Neurosurg. Psychiat.*, 1957, **20**, 11.

# LOSS OF RECENT MEMORY AFTER BILATERAL HIPPOCAMPAL LESIONS

BY

**WILLIAM BEECHER SCOVILLE and BRENDA MILNER**

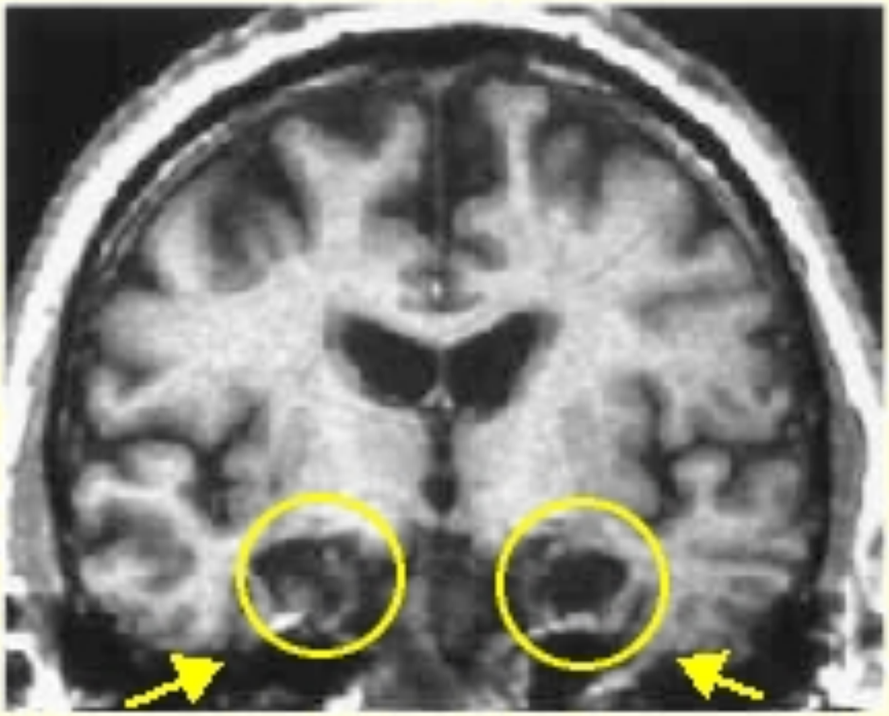
*From the Department of Neurosurgery, Hartford Hospital, and the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute, Canada*



**Le patient HM**

Henry Gustav Molaison

## MRI scan of "H.M."



NOTE THE RESULTS OF HIS BILATERAL MEDIAL TEMPORAL LOBE RESECTION AND THE REMOVAL OF THE HIPPOCAMPUS

**Musée Dupuytren**,
15 rue de l'École-de-Médecine, Paris

**Broca P.** 1861a. Perte de la parole, ramollissement chronique et destruction partielle du lobe antérieur gauche du cerveau. Bull Soc Anthropol. 2:235–238. 301–321.

**Broca P.** 1861b. Remarques sur le siège de la faculté du langage articulé; suivies d'une observation d'aphémie (perte de la parole). Bull Soc Anthropol. 36:330–357.

Opinion
TRENDS in Cognitive Sciences Vol.9 No.9 September 2005
Full text provided by www.sciencedirect.com

# On Broca, brain, and binding: a new framework

Peter Hagoort

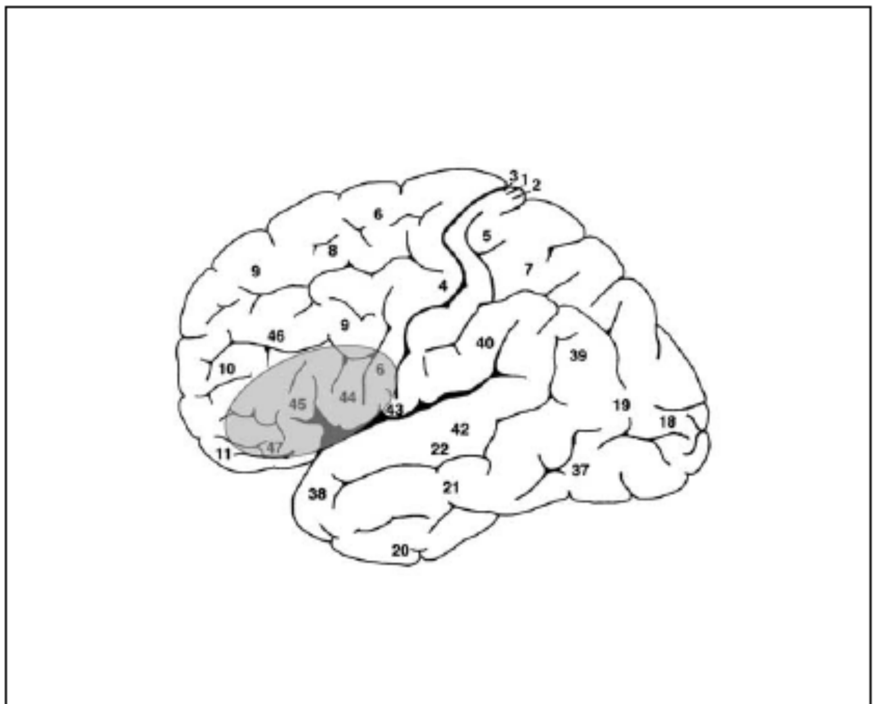
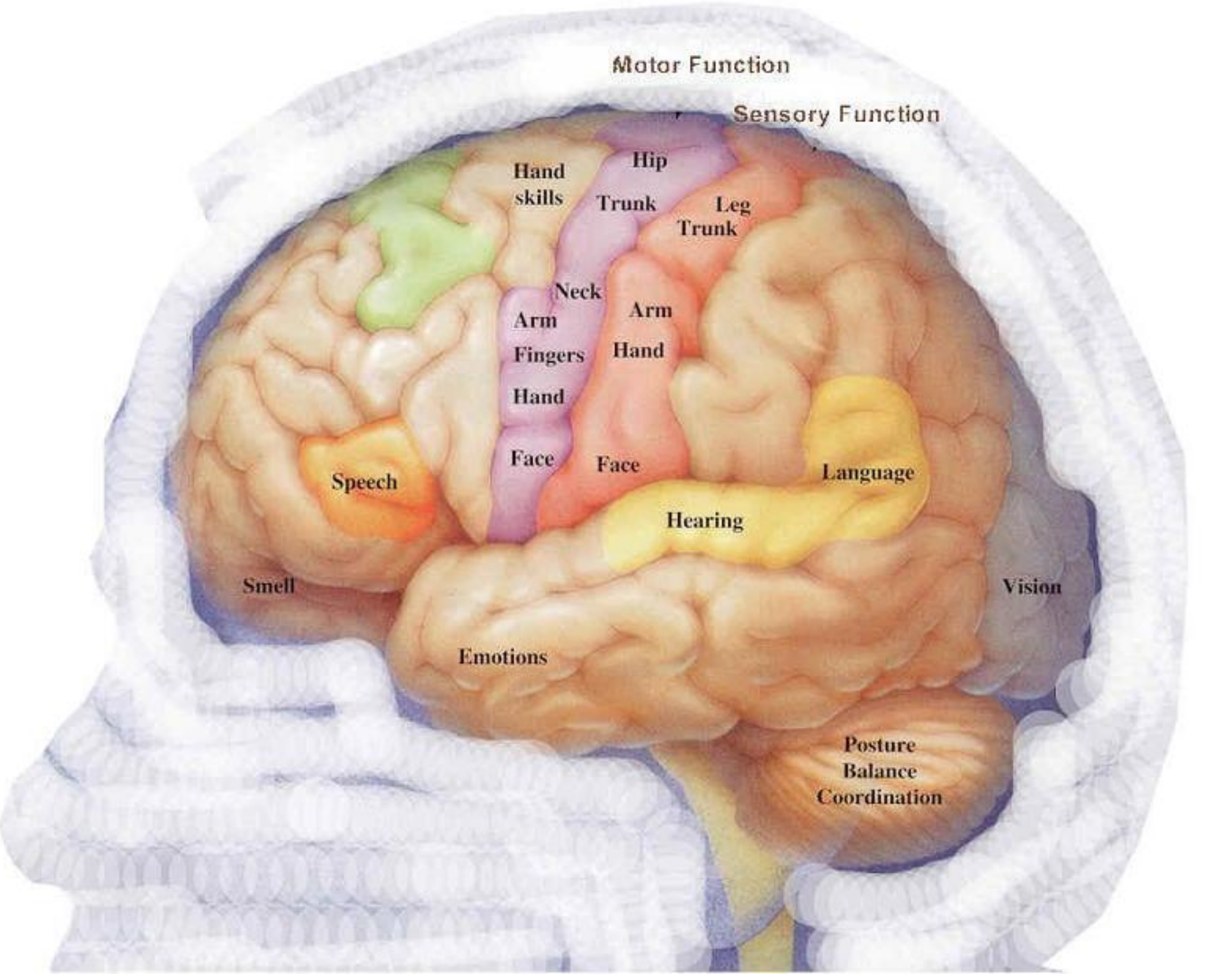



**Figure 3.** Lateral view of the left hemisphere. Brodmann's areas (BA) are marked by number. Classically, Broca's area comprises BA 44 and BA 45. Adjacent language-relevant cortex also includes BA 47 and ventral BA 6 (grey oval).


Motor Function
Sensory Function
Hand skills
Hip
Trunk
Leg
Trunk
Neck
Arm
Arm
Fingers
Hand
Hand
Face
Face
Speech
Language
Hearing
Smell
Vision
Emotions
Posture
Balance
Coordination

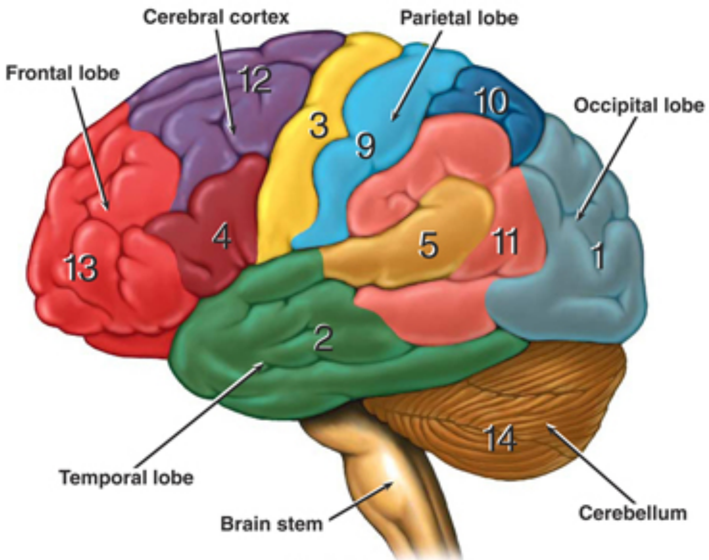
# Anatomy and Functional Areas of the Brain

## Functional Areas of the Cerebral Cortex

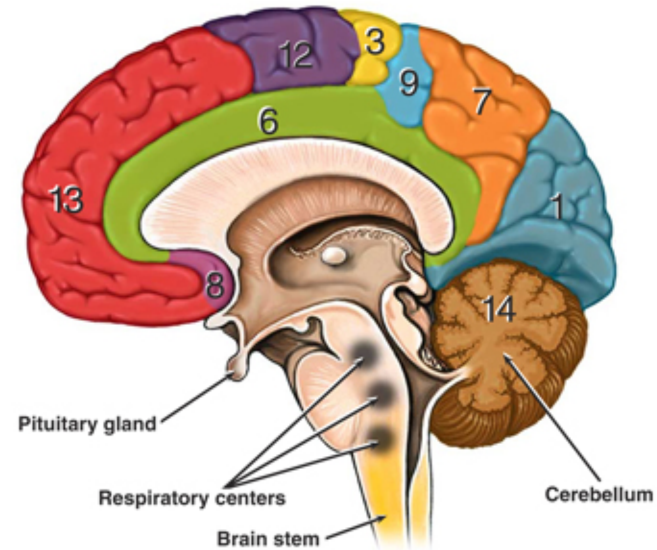
1. **Visual Area:**
   - Sight
   - Image recognition
   - Image perception
2. **Association Area**
   - Short-term memory
   - Equilibrium
   - Emotion
3. **Motor Function Area**
   - Initiation of voluntary muscles
4. **Broca's Area**
   - Muscles of speech
5. **Auditory Area**
   - Hearing
6. **Emotional Area**
   - Pain
   - Hunger
   - "Fight or flight" response
7. **Sensory Association Area**
8. **Olfactory Area**
   - Smelling
9. **Sensory Area**
   - Sensation from muscles and skin
10. **Somatosensory Association Area**
    - Evaluation of weight, texture, temperature, etc. for object recognition
11. **Wernicke's Area**
    - Written and spoken language comprehension
12. **Motor Function Area**
    - Eye movement and orientation
13. **Higher Mental Functions**
    - Concentration
    - Planning
    - Judgment
    - Emotional expression
    - Creativity
    - Inhibition

## Functional Areas of the Cerebellum

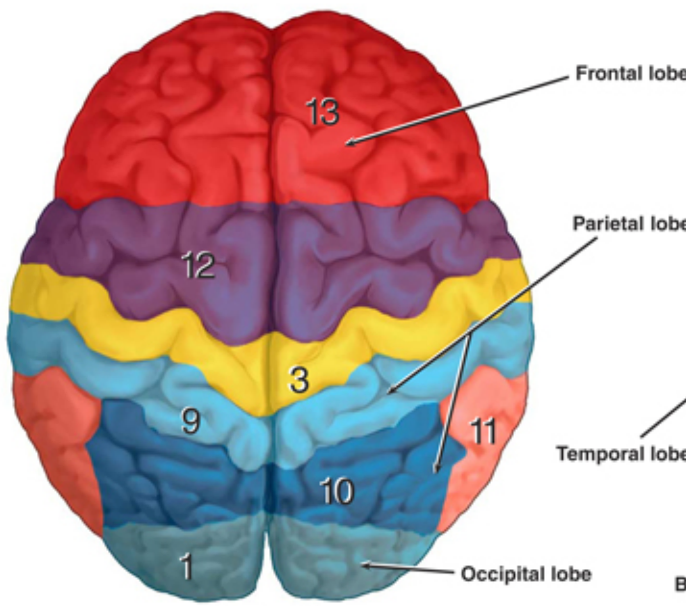
14. **Motor Functions**
    - Coordination of movement
    - Balance and equilibrium
    - Posture



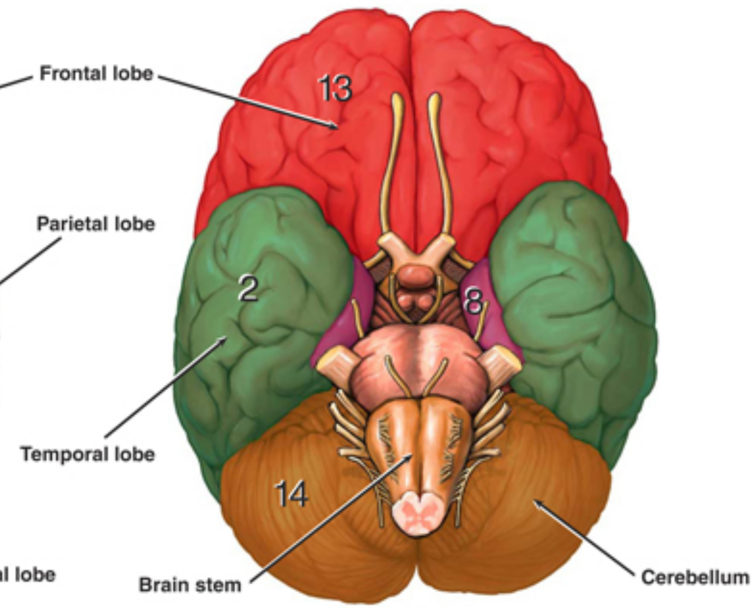

Lateral View




Sagittal View




Superior View




Inferior View

Le rôle critique joué par une structure (ou un circuit neural) dans un domaine spécifique de la cognition ou du comportement peut être testé en examinant la relation entre une lésion acquise de cette structure (ou système) et les déficits qui en découlent

- Problème : de plus en plus d'études montrent que des lésions de structures supposées être cruciales pour une fonction donnée ne sont pas nécessairement associées à des déficits de cette fonction

Neuropsychologia 46 (2008) 2662–2667

Contents lists available at ScienceDirect

Neuropsychologia

journal homepage: www.elsevier.com/locate/neuropsychologia

# Awareness of intending to act following parietal cortex resection

Gilles Lafargue [a,*], Hugues Duffau [b]

[a] *Laboratoire Neurosciences Fonctionnelles & Pathologies, CNRS, Université Lille Nord-de-France, France*
[b] *Département de neurochirurgie, CNRS FRE 2987, hôpital Gui-de-Chauliac, CHU de Montpellier, France*

Neuroimaging and neuropsychological studies have provided evidence suggesting that the inferior parietal lobule (IPL) plays a crucial role in the awareness of motor intentions. For instance, patients with IPL lesions caused by stroke selectively differ in the temporal judgements of their intentions to move compared with healthy controls [Sirigu, A., Daprati, E., Ciancia, S., Giraux, P., Nighoghossian, N., Posada, A., et al. (2004). Altered awareness of voluntary action after damage to the parietal cortex. *Nature Neuroscience*, *7*(1), 80–84]: they experience the will to move only at the moment they start moving, and not before, as it should normally be the case. In the study presented here, we failed to replicate the main behavioral findings of the study quoted above in three patients with surgical resection of the right IPL following slow-growing lesions. Their performances contrasted with that of stroke patients. The timing of their intentions to act but also the delay between their judgements of intention and movement onsets were in the normal range of values for matched controls, when tested with the temporal judgement task developed by Benjamin Libet. There are in the literature some reported cases of functional neuroplasticity following surgical resection of large amount of cerebral tissue. This mainly concerns the brain regions underpinning language and primary sensorimotor functions. Because of the small number of patients our data must be regarded cautiously. They provide preliminary behavioral support to extend to conscious awareness of willing the functional neuroplasticity potentialities of the brain, in human adults. A new perspective towards a hodological view for higher-order cognitive processes seems open.

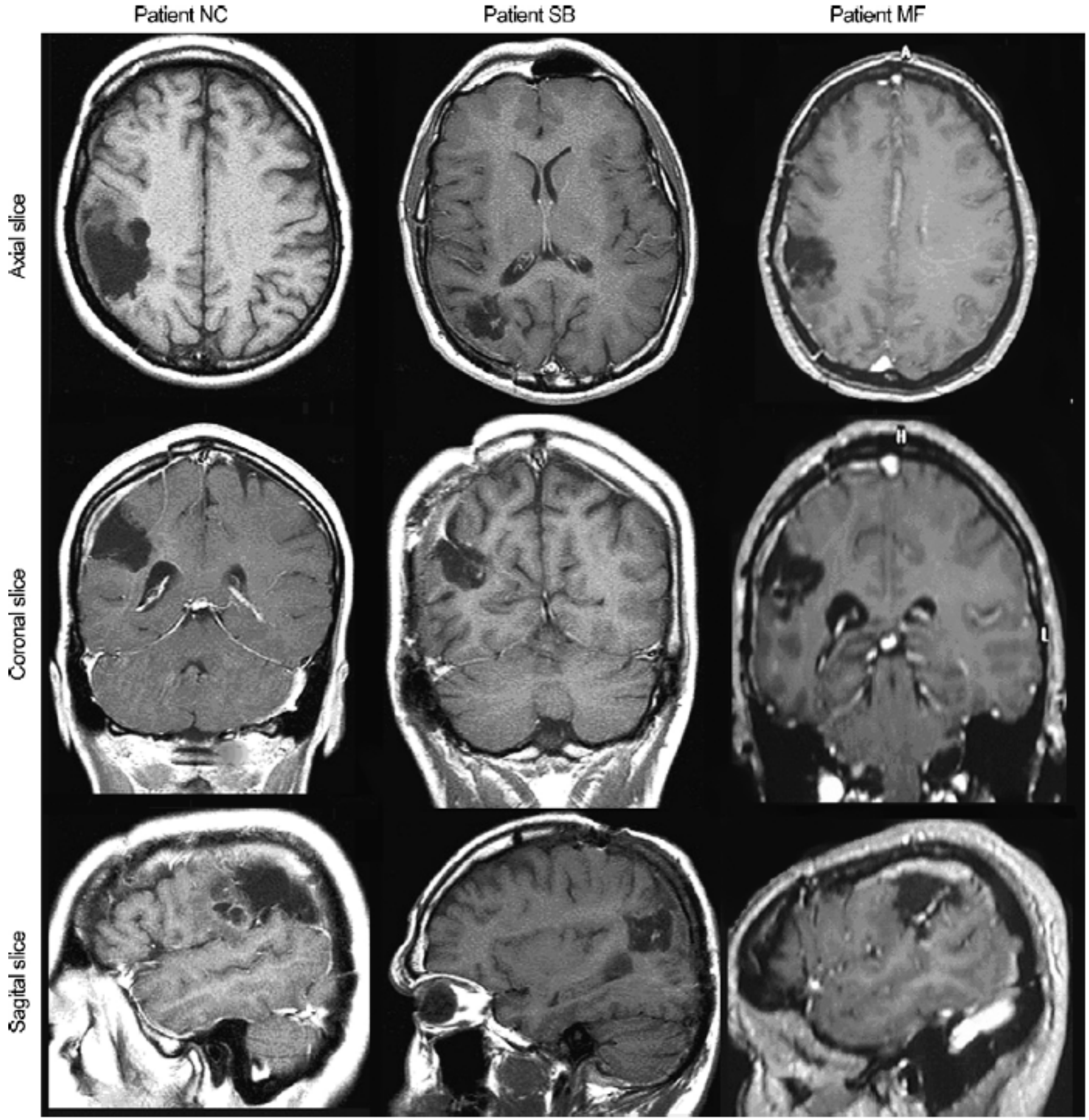
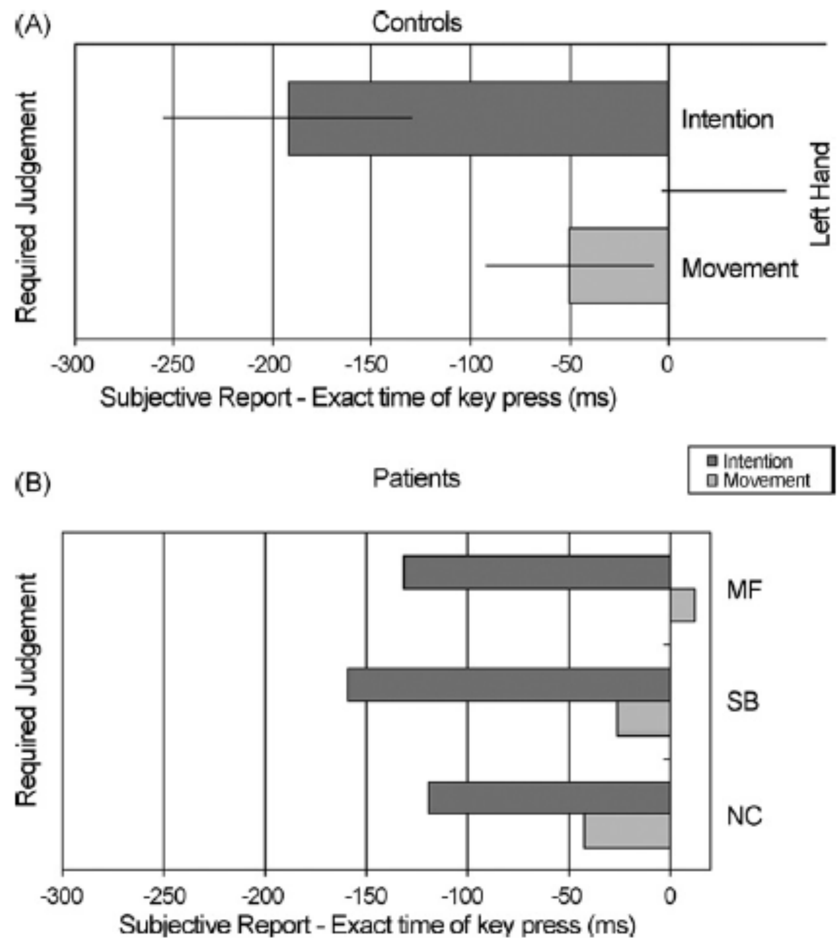



**Fig. 1.** Post-operative anatomical MRI of the patients confirms the resection of right IPL in the three patients.

0
2.56 sec
Clock appears
End 1st revolution
key press or Beep
Subject's response

(A)
Controls
Required Judgement
Intention
Movement
Left Hand
-300 -250 -200 -150 -100 -50 0
Subjective Report - Exact time of key press (ms)
(B)
Patients
Intention
Movement
Required Judgement
MF
SB
NC
-300 -250 -200 -150 -100 -50 0
Subjective Report - Exact time of key press (ms)

NEUROCASE
2009, i*First*, 1–17

Psychology Press
Taylor & Francis Group

# Speaking without Broca's area after tumor resection

**Monique Plaza, Peggy Gatignol, Marianne Leroy, and Hugues Duffau**

Laboratoire de Psychologie et Neurosciences Cognitives (UMR CNRS 8189), Université Paris Descartes, Service de Neurochirurgie, CHU Gui de Chauliac, Montpellier, France

FV was a 27-year-old right-handed man working as a computer engineer. Right-handedness was documented using the Edinburgh inventory questionnaire (Oldfield, 1971).

He had had word retrieval difficulties for 4–5 years, in marked increase for the past 2 years when he first consulted for generalized seizures. The neurological examination was normal, without either somosatosensory or motor deficit, but the MRI revealed a tumor invading the left frontal lobe.

NEUROCASE
2009, i*First*, 1–17

Psychology Press
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# Speaking without Broca's area after tumor resection

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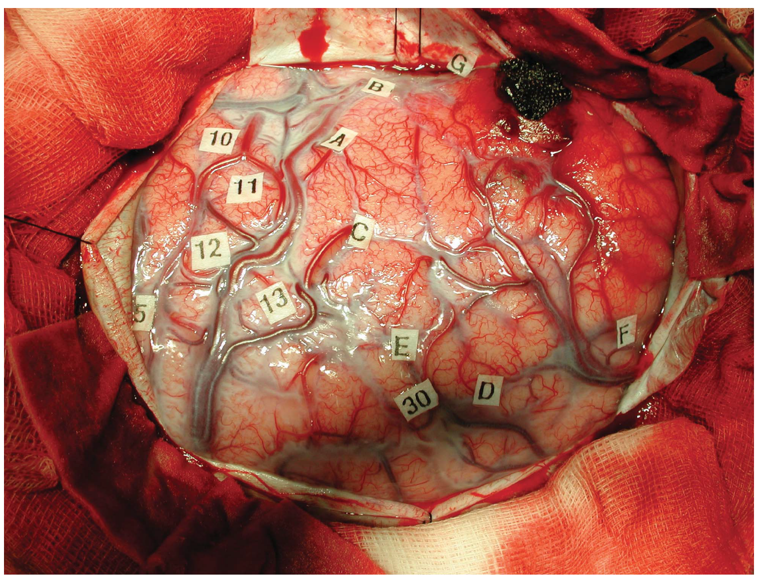
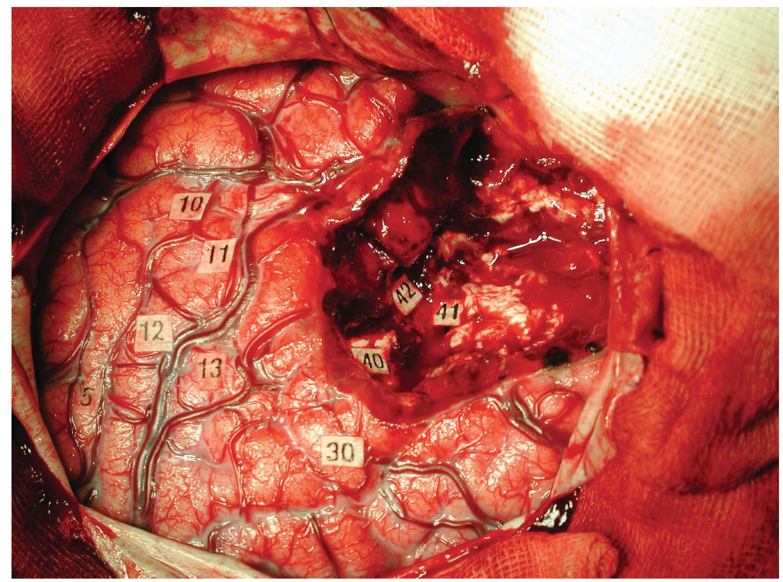


| *Tasks* | *Day −1* | *Day +5* | *Day +3 months* |
|---|---|---|---|
| Picture pointing | 72/72 | 72/72 | 72/72 |
| Body parts | 20/20 | 18/20 | 20/20 |
| Auditory instructions | 14/15 | 14/15 | 14/15 |
| Reasoning | 10/12 | 8/12 | 10/12 |
| Articulation | 7/7 | 5/7 | 7/7 |
| Fluency | 7/7 | 7/7 | 7/7 |
| Sequence repetition | 14/14 | 13/14 | 14/14 |
| Series | 9/9 | 9/9 | 9/9 |
| Automatic recitation | 2/2 | 2/2 | 2/2 |
| Words | 10/10 | 10/10 | 10/10 |
| Concrete Sentence repetition | 7/8 | 8/8 | 8/8 |
| Abstract sentence repetition | 8/8 | 6/8 | 7/8 |
| Oral words | 30/30 | 30/30 | 30/30 |
| Sentence reading | 10/10 | 10/10 | 10/10 |
| Definition | 30/30 | 30/30 | 30/30 |
| Picture naming | 105/105 | 105/105 | 105/105 |
| Body parts | 30/30 | 30/30 | 30/30 |
| Aphasic phonemic | 2 | 0 | 0 |
| Jargon | 0 | 0 | 0 |
| Letter discrimination | 10/10 | 10/10 | 10/10 |
| Verbal recitation | 8/8 | 8/8 | 8/8 |
| Spelled words | 8/8 | 8/8 | 8/8 |
| Word/picture matching | 10/10 | 10/10 | 10/10 |
| Text reading | 10/10 | 10/10 | 10/10 |
| Writing | 3/3 | 3/3 | 3/3 |
| Automatic | 46/46 | 46/46 | 46/46 |
| Dictation | 15/15 | 15/15 | 15/15 |
| Spelling | 10/10 | 9/10 | 10/10 |
| Graphic evocation | 10/10 | 8/10 | 9/10 |
| Sentence spelling | 12/12 | 9/12 | 12/12 |
| Description | 4/4 | 4/4 | 4/4 |
| Music song | 2/2 | 2/2 | 2/2 |
| Rhythm | 2/2 | 2/2 | 2/2 |
| *DO 80*: score | 77/80 | 80/80 | 80/80 |
| *DO 80*: time | 123 s | 129 s | 88 s |

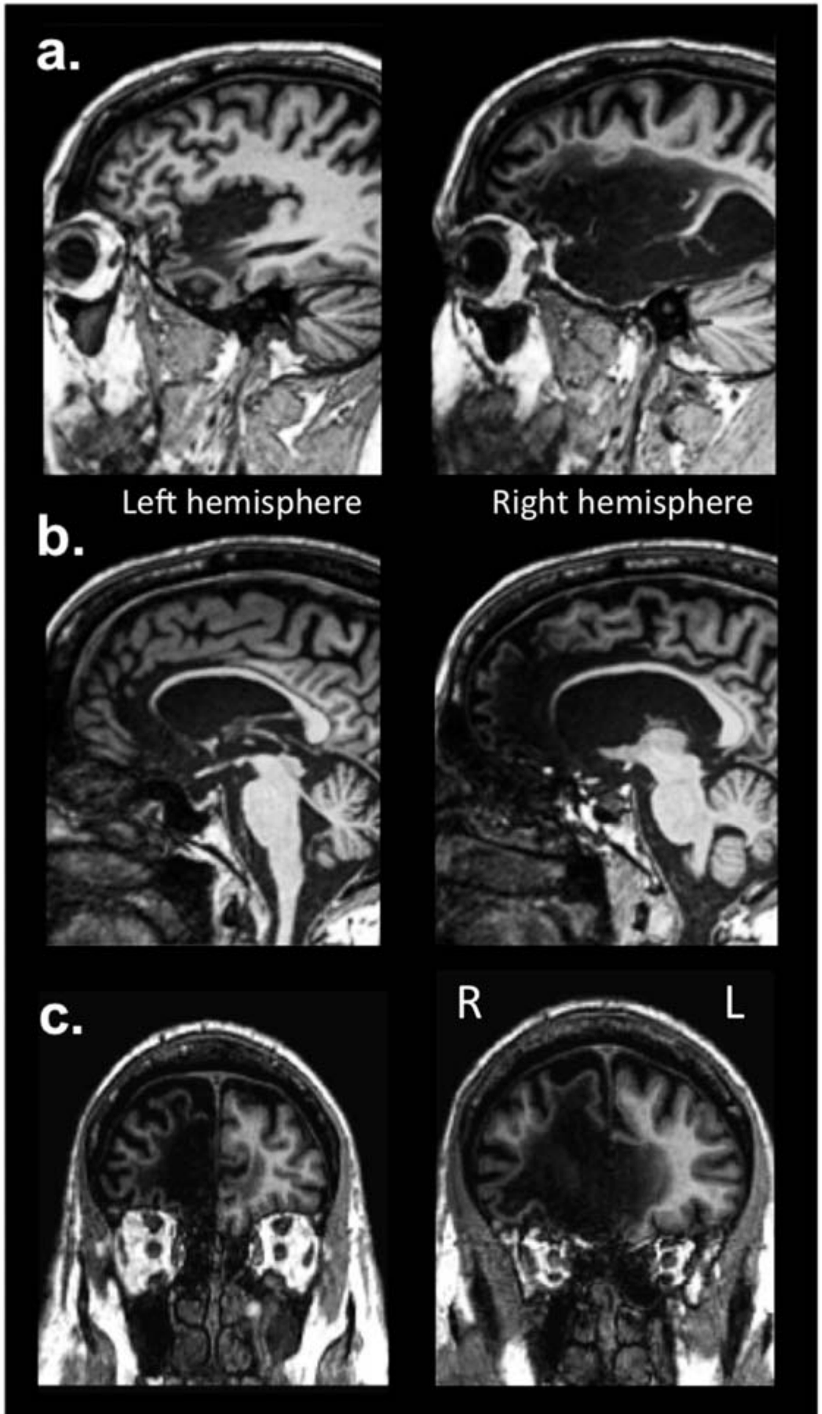
# Preserved Self-Awareness following Extensive Bilateral Brain Damage to the Insula, Anterior Cingulate, and Medial Prefrontal Cortices

**Carissa L. Philippi[1], Justin S. Feinstein[1*], Sahib S. Khalsa[2], Antonio Damasio[3], Daniel Tranel[1], Gregory Landini[4], Kenneth Williford[5], David Rudrauf[1*]**

**1** Division of Behavioral Neurology and Cognitive Neuroscience, Department of Neurology, University of Iowa, Iowa City, Iowa, United States of America, **2** Semel Institute for Neuroscience and Human Behavior, University of California Los Angeles, Los Angeles, California, United States of America, **3** Brain and Creativity Institute and Dornsife Cognitive Neuroscience Imaging Center, University of Southern California, Los Angeles, California, United States of America, **4** Department of Philosophy, University of Iowa, Iowa City, Iowa, United States of America, **5** Department of Philosophy, University of Texas Arlington, Arlington, Texas, United States of America

## Abstract

It has been proposed that self-awareness (SA), a multifaceted phenomenon central to human consciousness, depends critically on specific brain regions, namely the insular cortex, the anterior cingulate cortex (ACC), and the medial prefrontal cortex (mPFC). Such a proposal predicts that damage to these regions should disrupt or even abolish SA. We tested this prediction in a rare neurological patient with extensive bilateral brain damage encompassing the insula, ACC, mPFC, and the medial temporal lobes. In spite of severe amnesia, which partially affected his "autobiographical self", the patient's SA remained fundamentally intact. His Core SA, including basic self-recognition and sense of self-agency, was preserved. His Extended SA and Introspective SA were also largely intact, as he has a stable self-concept and intact higher-order metacognitive abilities. The results suggest that the insular cortex, ACC and mPFC are not required for most aspects of SA. Our findings are compatible with the hypothesis that SA is likely to emerge from more distributed interactions among brain networks including those in the brainstem, thalamus, and posteromedial cortices.




“Patient, R is a 57 year old, right-handed, college-educated, male, whose brain was damaged in 1980 following a severe episode of herpes simplex encephalitis. His brain damage is bilateral, more extensive on the right, and encompasses the target regions of the hypotheses under scrutiny: the insular cortex, the ACC, and the mPFC”

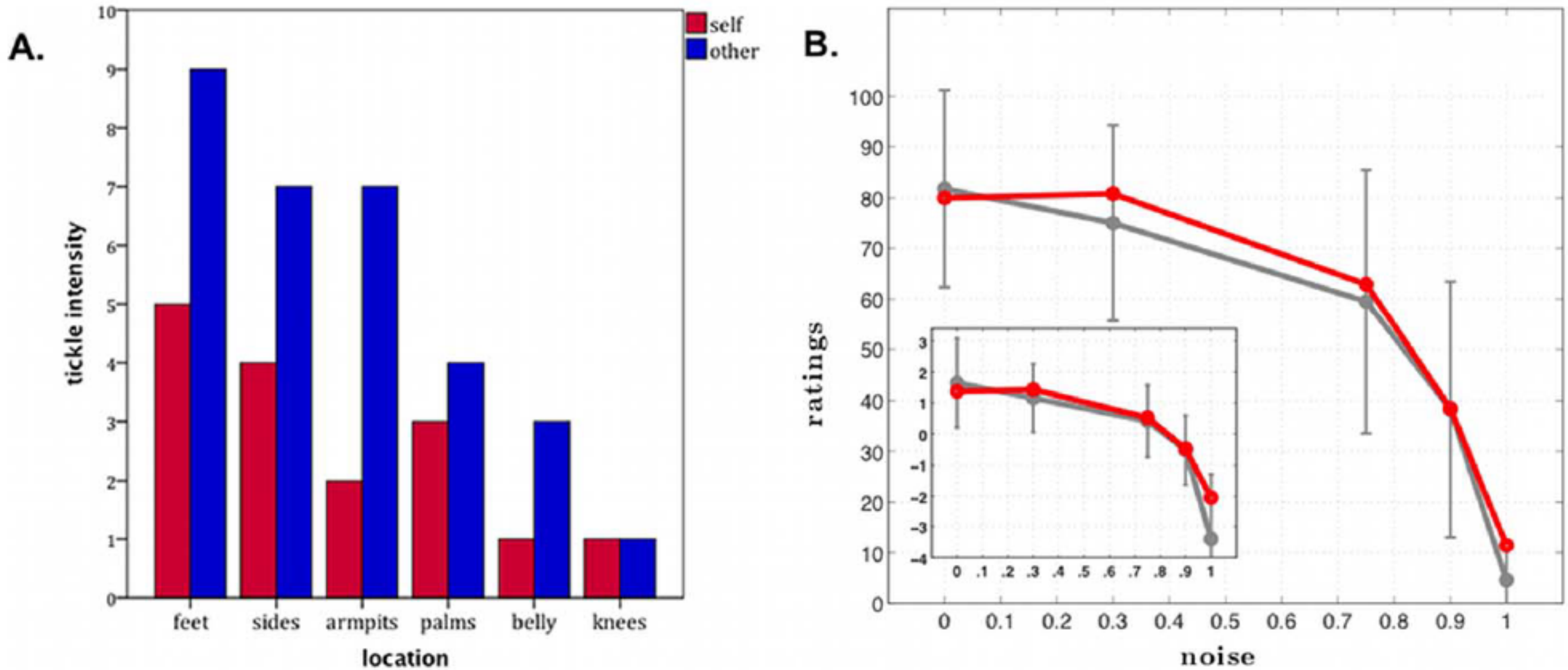
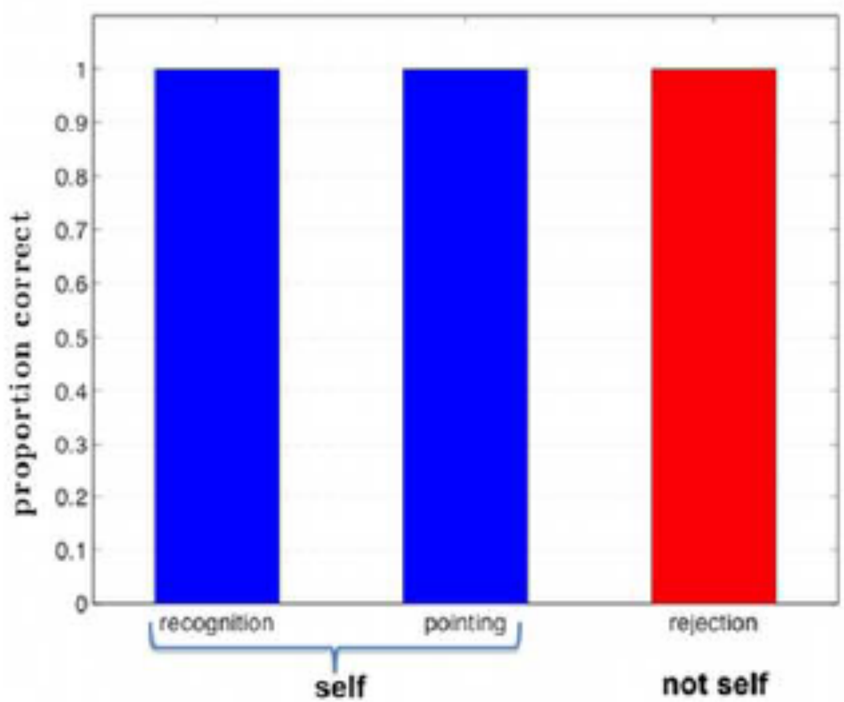
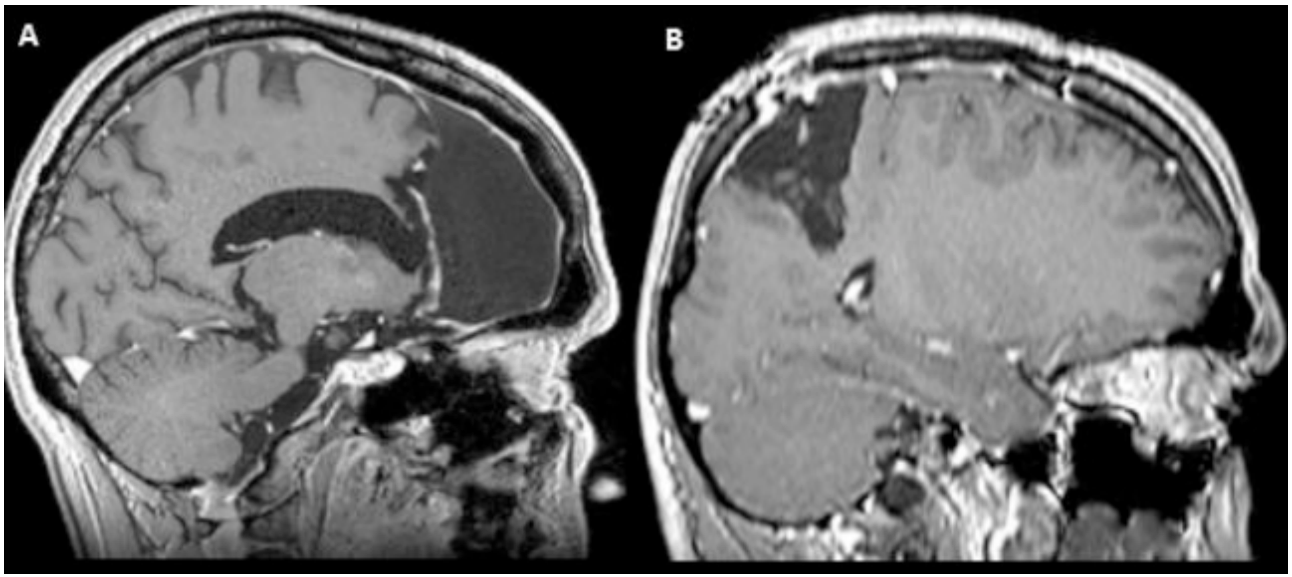



**Figure 7. Self-Agency.** A. Tickle test results. Tickle intensity ratings (y-axis) are plotted as a function of the body part being tickled (x-axis). Tickle condition is color coded: red = self-administered tickle, blue = experimenter-administered tickle. The graph shows normal ''feeling of agency'' in R, with lower intensity ratings in the self-administered tickle condition as compared to the experimenter-administered tickle condition (the scale goes from 0, ''not ticklish at all,'' to 10, ''extremely ticklish''). B. Self-agency judgment task results. Mean subjective ratings of control over the movement of the blue box (from 0 = ''no control'' to 100 = ''completely in control''), plotted as a function of objective variation in control (i.e., ''noise'' which is the proportion of time not in control during a trial). The group mean for each noise condition for healthy comparison participants are represented in gray, with error bars corresponding to 2 standard deviations from the mean. R's mean ratings are represented in red. For all participants, including R, the sense of control parametrically decreased as noise (i.e., objectively manipulated lack of control) increased. In all conditions, R's sense of self-agency was entirely within normal limits. Error bars = 2 standard deviations from the mean. Red = R's ratings. Gray = group mean of the healthy comparison participants.

A.



proportion correct
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
recognition
pointing
rejection
self
not self




(A) right prefrontal lobectomy and (B) right inferior parietal resection without inducing detectable cognitive abnormalities at month 3 after surgery

# Variabilité inter et intra-individuelle

# Cognitive Reserve

**Yaakov Stern**
Cognitive Neuroscience Division of the Taub Institute, and the Departments of Neurology and Psychiatry, Columbia University College of Physicians and Surgeons

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The concept of reserve has been proposed to account for the disjunction between the degree of brain damage or pathology and its clinical manifestations. For example, a head injury of the same magnitude can result in different levels of cognitive impairment, and that impairment can vary in its rate of recovery. Similarly, several prospective studies of aging have reported that up to 25% of elders whose neuropsychological testing is unimpaired prior to death meet full pathologic criteria for Alzheimer's disease (Ince, 2001), suggesting that this degree of pathology does not invariably result in clinical dementia. As will be described in detail below, many studies indicate that a set of life experiences such as educational and occupational exposure and leisure activities are associated with reduced risk of developing dementia and with a slower rate of memory decline in normal aging. Cognitive reserve (CR) postulates that individual differences in the cognitive processes or neural networks underlying task performance allow some people to cope better than others with brain damage. This paper attempts to produce a coherent theoretical account of reserve in general and of cognitive reserve in particular. It then reviews some of my group's epidemiologic and imaging research that has lent support to the concept of cognitive reserve and helped elucidate its neural underpinnings. It should be stressed that this review is focused on my group's work, and is not a thorough review on the entire literature on the topic.

*Lancet Neurol.* 2012 November ; 11(11): 1006–1012. doi:10.1016/S1474-4422(12)70191-6.

# Cognitive reserve in ageing and Alzheimer's disease

**Yaakov Stern, PhD**
Cognitive Neuroscience Division, Department of Neurology and Taub Institute, Columbia University College of physicians and Surgeons

## Abstract

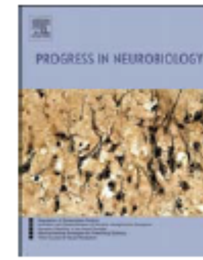
The concept of reserve accounts for individual differences in susceptibility to age-related brain changes or Alzheimer's disease-related pathology. There is evidence that some people can tolerate more of these changes than others and still maintain function. Epidemiologic studies suggest that lifetime exposures including educational and occupational attainment, and leisure activities in late life, can increase this reserve. For example, there is a reduced risk of developing Alzheimer's disease in individuals with higher educational or occupational attainment. It is convenient to think of two types of reserve: brain reserve, which refers to actual differences in the brain itself that may increase tolerance of pathology, and cognitive reserve. Cognitive reserve refers to individual differences in how tasks are performed that may allow some people to be more resilient than others. The concept of cognitive reserve holds out the promise of interventions that could slow cognitive aging or reduce the risk of dementia.

Progress in Neurobiology 89 (2009) 369–382

Contents lists available at ScienceDirect

Progress in Neurobiology

journal homepage: www.elsevier.com/locate/pneurobio




# The neurobiology of brain and cognitive reserve: Mental and physical activity as modulators of brain disorders

Jess Nithianantharajah [a,b], Anthony J. Hannan [a,c,*]

[a] Howard Florey Institute, Florey Neuroscience Institutes, University of Melbourne, Victoria 3010, Australia
[b] Genes to Cognition Program, Wellcome Trust Sanger Institute, Cambridge, UK
[c] Department of Anatomy and Cell Biology, University of Melbourne, Victoria, Australia

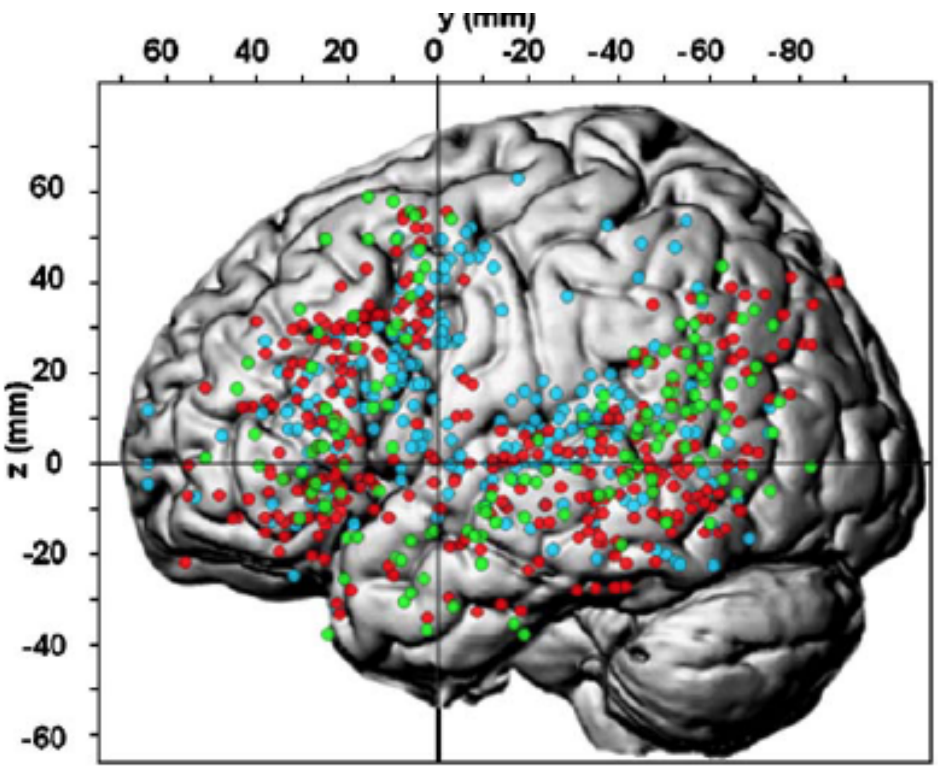
NeuroImage

www.elsevier.com/locate/ynimg
NeuroImage 30 (2006) 1414 – 1432

Review

# Meta-analyzing left hemisphere language areas: Phonology, semantics, and sentence processing

M. Vigneau,[a,1] V. Beaucousin,[a,1] P.Y. Hervé,[a] H. Duffau,[c] F. Crivello,[a]
O. Houdé,[a] B. Mazoyer,[a,b] and N. Tzourio-Mazoyer[a,*]




Phonologie

Sémantique

Syntaxe

730 activations issues de 130 études

REVIEW

Science AAAS

# Predispositions and Plasticity in Music and Speech Learning: Neural Correlates and Implications

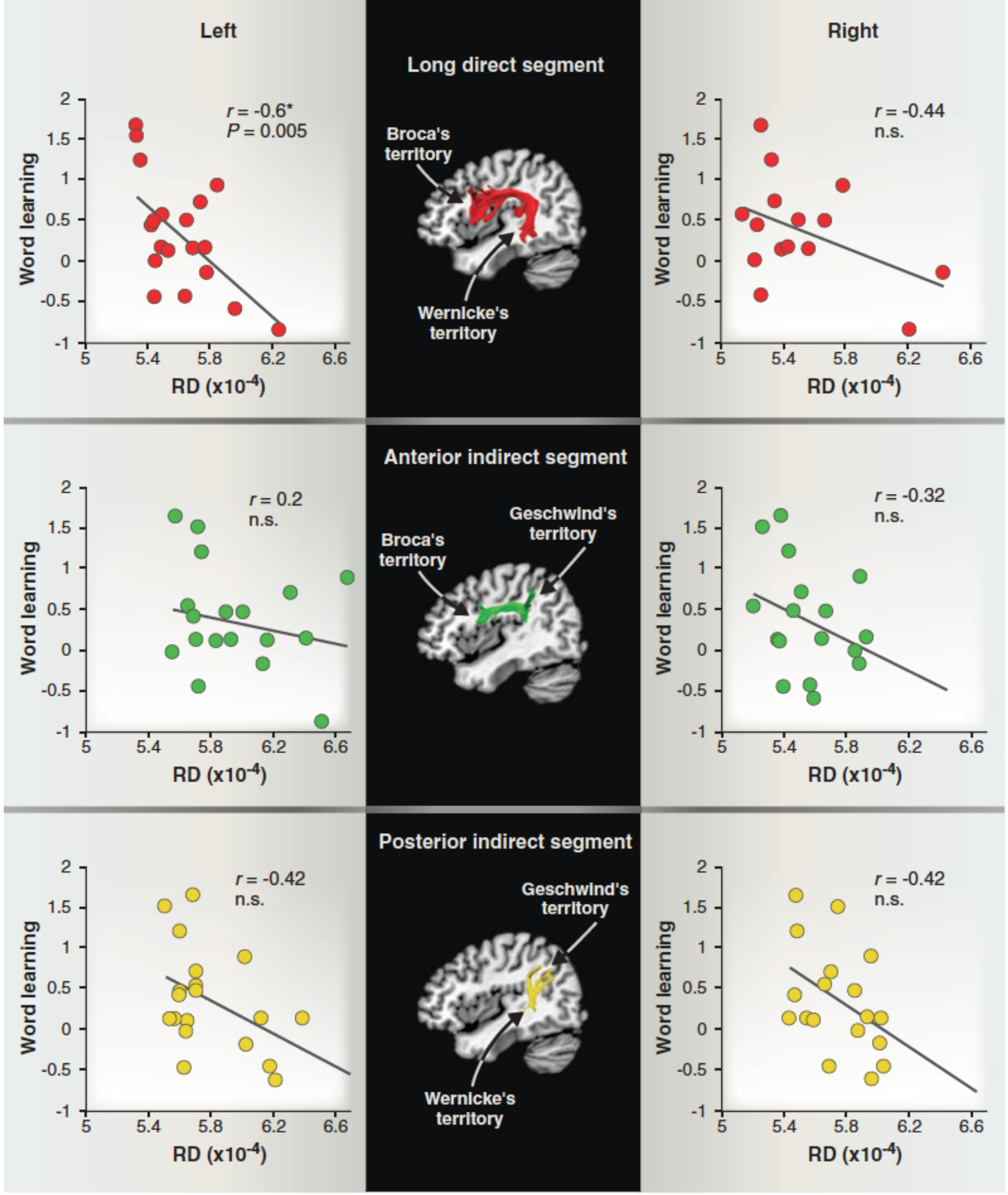
Robert J. Zatorre*

Speech and music are remarkable aspects of human cognition and sensory-motor processing. Cognitive neuroscience has focused on them to understand how brain function and structure are modified by learning. Recent evidence indicates that individual differences in anatomical and functional properties of the neural architecture also affect learning and performance in these domains. Here, neuroimaging findings are reviewed that reiterate evidence of experience-dependent brain plasticity, but also point to the predictive validity of such data in relation to new learning in speech and music domains. Indices of neural sensitivity to certain stimulus features have been shown to predict individual rates of learning; individual network properties of brain activity are especially relevant in this regard, as they may reflect anatomical connectivity. Similarly, numerous studies have shown that anatomical features of auditory cortex and other structures, and their anatomical connectivity, are predictive of new sensory-motor learning ability. Implications of this growing body of literature are discussed.

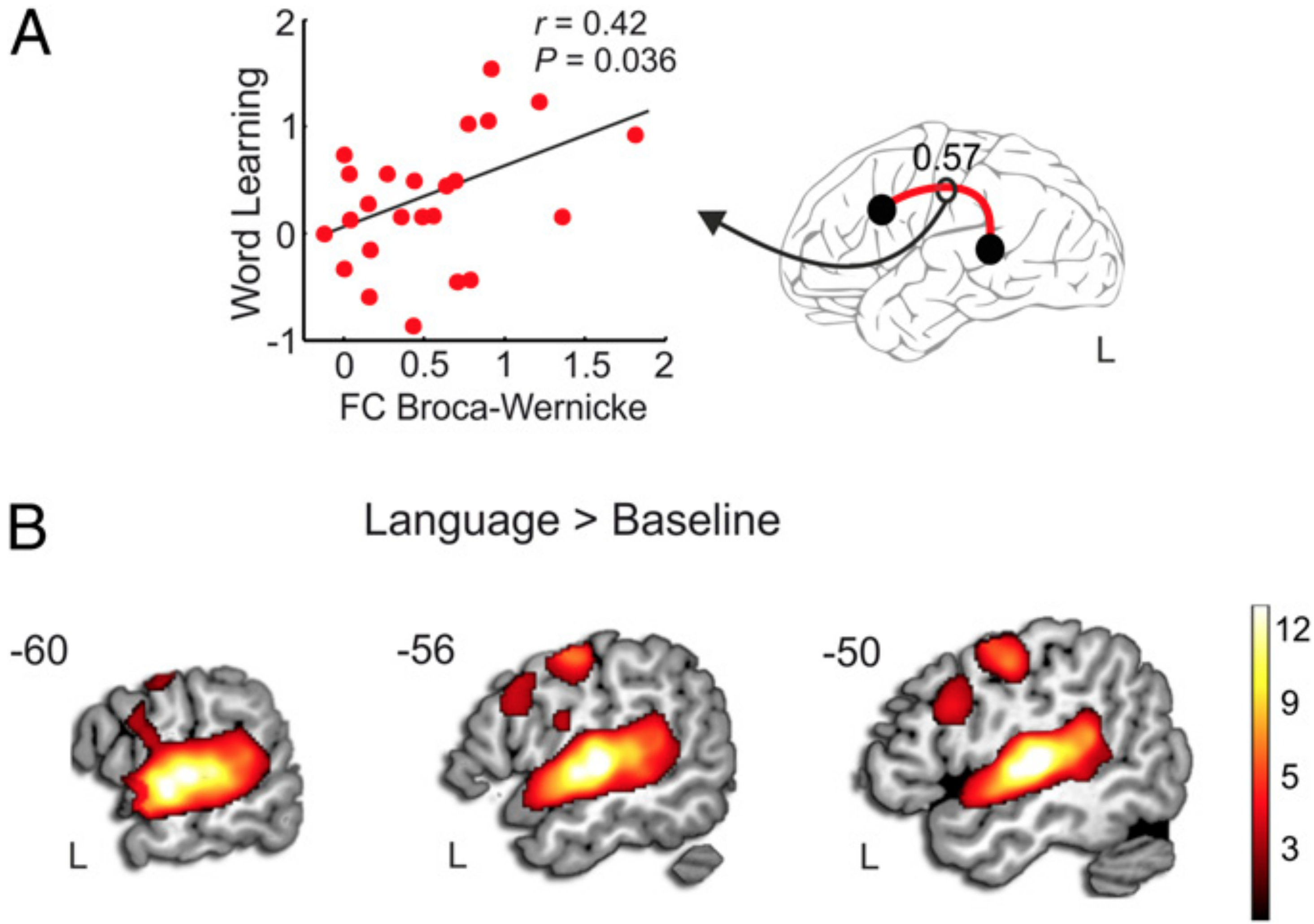
# Word learning is mediated by the left arcuate fasciculus

Diana López-Barroso[a,b,1], Marco Catani[c], Pablo Ripollés[a,b], Flavio Dell'Acqua[c,d,e], Antoni Rodríguez-Fornells[a,b,f], and Ruth de Diego-Balaguer[a,b,f]

[a]Cognition and Brain Plasticity Group, Bellvitge Biomedical Research Institute, L'Hospitalet de Llobregat, 08097 Barcelona, Spain; [b]Department of Basic Psychology, Campus Bellvitge, University of Barcelona, L'Hospitalet de Llobregat, 08097 Barcelona, Spain; [c]Natbrainlab, Department of Forensic and Neurodevelopmental Sciences, Institute of Psychiatry, and [d]Department of Neuroimaging, Institute of Psychiatry, King's College London, London SE5 8AF, United Kingdom; [e]National Institute for Health Research Biomedical Research Centre for Mental Health at South London and Maudsley National Health Service Foundation Trust and King's College London, Institute of Psychiatry, London SE5 8AF, United Kingdom; and [f]Institució Catalana de Recerca i Estudis Avançats, 08010 Barcelona, Spain



Left
Right
Long direct segment
Broca's territory
Wernicke's territory
r = -0.6*
P = 0.005
r = -0.44
n.s.
Anterior indirect segment
Broca's territory
Geschwind's territory
r = 0.2
n.s.
r = -0.32
n.s.
Posterior indirect segment
Geschwind's territory
Wernicke's territory
r = -0.42
n.s.
r = -0.42
n.s.
Word learning
RD (x10^-4)


A
r = 0.42
P = 0.036
Word Learning
FC Broca-Wernicke
2
1
0
-1
0
0.5
1
1.5
2
0.57
L
B
Language > Baseline
-60
-56
-50
L
L
L
12
9
5
3

# Word learning is mediated by the left arcuate fasciculus

Diana López-Barroso[a,b,1], Marco Catani[c], Pablo Ripollés[a,b], Flavio Dell'Acqua[c,d,e], Antoni Rodríguez-Fornells[a,b,f], and Ruth de Diego-Balaguer[a,b,f]

[a]Cognition and Brain Plasticity Group, Bellvitge Biomedical Research Institute, L'Hospitalet de Llobregat, 08097 Barcelona, Spain; [b]Department of Basic Psychology, Campus Bellvitge, University of Barcelona, L'Hospitalet de Llobregat, 08097 Barcelona, Spain; [c]Natbrainlab, Department of Forensic and Neurodevelopmental Sciences, Institute of Psychiatry, and [d]Department of Neuroimaging, Institute of Psychiatry, King's College London, London SE5 8AF, United Kingdom; [e]National Institute for Health Research Biomedical Research Centre for Mental Health at South London and Maudsley National Health Service Foundation Trust and King's College London, Institute of Psychiatry, London SE5 8AF, United Kingdom; and [f]Institució Catalana de Recerca i Estudis Avançats, 08010 Barcelona, Spain

**"Our results showed that performance in word learning correlates with micro- structural properties and strength of functional connectivity of the direct connections between Broca's and Wernicke's territories in the left hemisphere. This study suggests that our ability to learn new words relies on an efficient and fast communication between temporal and frontal areas. The absence of these connections in other animals may explain the unique ability of learning words in humans."**

13168–13173 | PNAS | August 6, 2013 | vol. 110 | no. 32

- Rôle supposé crucial de BA10 dans les capacités métacognitives

- Et il existe un lien entre les différences inter-individuelles de performances métacognitives et la structure de BA10

- La structure en soi est supposée être cruciale et son volume est associé à des différences de performances entre les individus

*Science*. 2010 September 17; 329(5998): 1541–1543. doi:10.1126/science.1191883.

Science AAAS

# Relating introspective accuracy to individual differences in brain structure

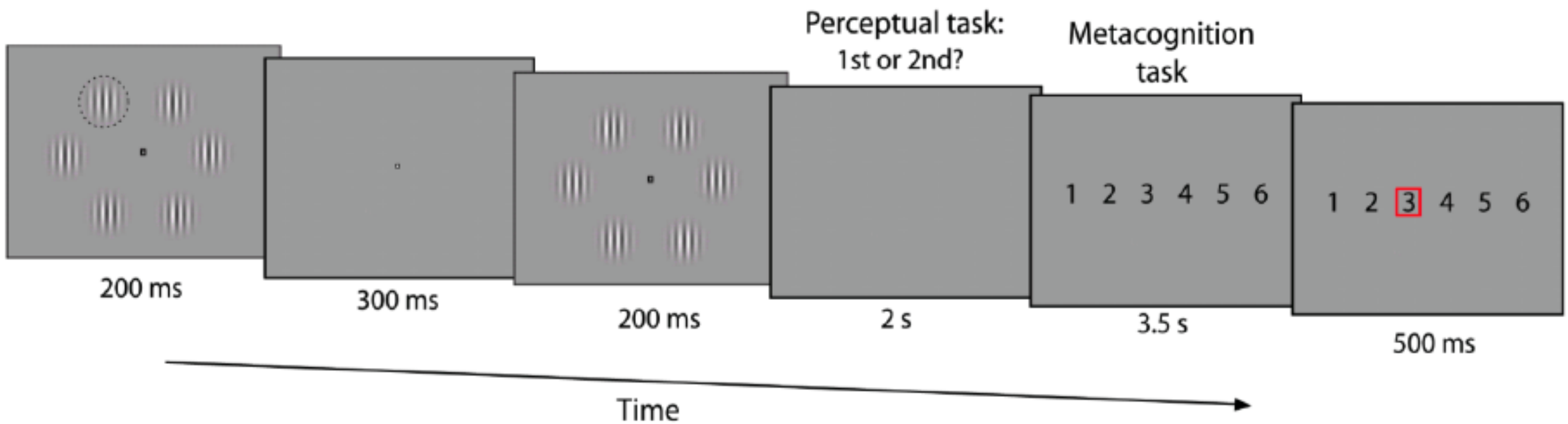
**Stephen M. Fleming**[*,1], **Rimona S. Weil**[*,1,2], **Zoltan Nagy**[1], **Raymond J. Dolan**[1], and **Geraint Rees**[1,2]

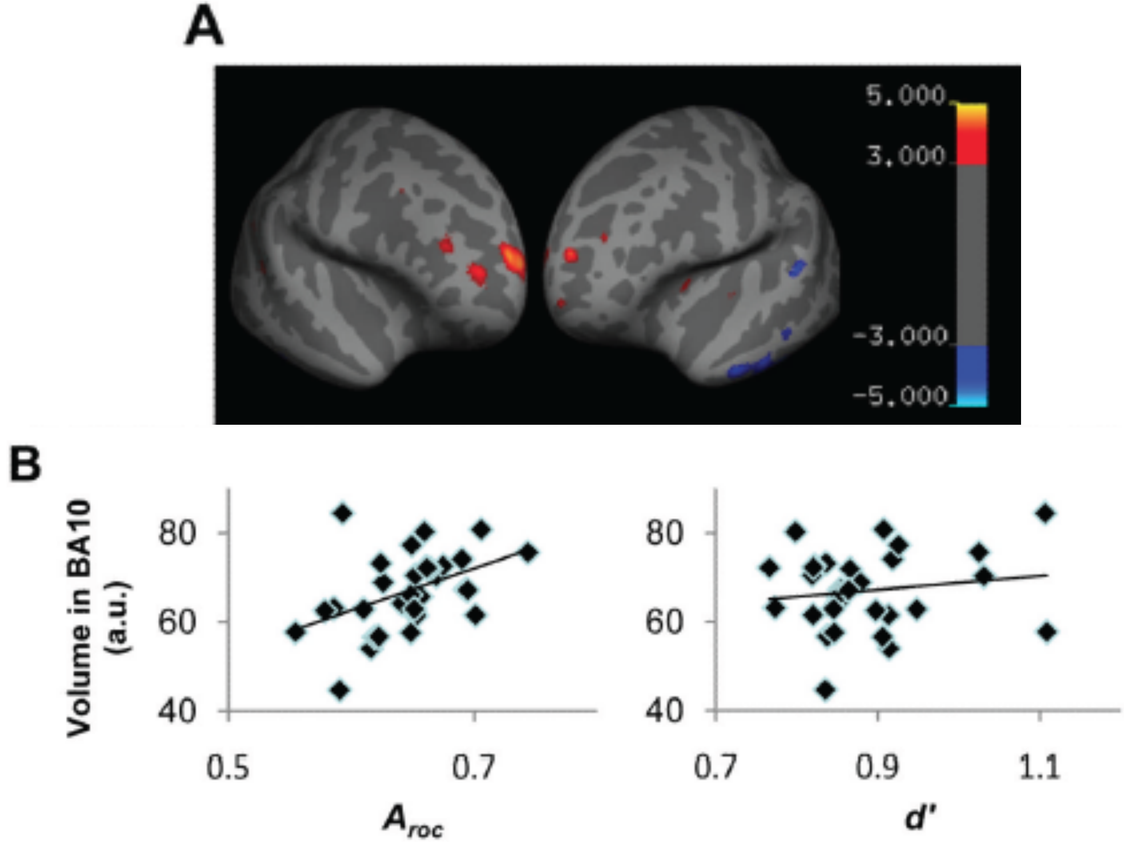
[1]Wellcome Trust Centre for Neuroimaging, University College London, 12 Queen Square, London WC1N 3BG

[2]Institute of Cognitive Neuroscience, University College London, 17 Queen Square, London WC1N 3AR

## Abstract

Our ability to introspect about self-performance is core to human subjective experience, but the neuroanatomical basis of this ability is unknown. Such accurate introspection requires discriminating correct from incorrect decisions, a capacity that varies substantially across individuals. We dissociated variation in introspective ability from objective performance in a simple perceptual decision task, allowing us to determine whether this inter-individual variability was associated with a distinct neural substrate. We show that introspective ability is correlated with gray matter volume in anterior prefrontal cortex, a region which shows striking evolutionary development in humans. Moreover, inter-individual variability in introspective ability also correlated with white matter microstructure connected with this area of prefrontal cortex. Our findings point to a focal neuroanatomical substrate for introspective ability, a substrate distinct from that supporting primary perception.


Perceptual task:
1st or 2nd?
Metacognition
task
1 2 3 4 5 6
1 2 3 4 5 6
200 ms
300 ms
200 ms
2 s
3.5 s
500 ms
Time




Gray matter volume correlated with introspective ability

(**A**) Projection of statistical ($T$) maps for positive (hot colormap) and negative (cool colormap) correlations with $A_{roc}$ onto an inflated cortical surface T1-weighted template, thresholded at $T > 3$ for display purposes. Significant clusters ($P < 0.05$, corrected for multiple comparisons) where metacognitive ability correlated with gray matter volume (see Methods) were found in right anterior prefrontal cortex (Brodmann area 10; positive

(**B**) Plot of grey matter volume in the right BA10 cluster against both $A_{roc}$ and $d'$ (see Methods for full details) indicating that the correlation with metacognitive ability was independent of task performance.

# Réorganisation des circuits cérébraux après une lésion cérébrale ou durant un apprentissage

*First publ. in: Science 270 (1995), pp. 305-307*

# Increased Cortical Representation of the Fingers of the Left Hand in String Players

Thomas Elbert, Christo Pantev, Christian Wienbruch, Brigitte Rockstroh, Edward Taub

Magnetic source imaging revealed that the cortical representation of the digits of the left hand of string players was larger than that in controls. The effect was smallest for the left thumb, and no such differences were observed for the representations of the right hand digits. The amount of cortical reorganization in the representation of the fingering digits was correlated with the age at which the person had begun to play. These results suggest that the representation of different parts of the body in the primary somatosensory cortex of humans depends on use and changes to conform to the current needs and experiences of the individual.

Nine musicians (six violinists, two cellists, and one guitarist) who had played their instruments for a mean period of 11.7 years (range, 7 to 17 years) served as subjects for our study. Six nonmusicians served as controls (*15*). The mean age for both groups was 24 ± 3 years. Before our investigation, the musicians kept a diary for 1 week, recording the amount of time practiced per day (mean 9.8 ± 8.4 hours per week), and had estimated the amount of time spent practicing during the previous month and year (10.8 ± 8.8 hours per week).

During the experimental session, somatosensory stimulation was delivered to the first digit and, in separate runs, to the fifth digit of either hand. Stimulation consisted of light superficial pressure applied by means of a pneumatic stimulator with the use of standard, nonpainful stimulation intensity (*9*, *16*, *17*). The data (Fig. 1) indi-

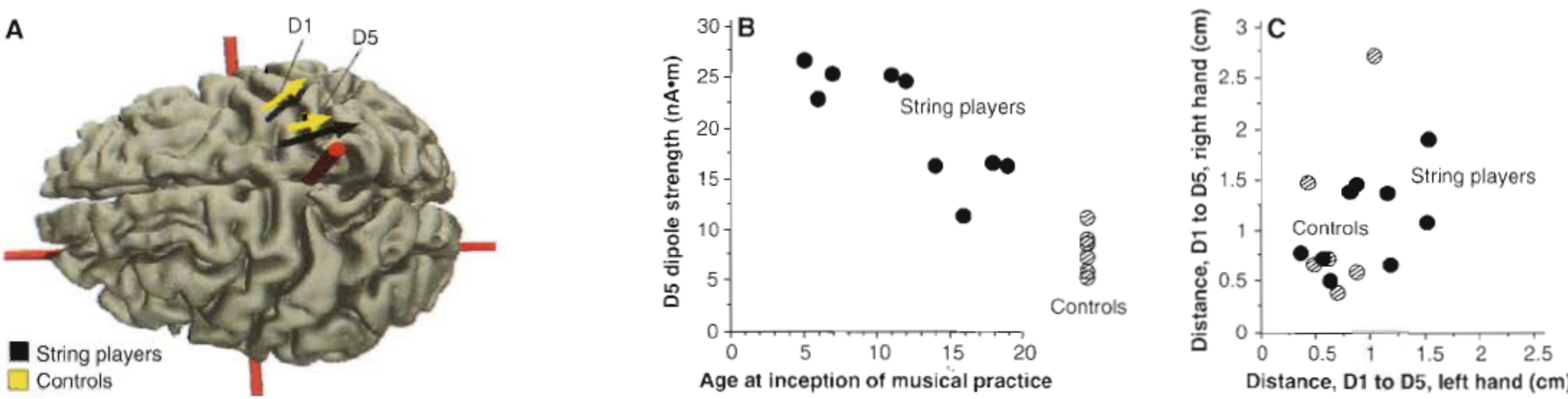
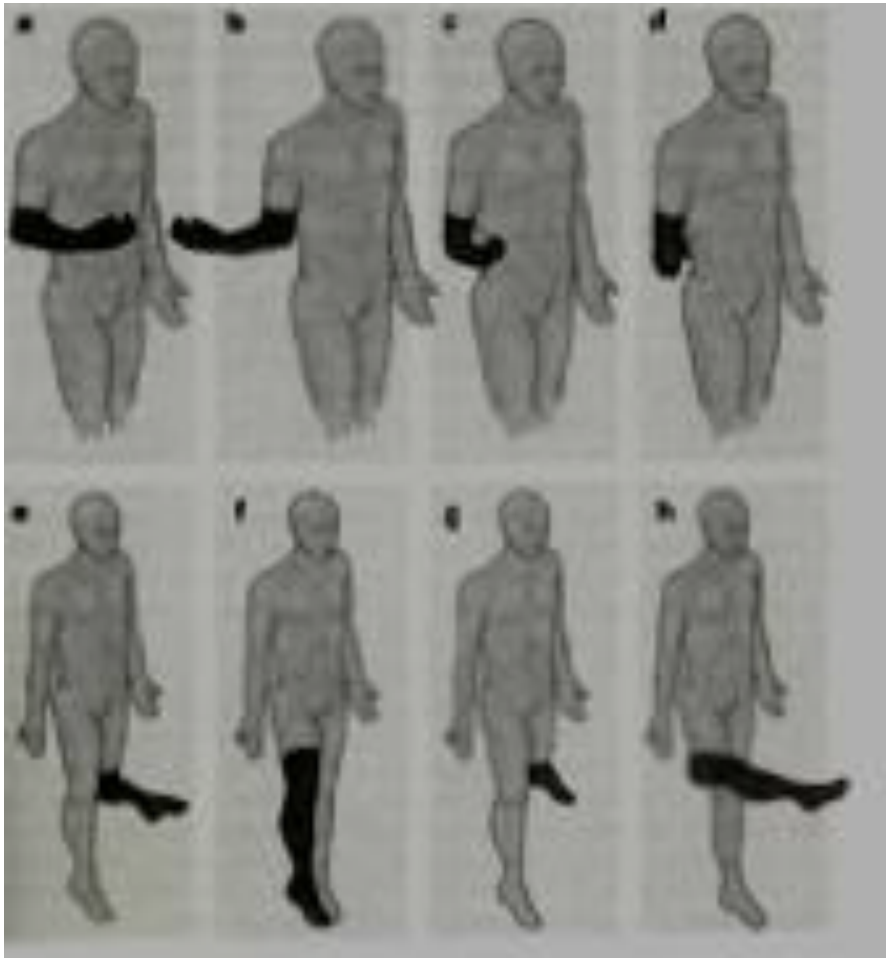
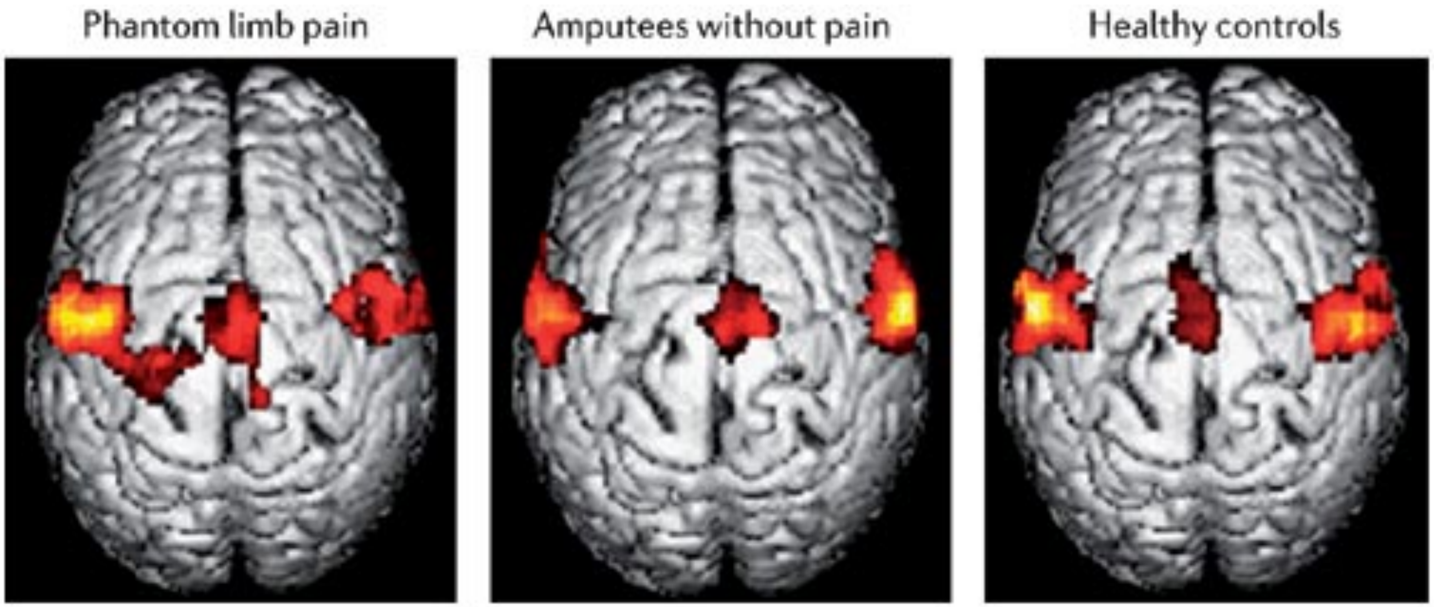



**Fig. 1.** (**A**) Equivalent current dipoles elicited by stimulation of the thumb (D1) and fifth finger (D5) of the left hand are superimposed onto an MRI (magnetic resonance imaging) reconstruction of the cerebral cortex of a control, who was selected to provide anatomical landmarks for the interpretation of the MEG-based localization. The arrows represent the location and orientation of the ECD vector for each of the two digits averaged across musicians (black) and controls (yellow). The length of the arrows represents the mean magnitude of the dipole moment for the two digits in each group. The average locations of D5 and D1 are shifted medially for the string players compared to controls; the shift is larger for D5 than for D1. The dipole moment is also larger for the musicians' D5, as indicated by the greater magnitude of the black arrow. (**B**) The magnitude of the dipole moment as a function of the age of inception of musical practice; string players are indicated by filled circles, control subjects by hatched circles. Note the larger dipole moment for individuals beginning musical practice before the age of 12. (**C**) Scatterplot of the Euclidean distances (in centimeters) between the cortical representations of D1 and D5. This distance for the musicians' left hands was greater than that in controls, but this difference is not statistically significant.

# Les membres fantômes





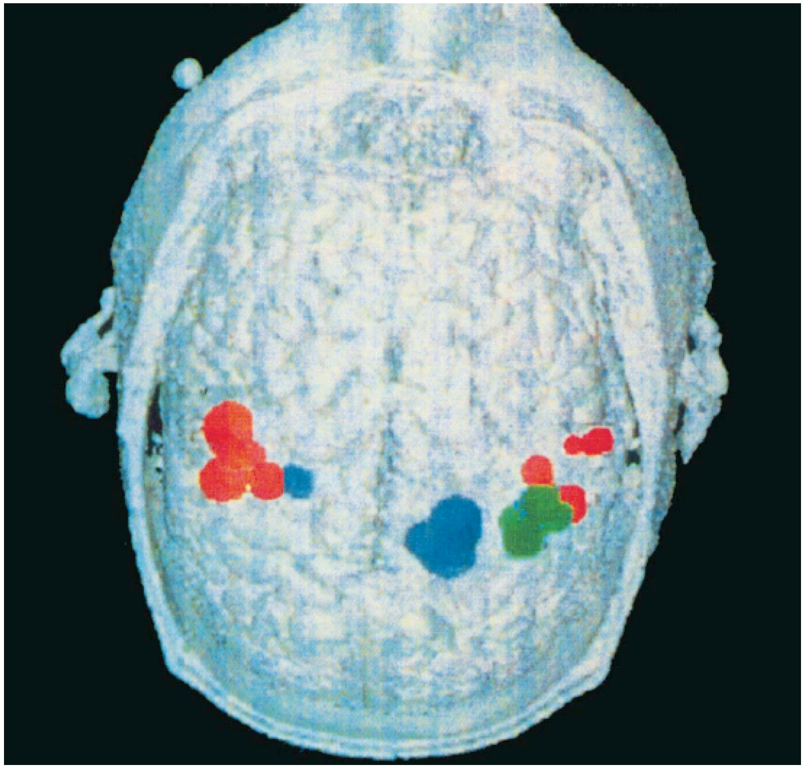

Flor *et al*. *Nature Reviews Neuroscience* **7**, 873–881 (November 2006) | doi:10.1038/nrn1991

nature REVIEWS NEUROSCIENCE

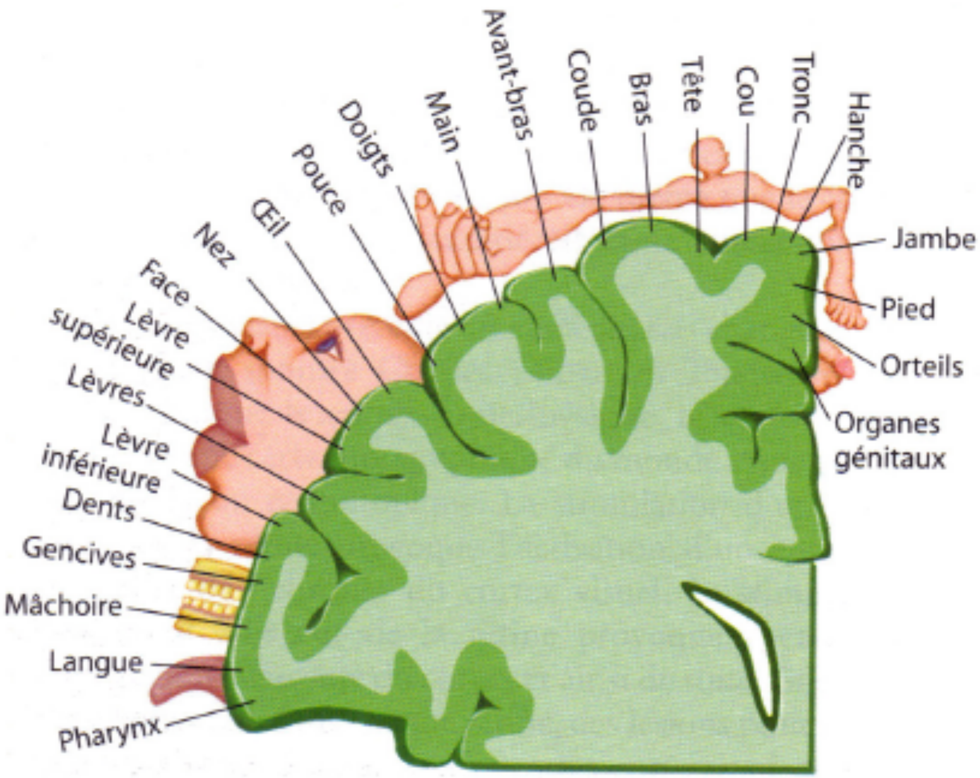
The JAMA Network

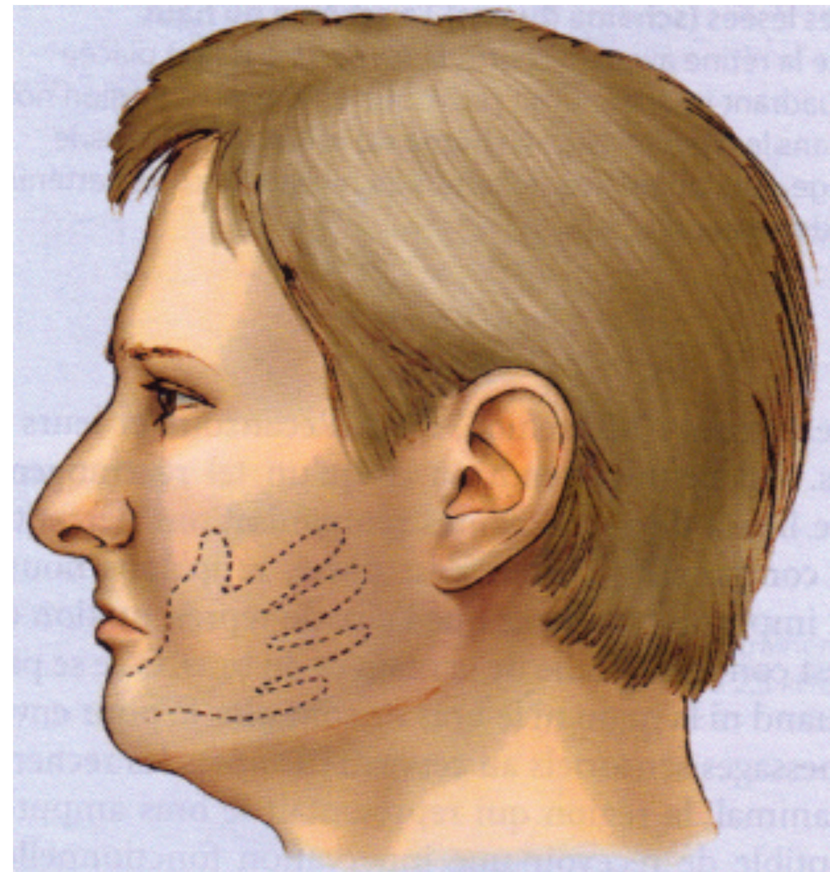
From: **Phantom Limbs and Neural Plasticity**
Ramachandran & Ramachandran

Arch Neurol. 2000;57(3):317-320. doi:10.1001/archneur.57.3.317



Changes in cortical topography in S1 revealed by magnetoencephalography. Top view of combined magnetoencephalography and 3-dimensional surface–rendered magnetic resonance image from an **adult whose right arm was amputated** below the elbow**. Red indicates face; green, hand; and blue,** upper arm. Notice **that the hand area (green) is missing from the left hemisphere** and is now being activated by sensory input from the flanking face region and upper arm.


Avant-bras
Coude
Bras
Tête
Cou
Tronc
Hanche
Main
Doigts
Pouce
Œil
Nez
Face
Lèvre supérieure
Lèvres
Lèvre inférieure
Dents
Gencives
Mâchoire
Langue
Pharynx
Jambe
Pied
Orteils
Organes génitaux



The JAMA Network

From: **Phantom Limbs and Neural Plasticity**

Arch Neurol. 2000;57(3):317-320. doi:10.1001/archneur.57.3.317


Figure Legend:

Points on the face of a patient that elicit precisely localized, modality-specific referral in the phantom limb 4 weeks after amputation of the left arm below the elbow. **Sensations were felt simultaneously on the face and phantom limb.**

# Cortical reorganization in motor cortex after graft of both hands

Pascal Giraux[1,2], Angela Sirigu[1], Fabien Schneider[3] and Jean-Michel Dubernard[4]

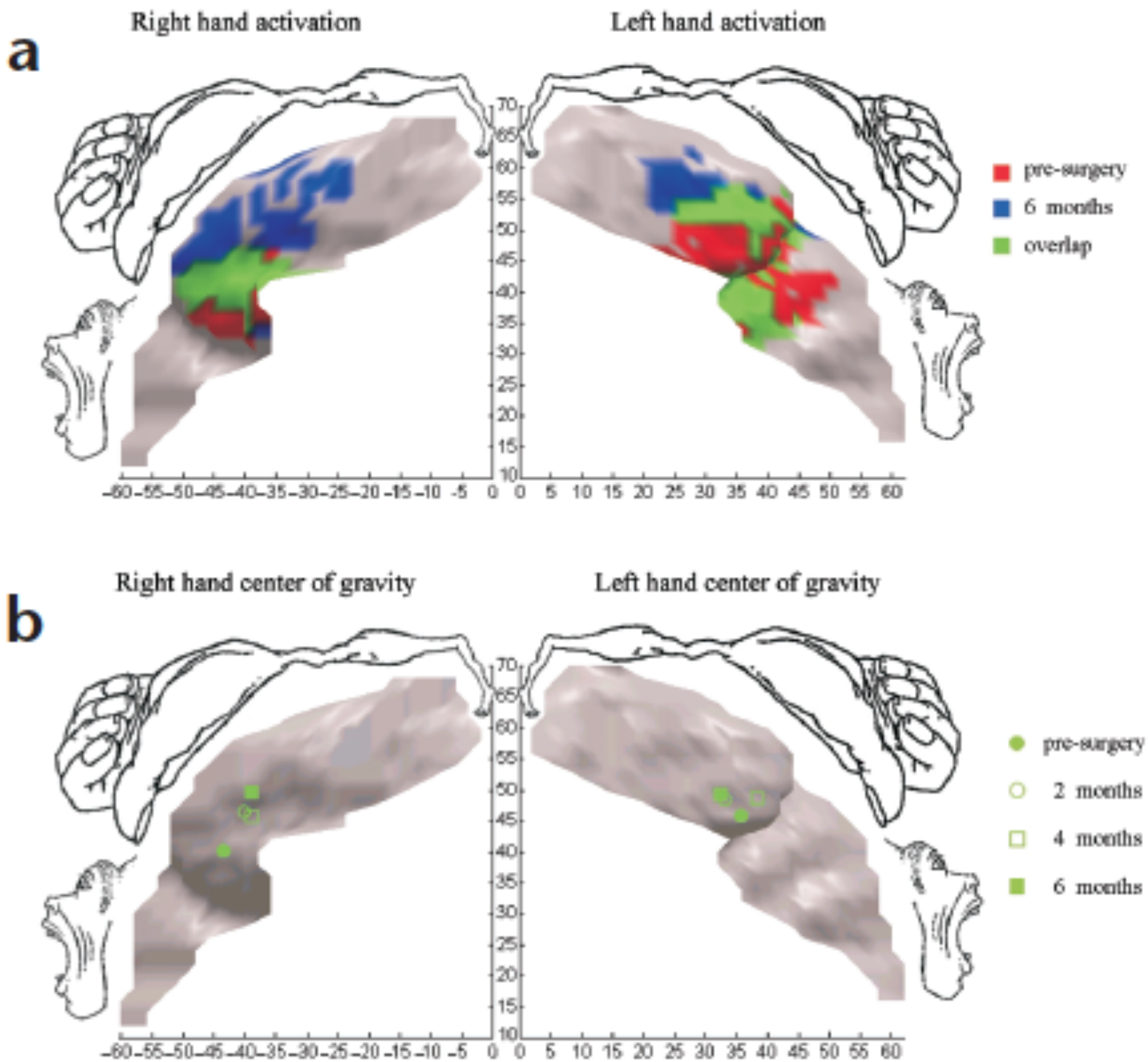
*[1] Institute for Cognitive Science, CNRS, 67 Bd Pinel, 69675 Bron, France*

*[2] Department of Physical Medicine, CHU, BD Pasteur, Saint-Etienne*

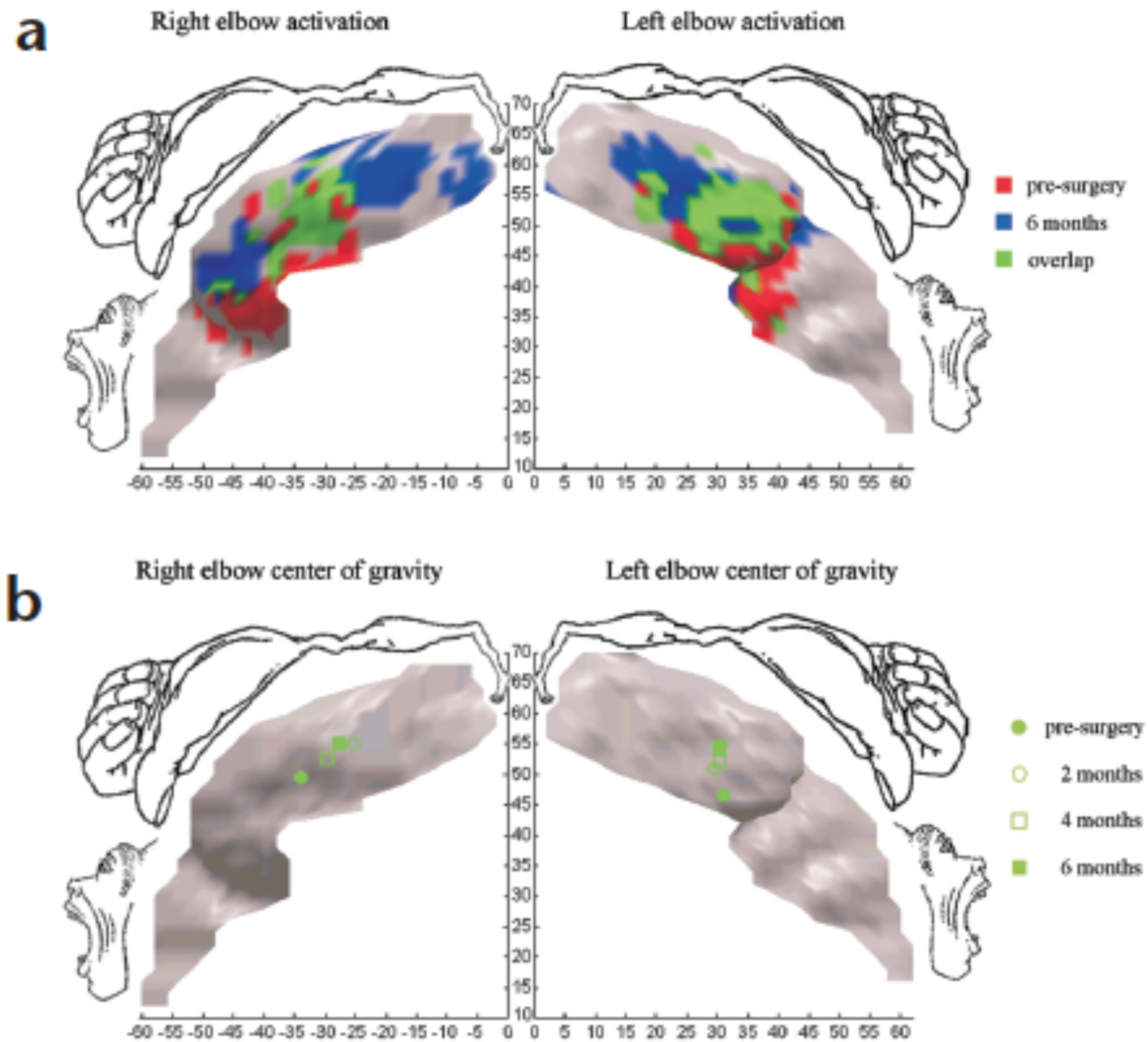
*[3] Radiology Department, CHU, BD Pasteur, Saint-Etienne*

*[4] Department of Surgical Transplant, E. Herriot Hospital, Place d'Arsonval, Lyon*

*Correspondence should be addressed to A.S. (sirigu@isc.cnrs.fr)*



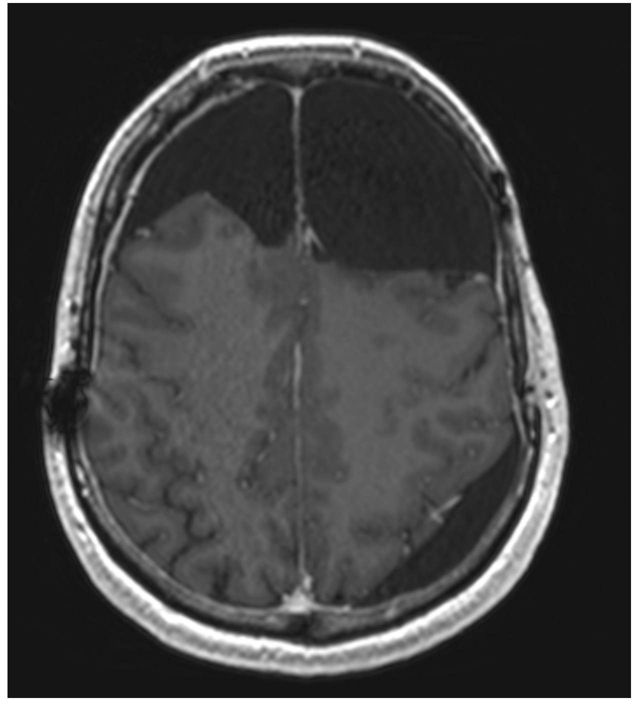
a
Right hand activation
Left hand activation
pre-surgery
6 months
overlap
b
Right hand center of gravity
Left hand center of gravity
pre-surgery
2 months
4 months
6 months

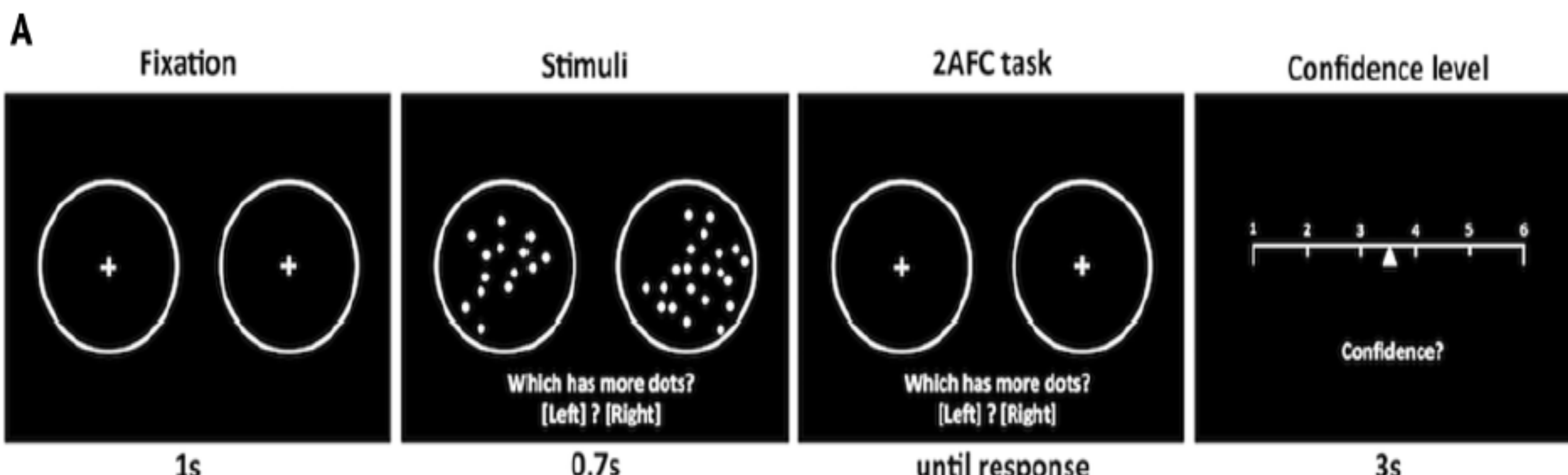

a
Right elbow activation
Left elbow activation
pre-surgery
6 months
overlap
b
Right elbow center of gravity
Left elbow center of gravity
pre-surgery
2 months
4 months
6 months

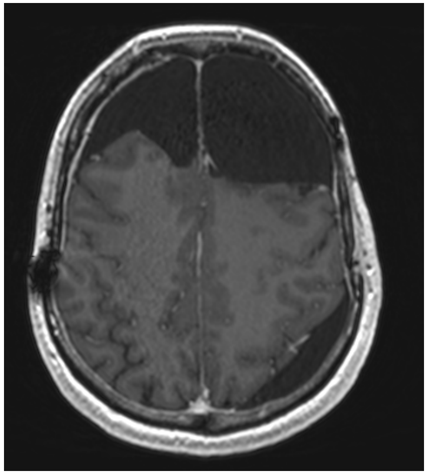
"If we assume that hand and elbow had preexisting connections, the elbow activation in the phase before surgery may emerge as a change in the weight of these connections; that is, the elbow connection may be enhanced at the expense of the deprived hand region. The hand transplant may have restored the efficacy of the original connections at the expense, this time, of the elbow representation, thus allowing typical features of cortical organization to reappear in the motor map."

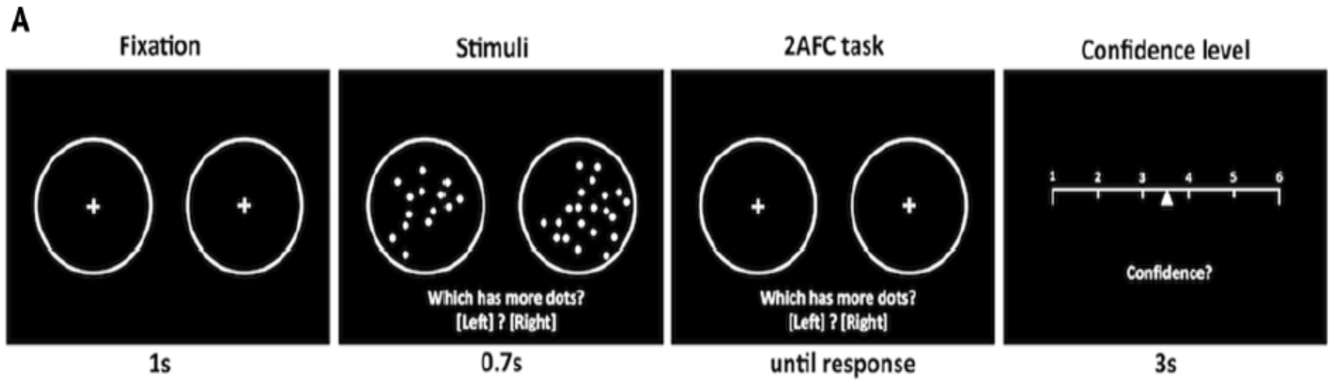
Anne-Laure Lemaitre et al. (en préparation) :

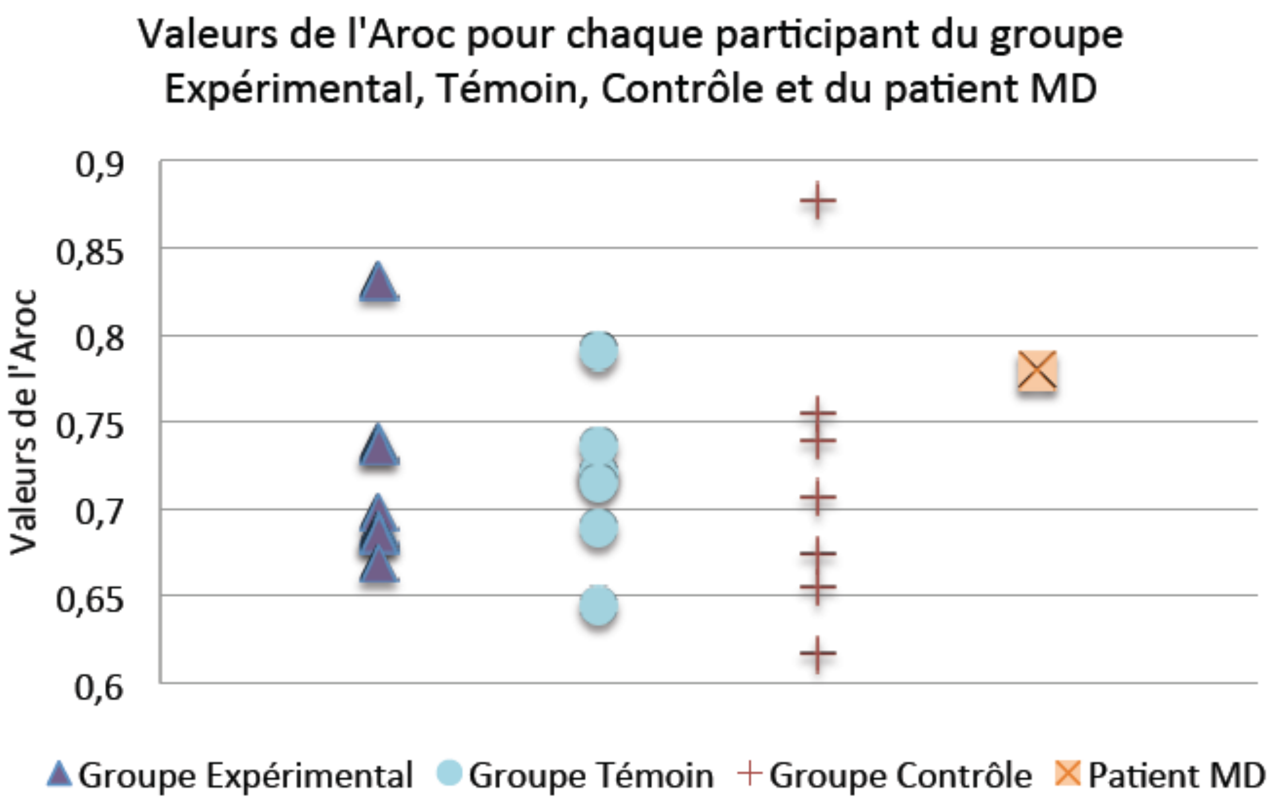
**« Capacités métacognitives intactes suite à une résection bilatérale du cortex préfrontale »**




A
Fixation
Stimuli
2AFC task
Confidence level
1
2
3
4
5
6
Confidence?
Which has more dots?
[Left] ? [Right]
Which has more dots?
[Left] ? [Right]
1s
0.7s
until response
3s



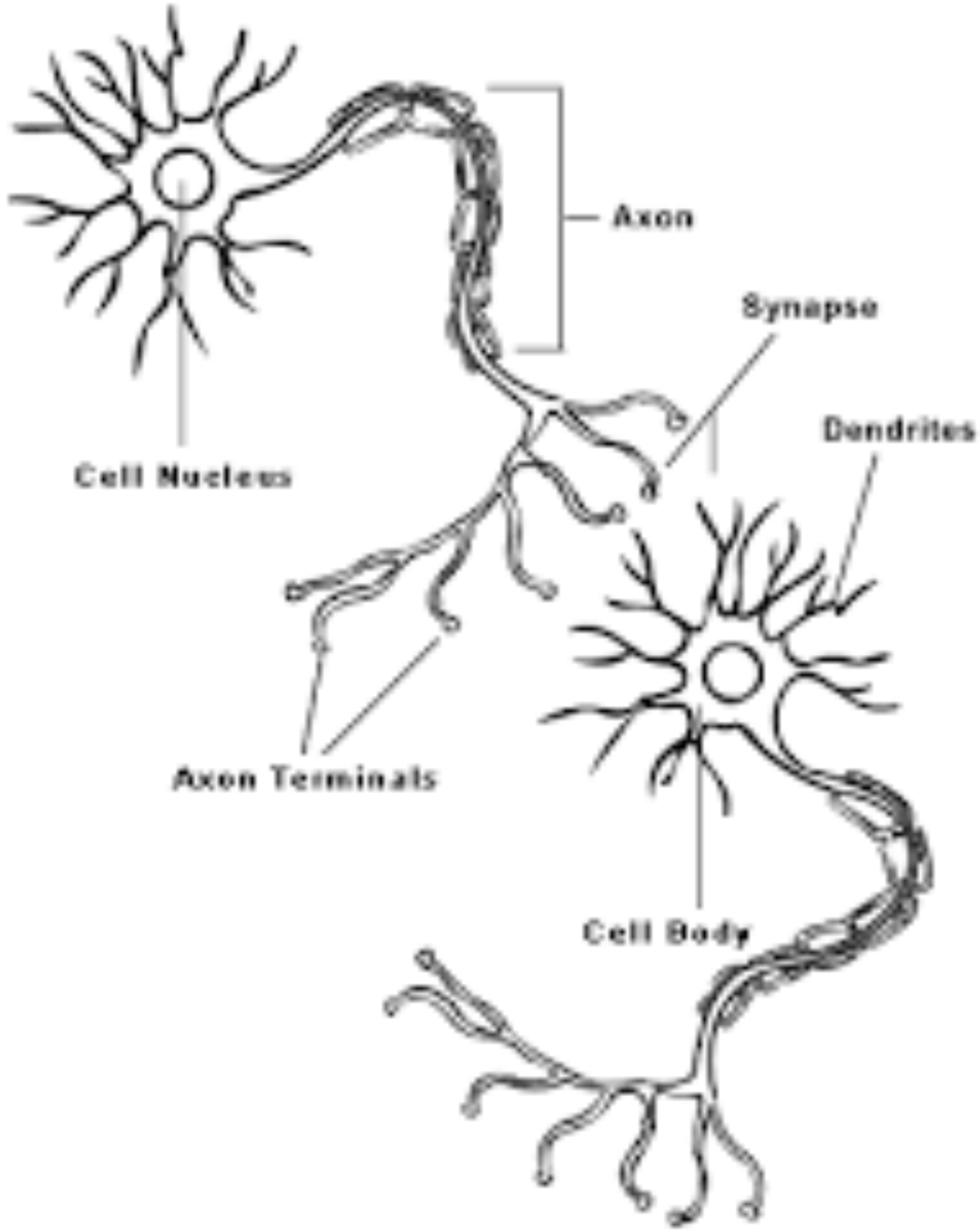

A
Fixation
Stimuli
2AFC task
Confidence level
Which has more dots?
[Left] ? [Right]
Which has more dots?
[Left] ? [Right]
1
2
3
4
5
6
Confidence?
1s
0.7s
until response
3s


Valeurs de l'Aroc pour chaque participant du groupe
Expérimental, Témoin, Contrôle et du patient MD
Valeurs de l'Aroc
0,9
0,85
0,8
0,75
0,7
0,65
0,6
Groupe Expérimental
Groupe Témoin
Groupe Contrôle
Patient MD

# La neuroplasticité - définition

"Neural plasticity is the ability of the central nervous system (CNS) to change and adapt in response to environmental cues, experience, behavior, injury or disease. Neural plasticity can result from a change in function within a particular neural substrate in the CNS through alterations in synaptic strength, neuronal excitability, neurogenesis or cell death (Brosh & Barkai, 2004)."

Translating Principles of Neural Plasticity into Research on Speech Motor Control Recovery and Rehabilitation*. J Speech Lang Hear Res.* 2008 February ; 51(1): S240–S258


Axon
Synapse
Dendrites
Cell Nucleus
Axon Terminals
Cell Body

# Neuroplasticité structurelle

OPINION

# The musician's brain as a model of neuroplasticity

*Thomas F. Münte, Eckart Altenmüller and Lutz Jäncke*

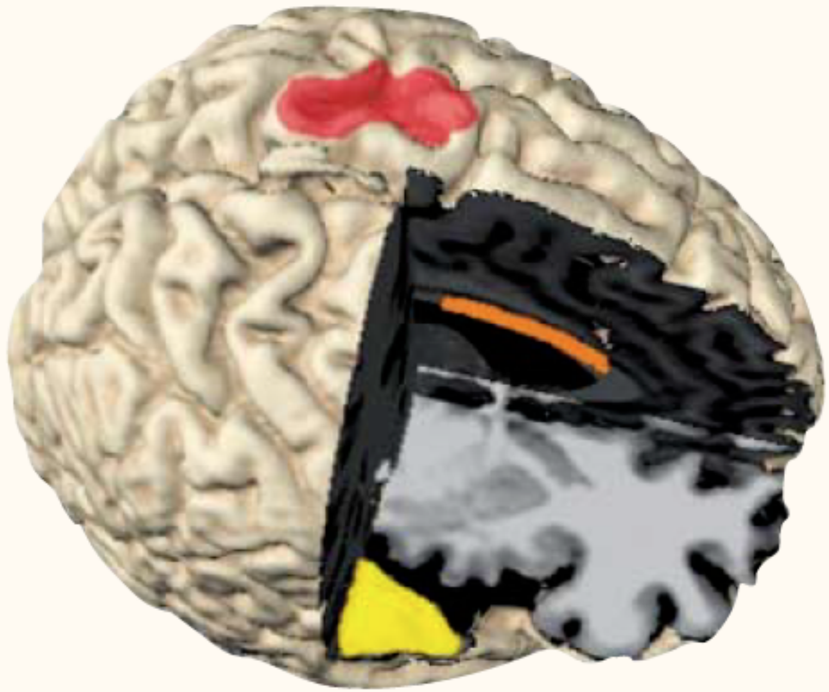


Figure 2 | **Structural changes in the brains of musicians.** Some of the brain areas that have been found to be enlarged in musicians in morphometric studies based on structural magnetic resonance imaging. Red, primary motor cortex; yellow, planum temporale; orange, anterior part of the corpus callosum.

# Changes in grey matter induced by training

## Newly honed juggling skills show up as a transient feature on a brain-imaging scan.

Does the structure of an adult human brain alter in response to environmental demands[1,2]? Here we use whole-brain magnetic-resonance imaging to visualize learning-induced plasticity in the brains of volunteers who have learned to juggle. We find that these individuals show a transient and selective structural change in brain areas that are associated with the processing and storage of complex visual motion. This discovery of a stimulus-dependent alteration in the brain's macroscopic structure contradicts the traditionally held view that cortical plasticity is associated with functional rather than anatomical changes.

Animal studies indicate that experience-related changes may occur in mammalian brain structures, but so far there has been no evidence of comparable alterations in the human brain[3–5]. To investigate this possibility, we divided a homogeneous group of volunteers (21 female, 3 male; mean age, 22 yr ± 1.6 s.d.), who were matched for sex and age, into two groups, designated as jugglers and non-jugglers. Both groups were inexperienced in juggling at the time of their first brain scan.

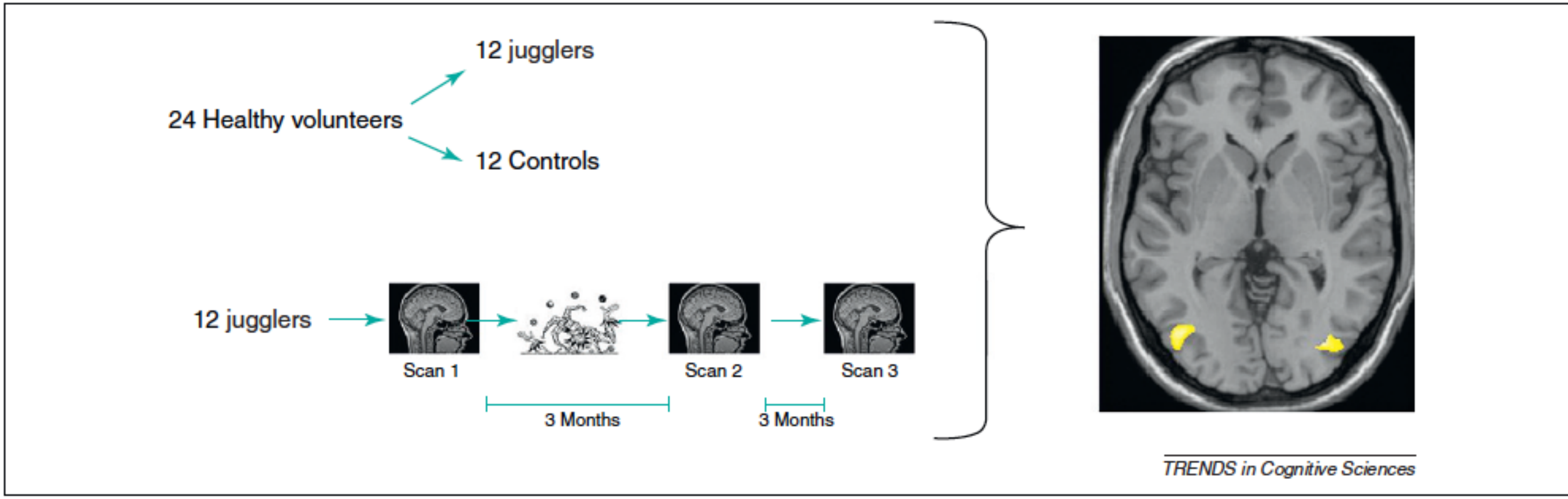
Subjects in the juggler group were given 3 months to learn a classic three-ball cascade juggling routine. A second brain scan was performed when they had become skilled performers (that is, when they could sustain juggling for at least 60 seconds). A third scan was carried out 3 months later; during the intervening period, none of the jugglers practised or attempted to extend their skills — for example, by learning a four-ball or a reverse cascade. In fact, most subjects were no longer fluent in three-ball cascade juggling by the time of the third scan.

We used voxel-based morphometry, a sophisticated objective whole-brain technique, to investigate subtle, region-specific changes in grey and white matter by averaging results across the volunteers. This method is based on high-resolution, three-dimensional magnetic-resonance imaging, registered in a common stereotactic space, and is designed to find significant regional differences by applying voxel-wise statistics in the context of gaussian random fields[6,7].

Group comparison at the beginning (the baseline) showed no significant regional differences in grey matter between jugglers and non-jugglers. In the longitudinal analysis, the juggler group demonstrated a significant (44 d.f., $P<0.05$) transient bilateral expansion in grey matter in the mid-temporal area (hMT/V5) and in the left posterior intraparietal sulcus between the first and the

THE IMAGE BANK / GETTY

second scans. This expansion decreased in the third scan (Fig. 1). We found a close rela-




The longitudinal analysis demonstrated transient structural changes in the ‘jugglers’ group opposed to the ‘nonjugglers’. A significant gray matter expansion between the first and the second scan was found in the midtemporal area (hMT/V5) bilaterally and in the left posterior intraparietal sulcus, which had decreased by the time of the third scan.


Draganski, B. et al. (2004) Neuroplasticity: changes in grey matter induced by training. ***Nature*** 427, 311–**312**

# Training-Induced Brain Structure Changes in the Elderly

**Janina Boyke,[1] Joenna Driemeyer,[1] Christian Gaser,[2] Christian Büchel,[1] and Arne May[1]**
[1]Department of Systems Neuroscience, University of Hamburg, D-22046 Hamburg, Germany, and [2]Department of Psychiatry, University of Jena, 07740 Jena, Germany

It has been suggested that learning is associated with a transient and highly selective increase in brain gray matter in healthy young volunteers. It is not clear whether and to what extent the aging brain is still able to exhibit such structural plasticity. We built on our original study, now focusing on healthy senior citizens. We observed that elderly persons were able to learn three-ball cascade juggling, but with less proficiency compared with 20-year-old adolescents. Similar to the young group, gray-matter changes in the older brain related to skill acquisition were observed in area hMT/V5 (middle temporal area of the visual cortex). In addition, elderly volunteers who learned to juggle showed transient increases in gray matter in the hippocampus on the left side and in the nucleus accumbens bilaterally.

*Key words:* age; brain; plasticity; learning; voxel-based morphometry; hippocampus

**- Age moyen 60 ans**

## Materials and Methods

*Volunteers.* We studied 93 healthy volunteers (54 female, 39 male; mean age, 60 years). Twenty-four participants did not complete the study, leaving 69 complete data sets with three time points. None of the volunteers could juggle. The subjects were recruited locally and they were informed that the purpose of the current study was to investigate the adaptive behavior of the CNS to learning to juggle. All of the volunteers were completely healthy; particularly, none suffered from dementia, Parkinson's disease, diabetes, or hypertension. The study received ethical approval by the local Ethics committee and written informed consent was obtained from all study participants before examination.

# Navigation-related structural change in the hippocampi of taxi drivers

Eleanor A. Maguire*[†], David G. Gadian[‡], Ingrid S. Johnsrude[†], Catriona D. Good[†], John Ashburner[†], Richard S. J. Frackowiak[†], and Christopher D. Frith[†]

[†]Wellcome Department of Cognitive Neurology, Institute of Neurology, University College London, Queen Square, London WC1N 3BG, United Kingdom; and [‡]Radiology and Physics Unit, Institute of Child Health, University College London, London WC1N 1EH, United Kingdom

Communicated by Brenda Milner, McGill University, Montreal, Canada, January 28, 2000 (received for review November 10, 1999)

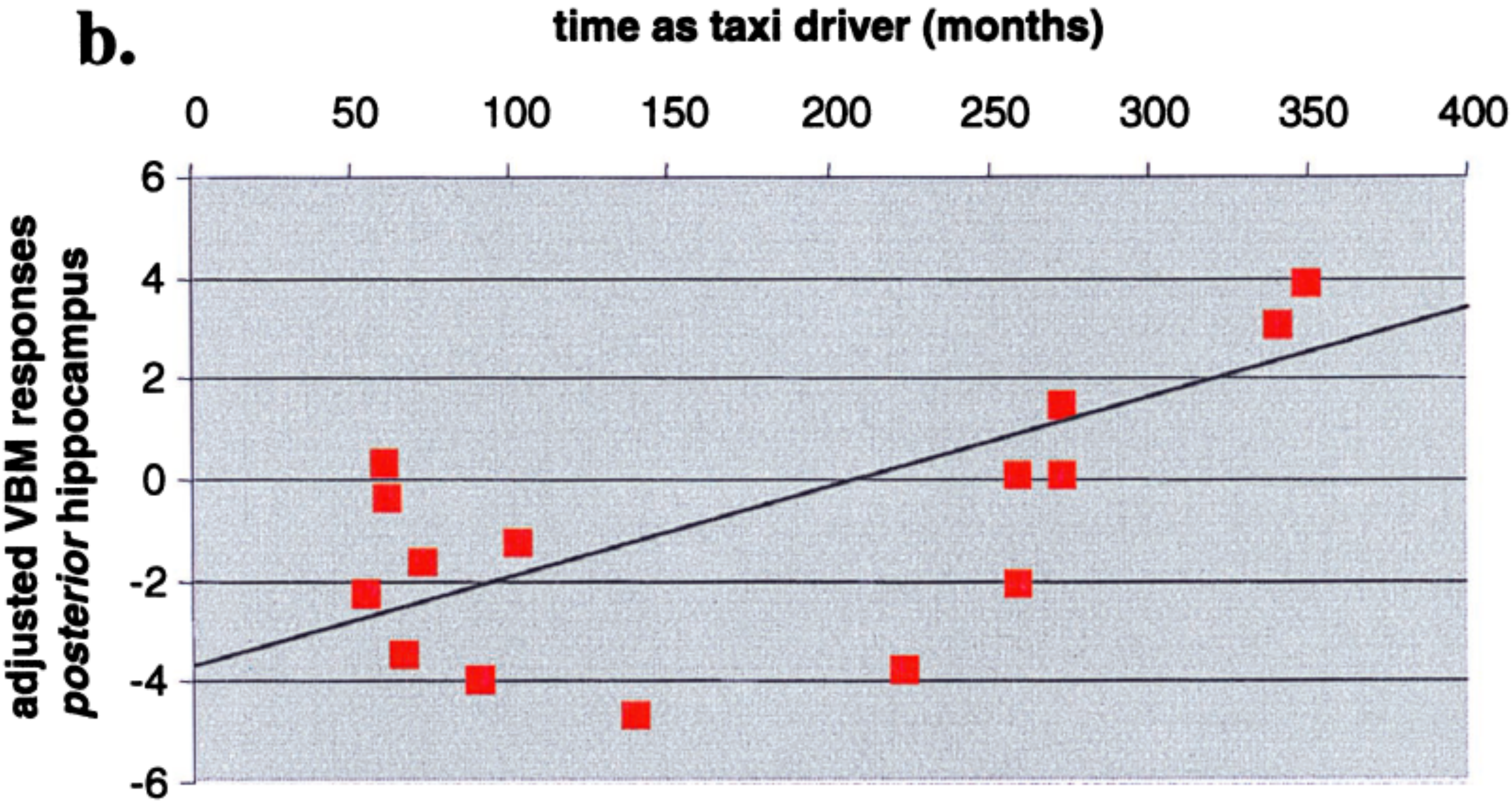
**Structural MRIs of the brains of humans with extensive navigation experience, licensed London taxi drivers, were analyzed and compared with those of control subjects who did not drive taxis. The posterior hippocampi of taxi drivers were significantly larger relative to those of control subjects. A more anterior hippocampal region was larger in control subjects than in taxi drivers. Hippocampal volume correlated with the amount of time spent as a taxi driver (positively in the posterior and negatively in the anterior hippocampus). These data are in accordance with the idea that the posterior hippocampus stores a spatial representation of the environment and can expand regionally to accommodate elaboration of this representation in people with a high dependence on navigational skills. It seems that there is a capacity for local plastic change in the structure of the healthy adult human brain in response to environmental demands.**

*a priori* regions of interest. The data were also analyzed by using a second and completely independent pixel-counting technique within the hippocampus proper. Comparisons were made between the brain scans of taxi drivers, who had all acquired a significant amount of large-scale spatial information (as evidenced by passing the licensing examinations), and those of a comparable group of control subjects who lacked such extensive navigation exposure.

## Methods

**Subjects.** Right-handed male licensed London taxi drivers ($n$ = 16; mean age 44 years; range 32–62 years) participated. All had been licensed London taxi drivers for more than 1.5 years (mean time as taxi driver = 14.3 years; range = 1.5–42 years). The average time spent training to be a taxi driver before passing the

PNAS, 2000 u vol. 97 u no. 8




**Le volume de l’hippocampe droit corrèle avec le nombre d’années passées à être chauffeur de taxi à Londres**

*HIPPOCAMPUS 16:1091–1101 (2006)*

# London Taxi Drivers and Bus Drivers: A Structural MRI and Neuropsychological Analysis

Eleanor A. Maguire,* Katherine Woollett, and Hugo J. Spiers

**ABSTRACT:** Licensed London taxi drivers show that humans have a remarkable capacity to acquire and use knowledge of a large complex city to navigate within it. Gray matter volume differences in the hippocampus relative to controls have been reported to accompany this expertise. While these gray matter differences could result from using and updating spatial representations, they might instead be influenced by factors such as self-motion, driving experience, and stress. We examined the contribution of these factors by comparing London taxi drivers with London bus drivers, who were matched for driving experience and levels of stress, but differed in that they follow a constrained set of routes. We found that compared with bus drivers, taxi drivers had greater gray matter volume in mid-posterior hippocampi and less volume in anterior hippocampi. Furthermore, years of navigation experience correlated with hippocampal gray matter volume only in taxi drivers, with right posterior gray matter volume increasing and anterior volume decreasing with more navigation experience. This suggests that spatial knowledge, and not stress, driving, or self-motion, is associated with the pattern of hippocampal gray matter volume in taxi drivers. We then tested for functional differences between the groups and found that the ability to acquire new visuo-spatial information was worse in taxi drivers than in bus drivers. We speculate that a complex spatial representation, which facilitates expert navigation and is associated with greater posterior hippocampal gray matter volume, might come at a cost to new spatial memories and gray matter volume in the anterior hippocampus. 

"If gray matter volume can be influenced by navigation experience, this has important implications for understanding the mechanisms of hippocampal operation, and for rehabilitation of memory-impaired patients. However, several other factors may have affected the findings. **Navigation around London by taxi drivers necessarily involves self-motion**. Since spatially selective hippocampal activity and theta oscillations require self-motion (Foster et al., 1989; O'Keefe and Recce, 1993; Terrazas et al., 2005), **it could be argued that the structural changes observed are not the result of using and updating spatial representations but are instead the result of increased hippocampal activity caused by self-motion.** Furthermore, movement around London is achieved by driving, which itself comprises multiple elements such as vigilance, attention, motor planning, and execution. In addition, driving all day in the poor air of a large city, dealing with customers, traffic, and fellow road users could be regarded as stressful, which might have impacted upon hippocampal gray matter (McEwen, 2001; McEwan and Magarinos, 2001)."

*Participant Characteristics*

| | London taxi drivers | London bus drivers |
|---|---|---|
| Mean age (yr) | 39.33 (4.49) | 35.88 (5.79) |
| Mean full-time driving experience in London (yr) | 10.94 (5.25) | 7.71 (6.47) |
| Mean age at leaving school (yr) | 16.50 (0.90) | 16.53 (1.00) |
| Mean laterality index (handedness) | 69.72 (43.40) | 57.12 (51.15) |
| Mean scaled score on matrix reasoning | 11.61 (1.76) | 11.59 (2.26) |

SDs in parentheses. Group comparisons revealed no significant differences on any of these background characteristics (see text).

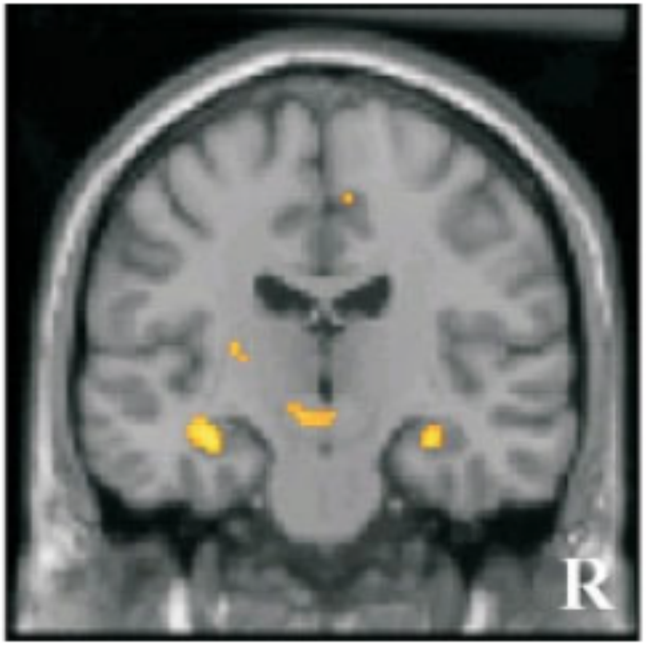
18 taxi drivers
17 bus drivers

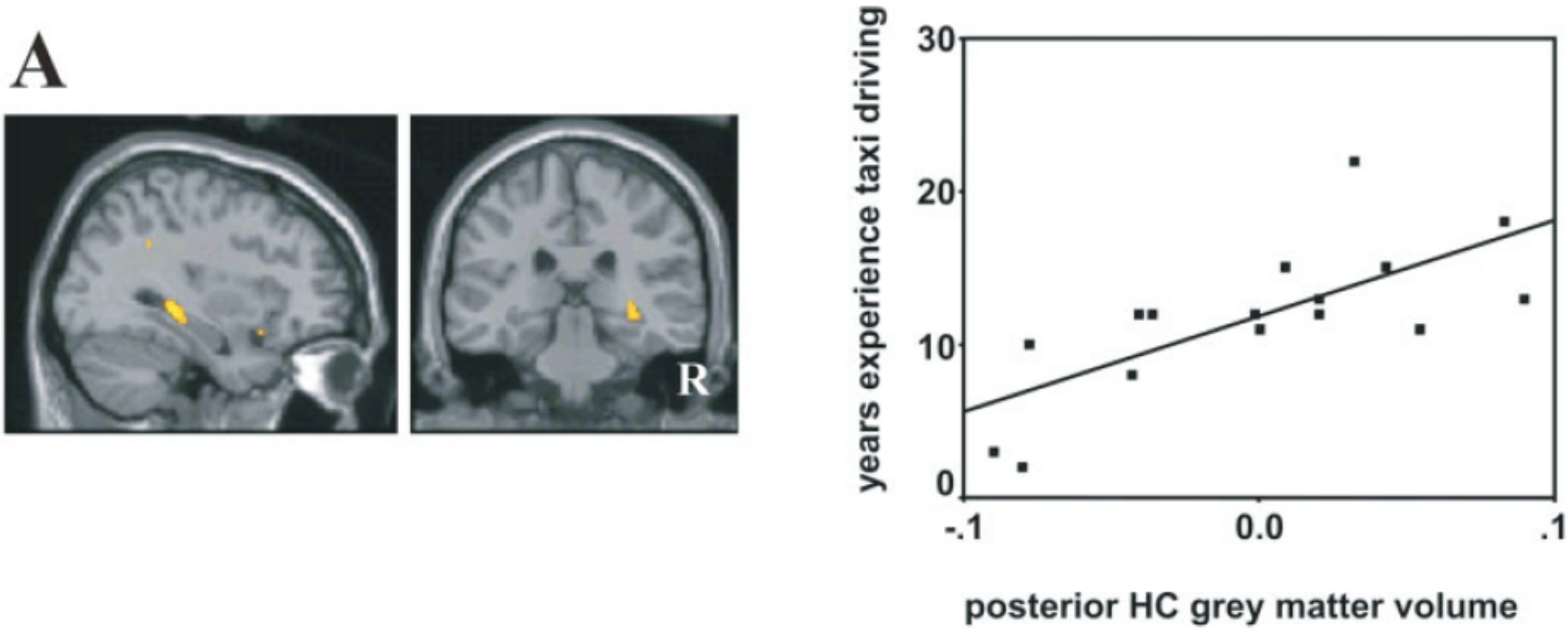
*Mean Scores on Stress and Anxiety Measures*

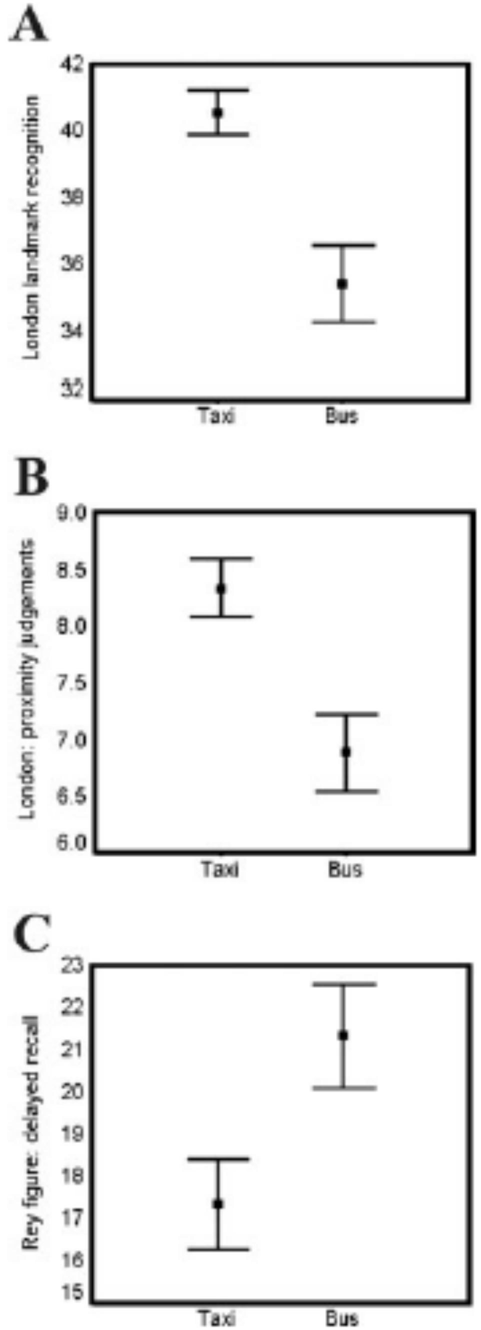
| | London taxi drivers | London bus drivers |
|---|---|---|
| Perceived stress sale | 16.39 (7.96) | 15.59 (5.68) |
| Life stress rating | 5.50 (2.72) | 4.29 (1.75) |
| Job stress rating | 4.94 (2.55) | 4.29 (1.96) |
| State trait anxiety inventory state | 29.50 (7.99) | 26.41 (9.46) |
| State trait anxiety inventory trait | 38.11 (12.31) | 34.35 (9.91) |

SDs in parentheses. Group comparisons revealed no significant differences on any of these measures (see text).

**Taxi > Bus**




A
R
years experience taxi driving
30
20
10
0
-.1
0.0
.1
posterior HC grey matter volume



A
London landmark recognition
42
40
38
36
34
32
Taxi
Bus
B
London: proximity judgements
9.0
8.5
8.0
7.5
7.0
6.5
6.0
Taxi
Bus
C
Rey figure: delayed recall
23
22
21
20
19
18
17
16
15
Taxi
Bus

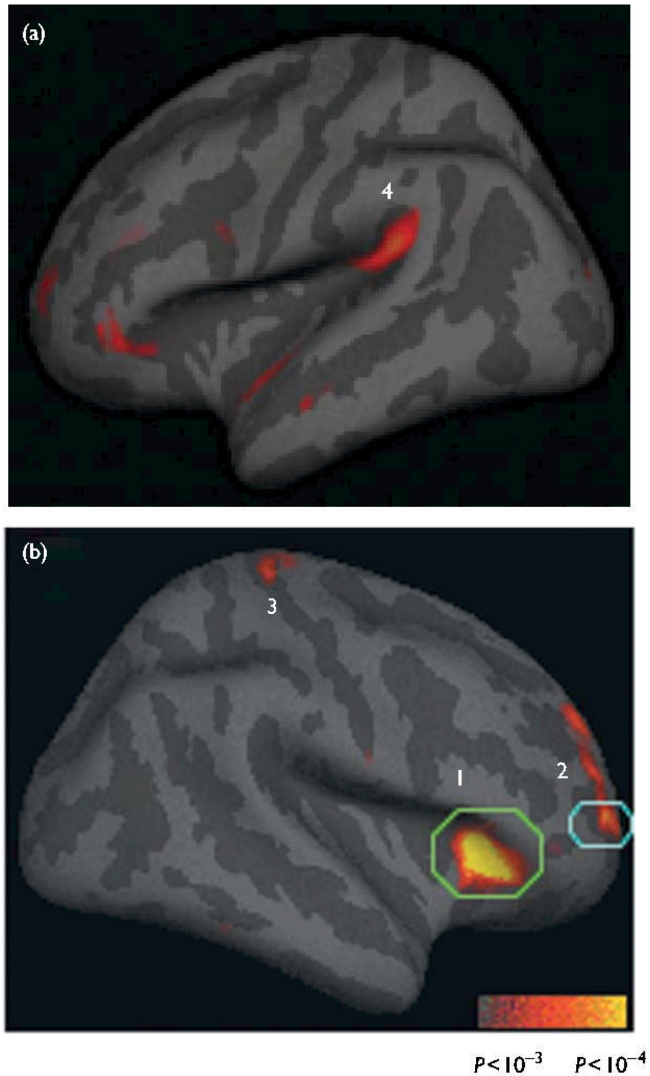
*Neuroreport*. 2005 November 28; 16(17): 1893–1897.

# Meditation experience is associated with increased cortical thickness

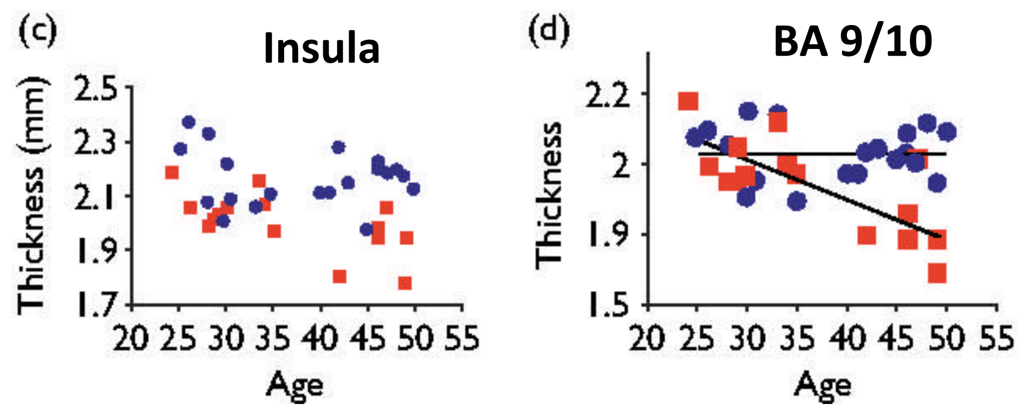
**Sara W. Lazar**[a], **Catherine E. Kerr**[b], **Rachel H. Wasserman**[a,b], **Jeremy R. Gray**[c], **Douglas N. Greve**[d], **Michael T. Treadway**[a], **Metta McGarvey**[e], **Brian T. Quinn**[d], **Jeffery A. Dusek**[f,g], **Herbert Benson**[f,g], **Scott L. Rauch**[a], **Christopher I. Moore**[h,i], and **Bruce Fischl**[d,j]
*aPsychiatric Neuroimaging Research Program, Massachusetts General Hospital*

- Participants

  **Twenty participants** with extensive training in Insight meditation were recruited from local meditation communities. These participants were not monks, but **rather typical Western meditation practitioners** who incorporate their practice into a daily routine involving career, family, friends and outside interests. Two participants were full-time meditation teachers, three were part-time yoga or meditation teachers and the rest meditated an average of once a day for 40 min, while pursuing traditional careers in fields such as **healthcare and law. On average, participants had 9.1 ± 7.1 years of meditation experience and practiced 6.2 ± 4.0 h per week.** Participants were required to have participated in at least 1 week-long Insight meditation retreat, which entails approximately 10 h of meditation per day. Fifteen control participants with no meditation or yoga experience were also recruited.




**Cortical regions thicker in meditators than in controls. (a and b) :** : (1) insula**, (2) Brodmann area (BA) 9/10**, (3) somatosensory cortex, (4) auditory cortex




**Meditation participants: blue circles; control participants: red squares.**

*Neuroreport*. 2005 November 28; 16(17): 1893–1897.

# Meditation experience is associated with increased cortical thickness

**Sara W. Lazar**[a], **Catherine E. Kerr**[b], **Rachel H. Wasserman**[a,b], **Jeremy R. Gray**[c], **Douglas N. Greve**[d], **Michael T. Treadway**[a], **Metta McGarvey**[e], **Brian T. Quinn**[d], **Jeffery A. Dusek**[f,g], **Herbert Benson**[f,g], **Scott L. Rauch**[a], **Christopher I. Moore**[h,i], and **Bruce Fischl**[d,j]
*aPsychiatric Neuroimaging Research Program, Massachusetts General Hospital*

## Conclusion

Our initial results suggest that meditation may be associated with structural changes in areas of the brain that are important for sensory, cognitive and emotional processing. **The data further suggest that meditation may impact age-related declines in cortical structure.**

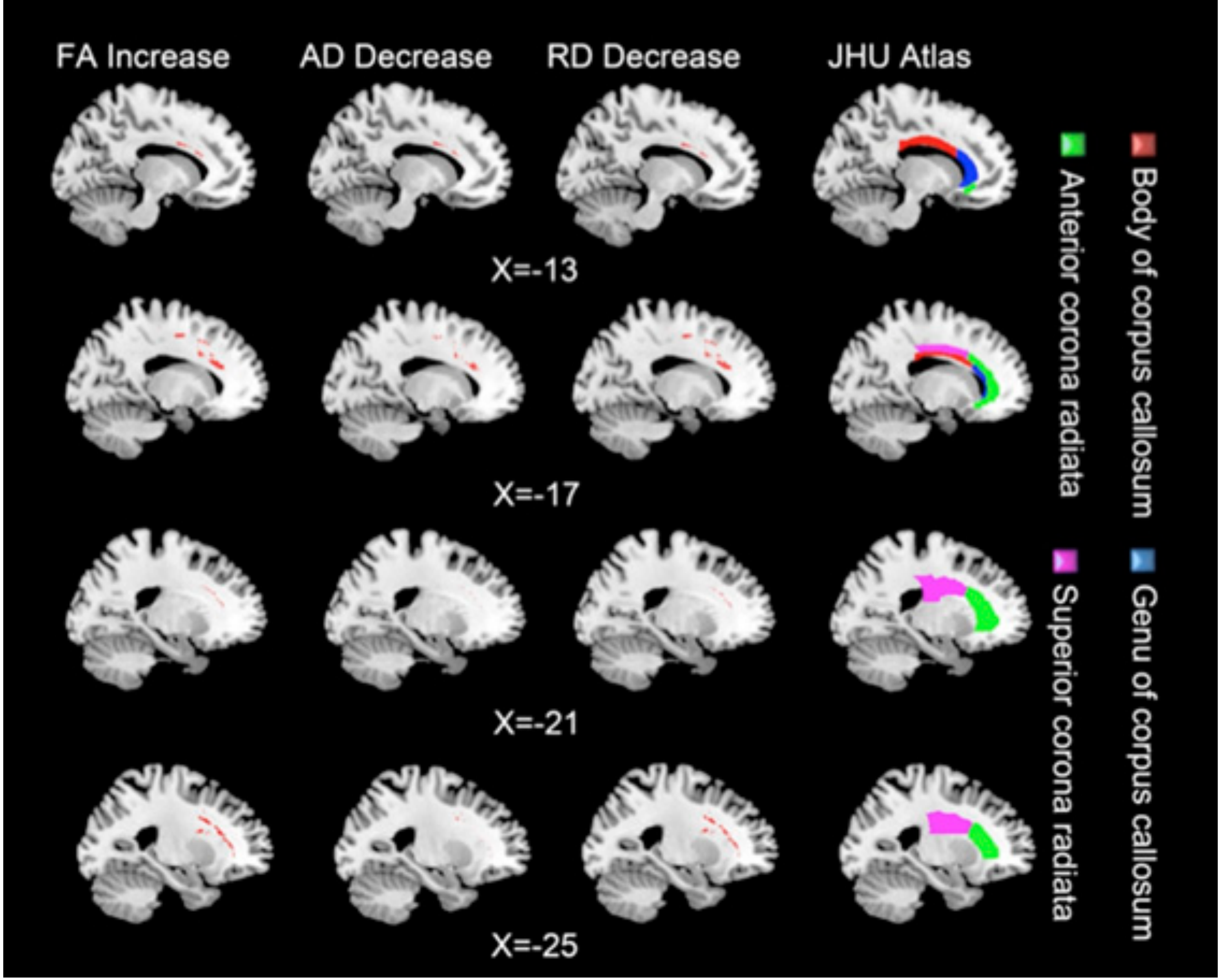
# Mechanisms of white matter changes induced by meditation

Yi-Yuan Tang[a,b,c,1], Qilin Lu[b], Ming Fan[d], Yihong Yang[e], and Michael I. Posner[c,1]

[a]Department of Psychology, Texas Tech Neuroimaging Institute, Texas Tech University, Lubbock, TX 79409; [b]Institute of Neuroinformatics and Laboratory for Body and Mind, Dalian University of Technology, Dalian 116024, China; [c]Department of Psychology, University of Oregon, Eugene, OR 97403; [d]Institute of Basic Medical Sciences, Beijing 100850, China; and [e]Neuroimaging Research Branch, National Institute on Drug Abuse-Intramural Research Program, Baltimore, MD 21224

Our studies used a form of mindfulness meditation, integrative body-mind training (IBMT) in comparison with relaxation training (RT), which served as an active control (Tang et al., 2007). **We used diffusion tensor imaging (DTI) before and after 4 weeks of training with IBMT and RT (Tang et al., 2010).**

We found significantly greater increases in fractional anisotropy (FA) following IBMT than after the RT control. The training effect was in white matter pathways connecting the anterior cingulate cortex (ACC) to other brain areas (Tang et al., 2010). We also found that after 2 weeks the FA change was entirely due to axial diffusivity (AD), which declined significantly more following IBMT than RT (Tang et al., 2012a). AD is thought to relate to changes in axonal density (Kumar et al., 2010, 2012). After 4 weeks FA involved changes in both axial and radial diffusivity (RD). RD is thought to reflect myelination (Song et al., 2002, 2003)**. This evidence suggests that meditation can influence brain areas known to be involved in self control in children and adults** (Posner and Rothbart, 2007).




FA+ = Efficiency +
AD- et RD-= myelinisation +

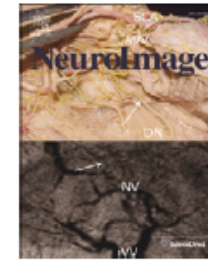
“Our studies have shown that short-term meditation training increases the ability to resolve conflict in a cognitive task, altered neural activity in the ACC, and improved connectivity of the ACC to other brain regions (5, 16, 17, 19, 20). The ACC has been associated with the ability to resolve conflict and to exercise control of cognition and emotion (21). **One study found a correlation between the ability to resolve conflict and FA in the anterior corona radiata, a major pathway connecting the ACC to other brain areas (22**). Thus, the improved self-regulation following IBMT may be mediated by the increase of communication efficiency between the ACC and other brain areas (5, 16).”

NeuroImage 63 (2012) 240–244

Contents lists available at SciVerse ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg




# Growth of language-related brain areas after foreign language learning

Johan Mårtensson [a,*], Johan Eriksson [b], Nils Christian Bodammer [c], Magnus Lindgren [a], Mikael Johansson [a], Lars Nyberg [b], Martin Lövdén [a,c,d]

[a] *Department of Psychology, Lund University, 22100 Lund, Sweden*

The influence of adult foreign-language acquisition on human brain organization is poorly understood. **We studied cortical thickness and hippocampal volumes of conscript interpreters before and after three months of intense language studies.**

Results revealed increases in hippocampus volume and in cortical thickness of the left middle frontal gyrus, inferior frontal gyrus, and superior temporal gyrus for interpreters relative to controls.

These findings con- firm structural changes in brain regions known to serve language functions during foreign-language acquisition.

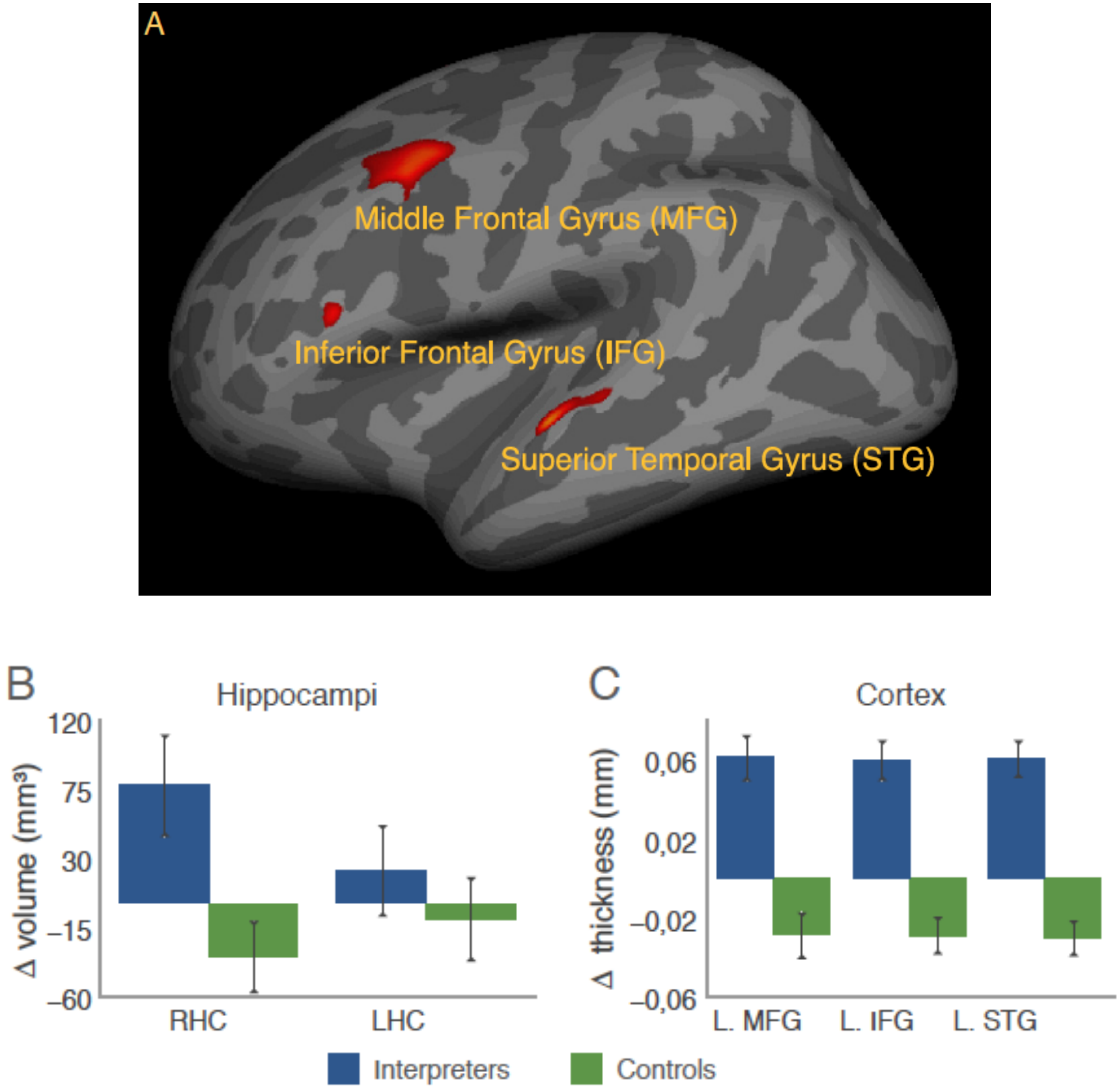



**Fig. 1.** Increases in cortical thickness and hippocampal volume accompany foreign language acquisition. (A) As compared with controls, conscript interpreters showed larger increases ($p<.001$; cluster size > 100) in the left middle frontal gyrus (MFG), inferior frontal gyrus (IFG), and superior temporal gyrus (STG). (B) Change (posttest value–pretest value) of right hippocampal volume (RHC) and left hippocampal volume (LHC) for interpreters and controls. (C) Changes in cortical thickness in the left MFG, IFG and STG.

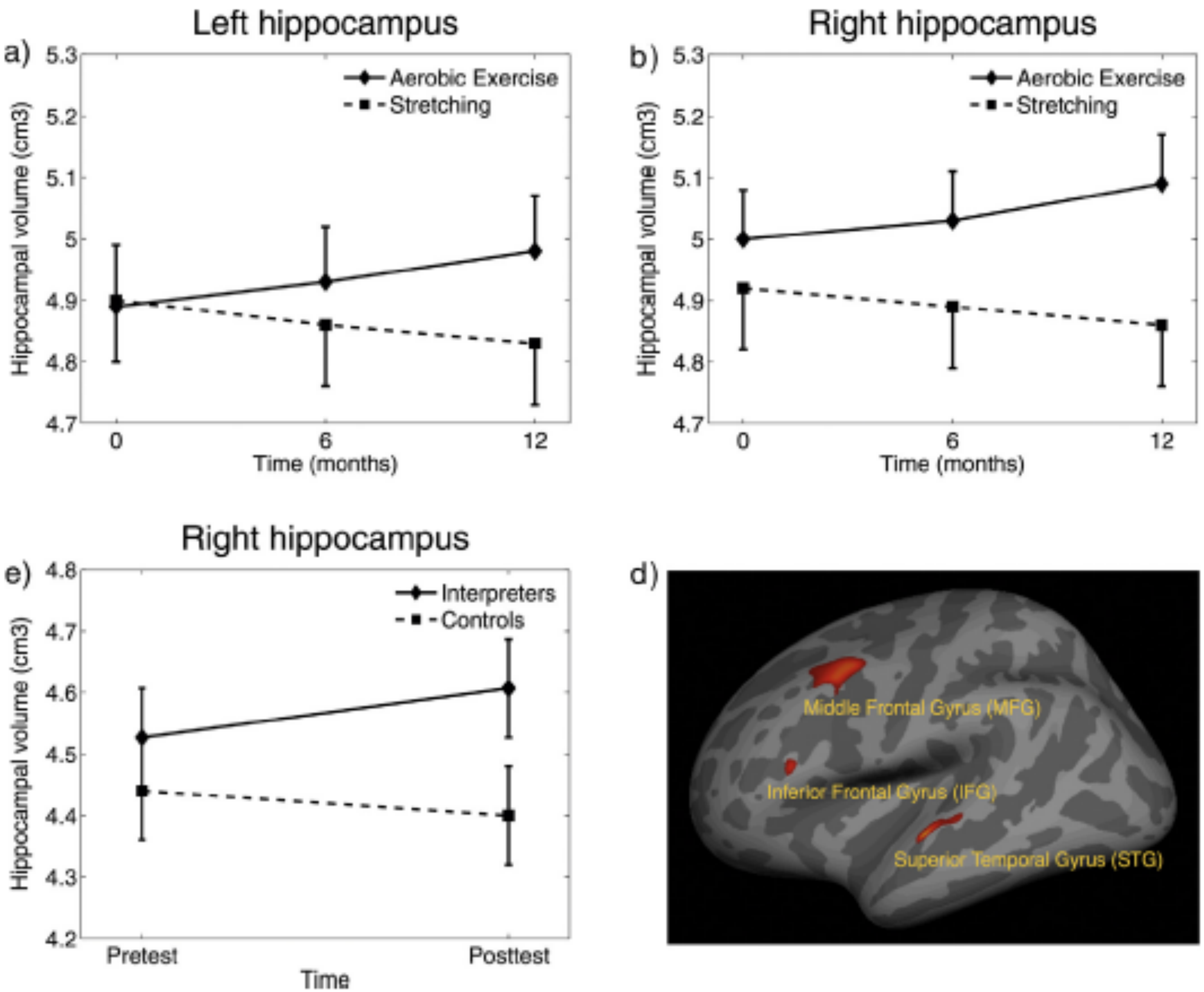
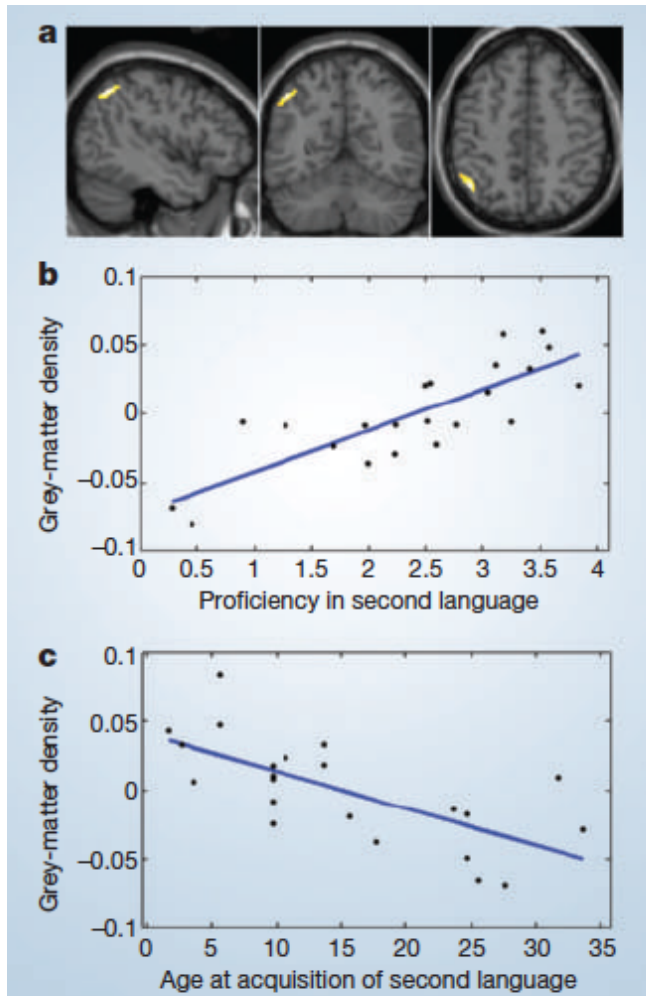



**Fig. 1.** Examples of experience-dependent change in hippocampal volume and cortical thickness in human adulthood. (A, B) Hippocampal volumes (*M*; *SEM*) of older adults in a 12-month aerobic exercise intervention increased, whereas the volumes of a stretching control group declined in the range of normal age-related loss (Erickson et al., 2011). (C) Selective increases in hippocampal volume (*M*; *SEM*) and (D) Cortical thickness for young military conscript interpreters after three months of foreign language acquisition as compared to university student controls.

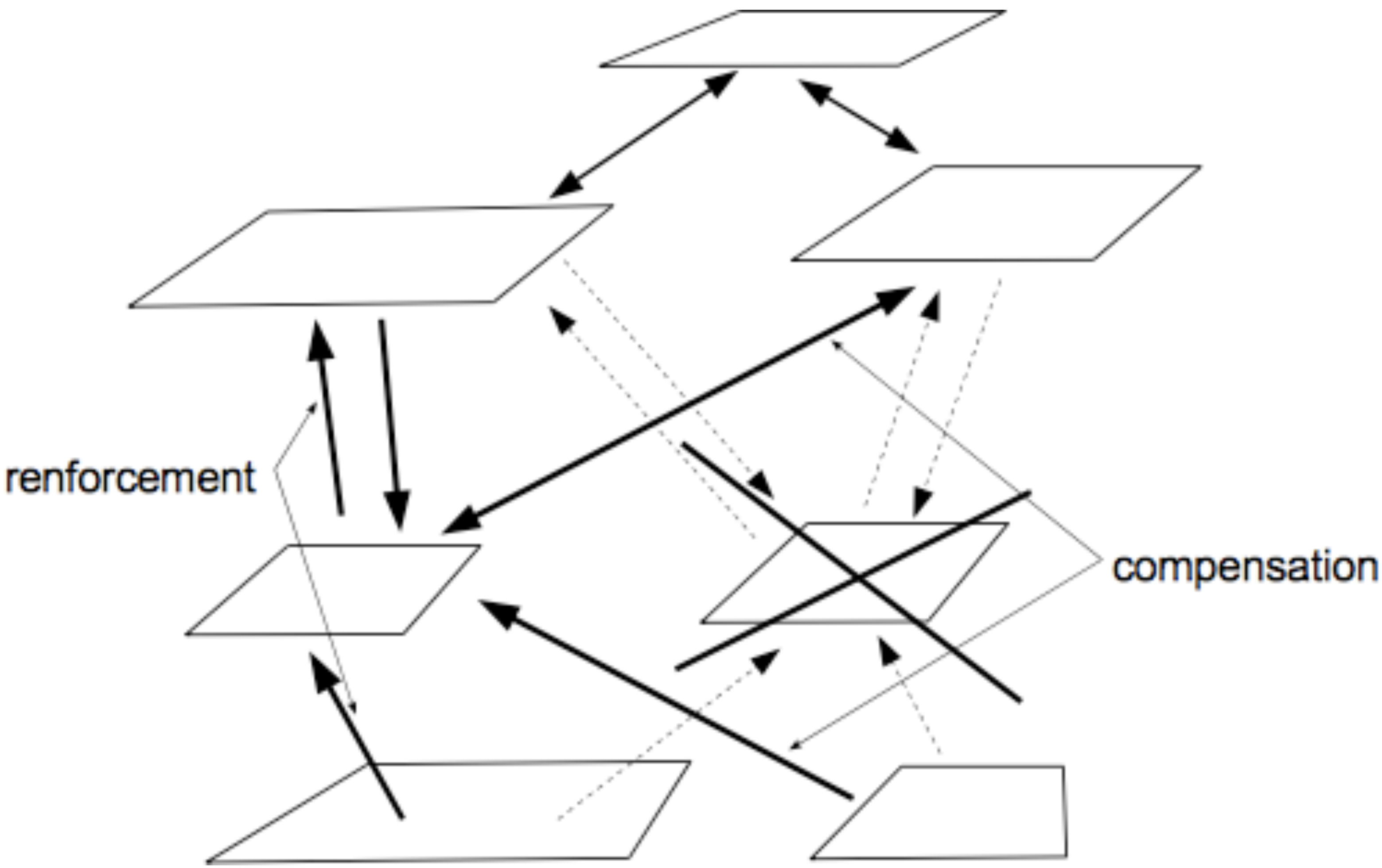
# Structural plasticity in the bilingual brain

Proficiency in a second language and age at acquisition affect grey-matter density.

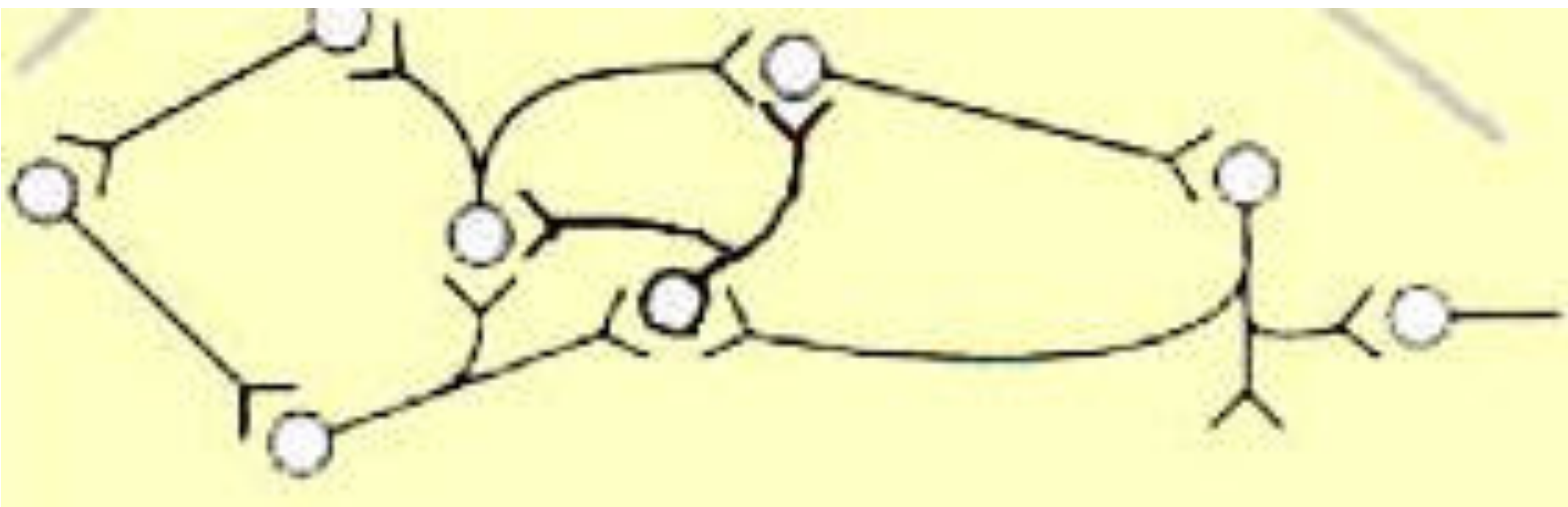


# Les différentes formes de plasticité neurale

# Les principes de la plasticité neurale



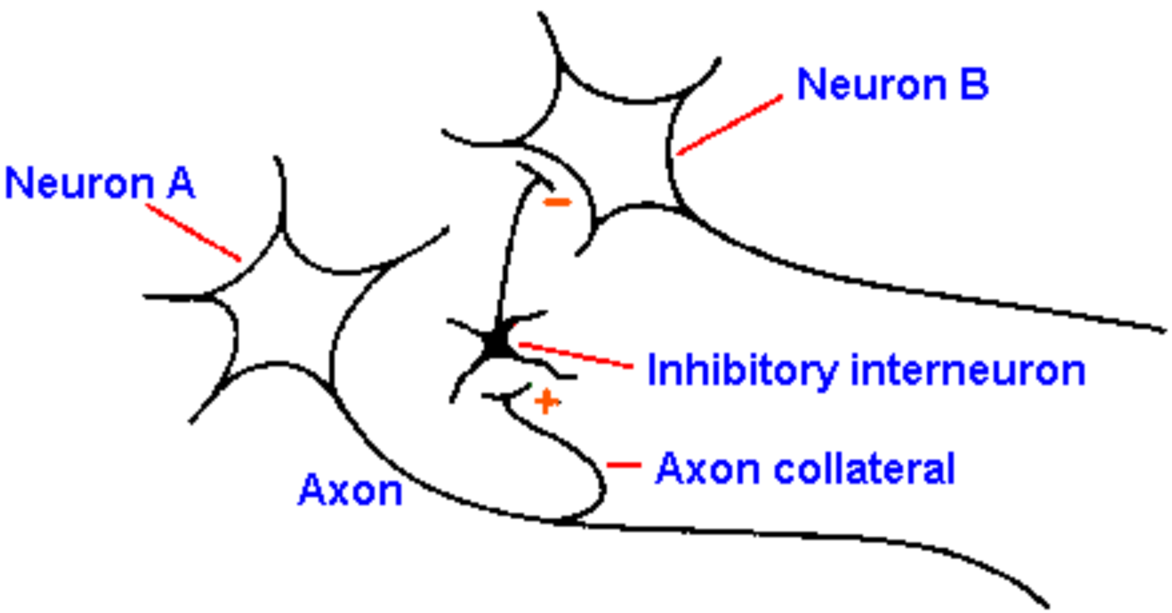
# Changements fonctionnels



# Changements fonctionnels

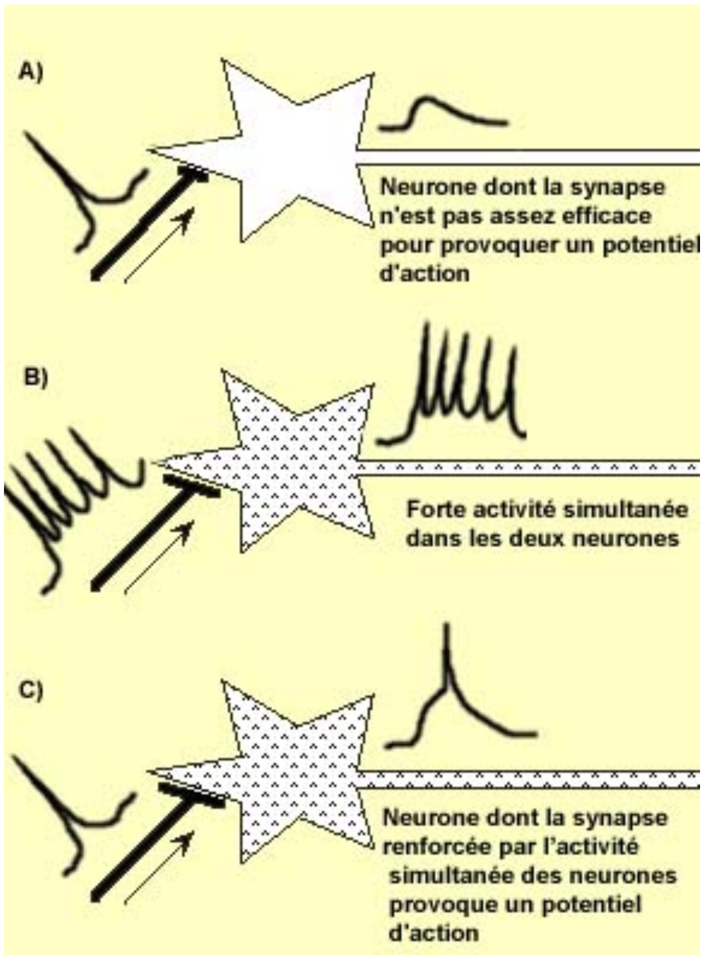
Démasquage de synapses inactives

Changements des effets modulateurs de connexions latérales



# Changements fonctionnels

## renforcement / affaiblissement synaptique

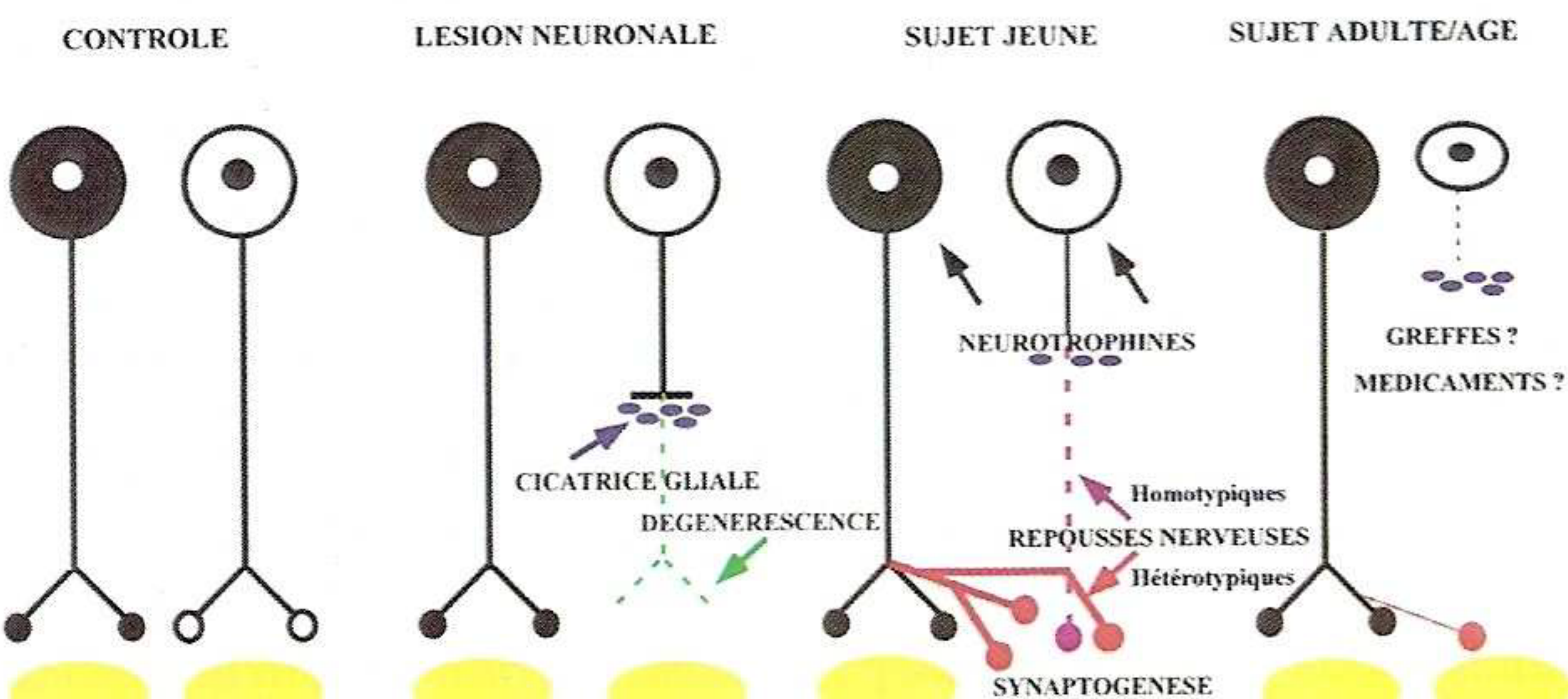



**la loi de Hebb (1949)**

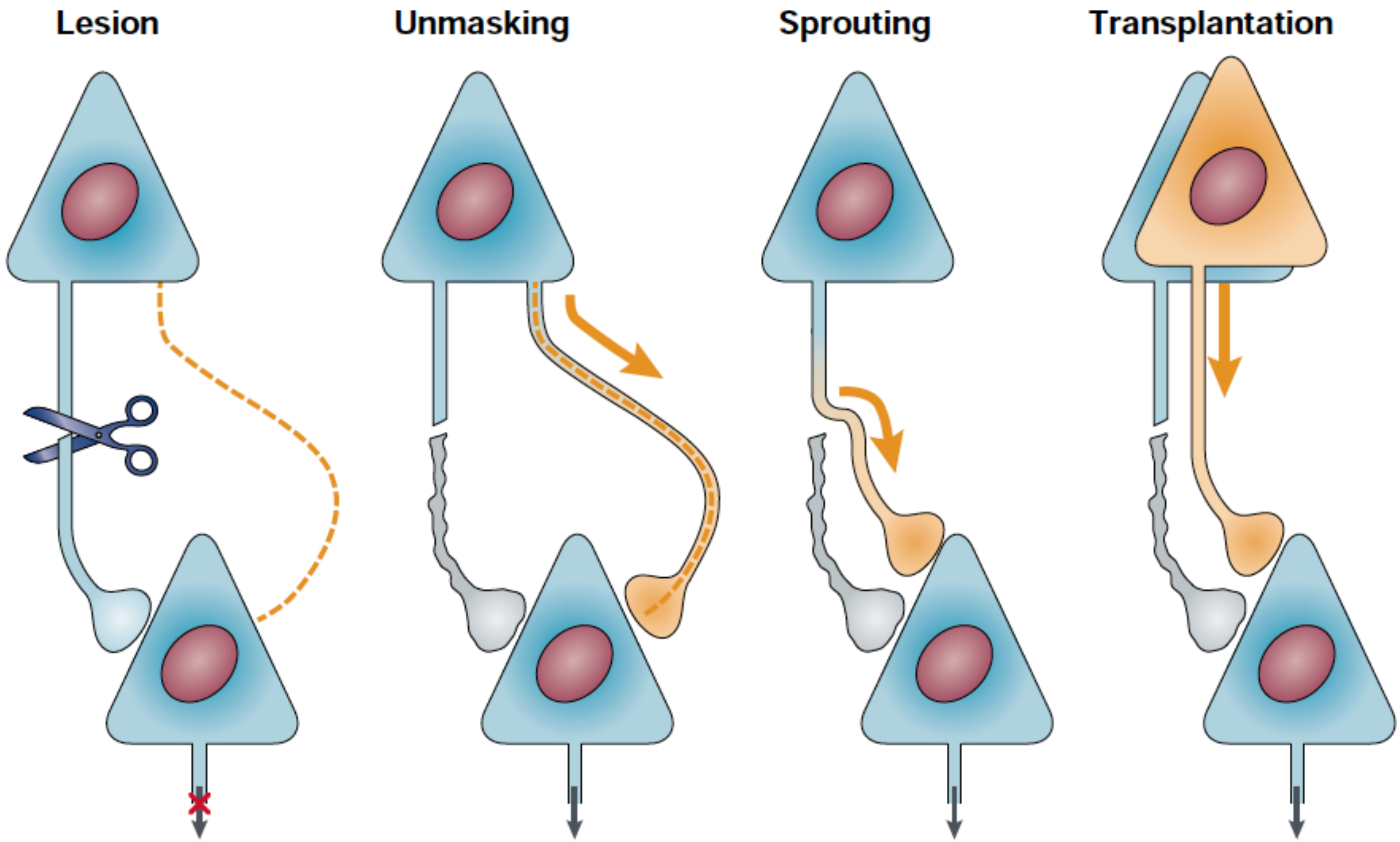
1. **Renforcement synaptique** : si deux neurones de chaque côté d'une connexion sont activés simultanément (de manière synchrone), alors la force de cette connexion est sélectivement renforcée
2. **Affaiblissement synaptique** : si deux neurones de chaque côté d'une connexion sont activés de manière asynchrone, alors cette connexion est sélectivement affaiblie ou éliminée

# Changements structurels

La synaptogénèse

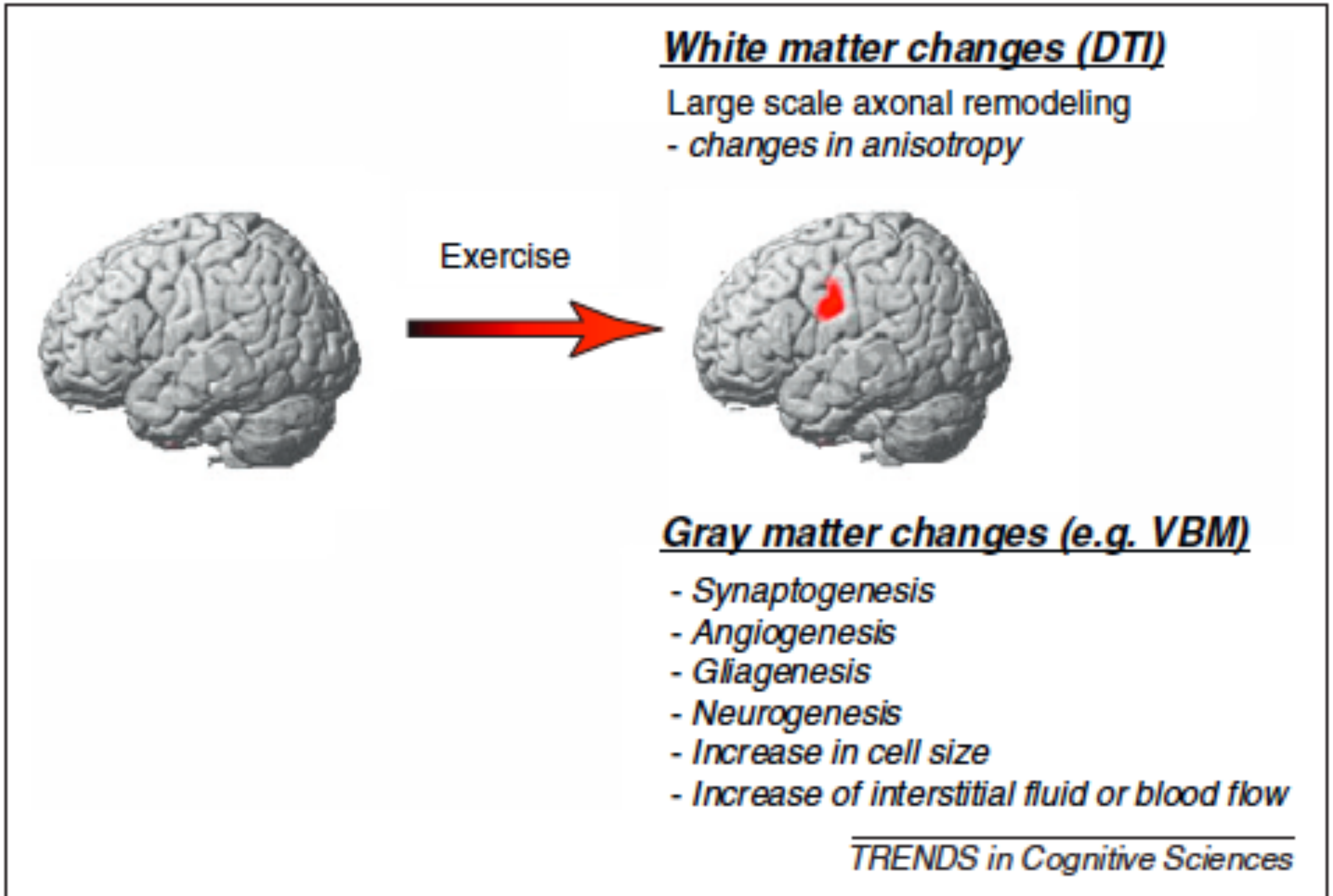


# Les différentes formes de plasticité neurale

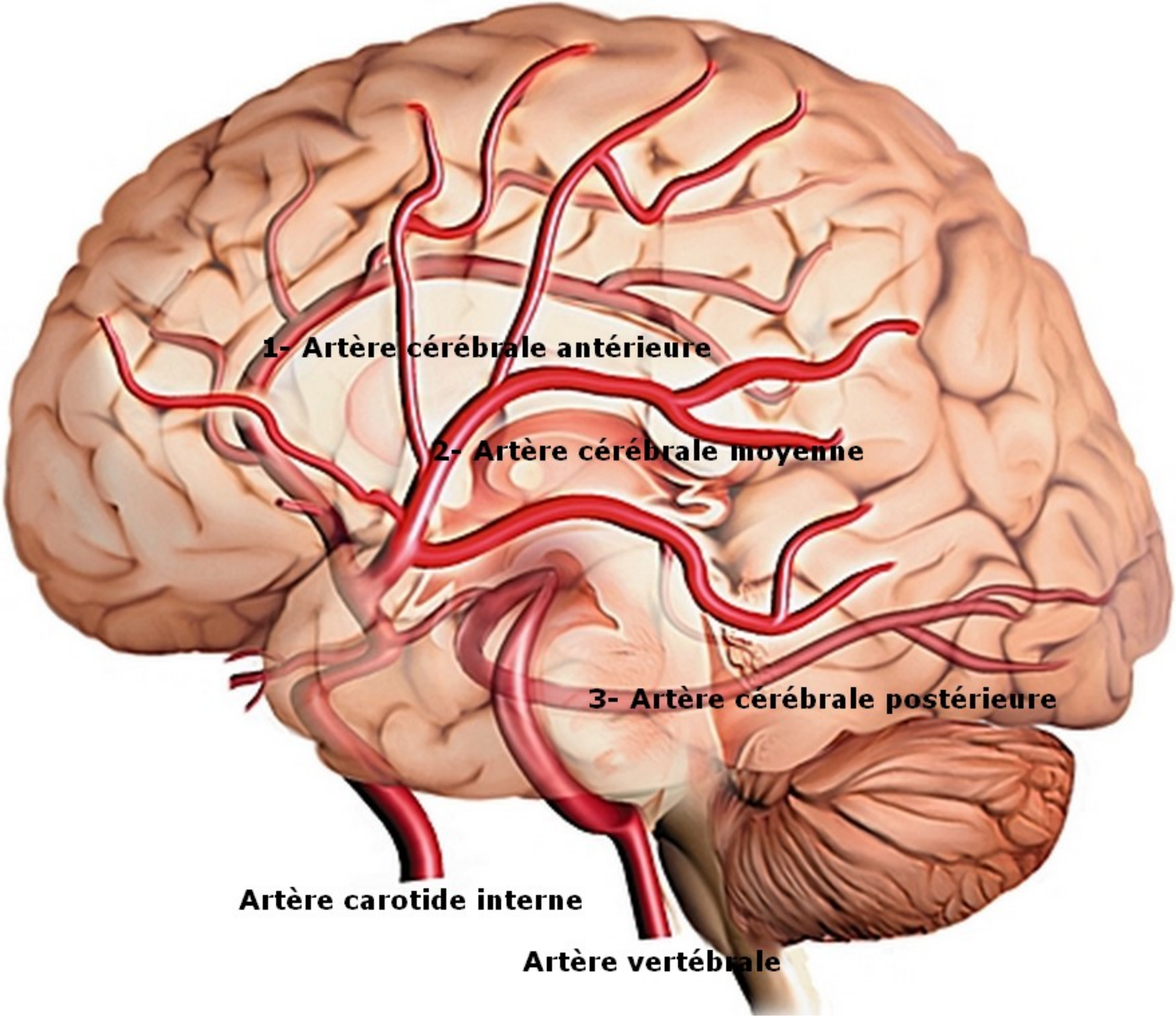


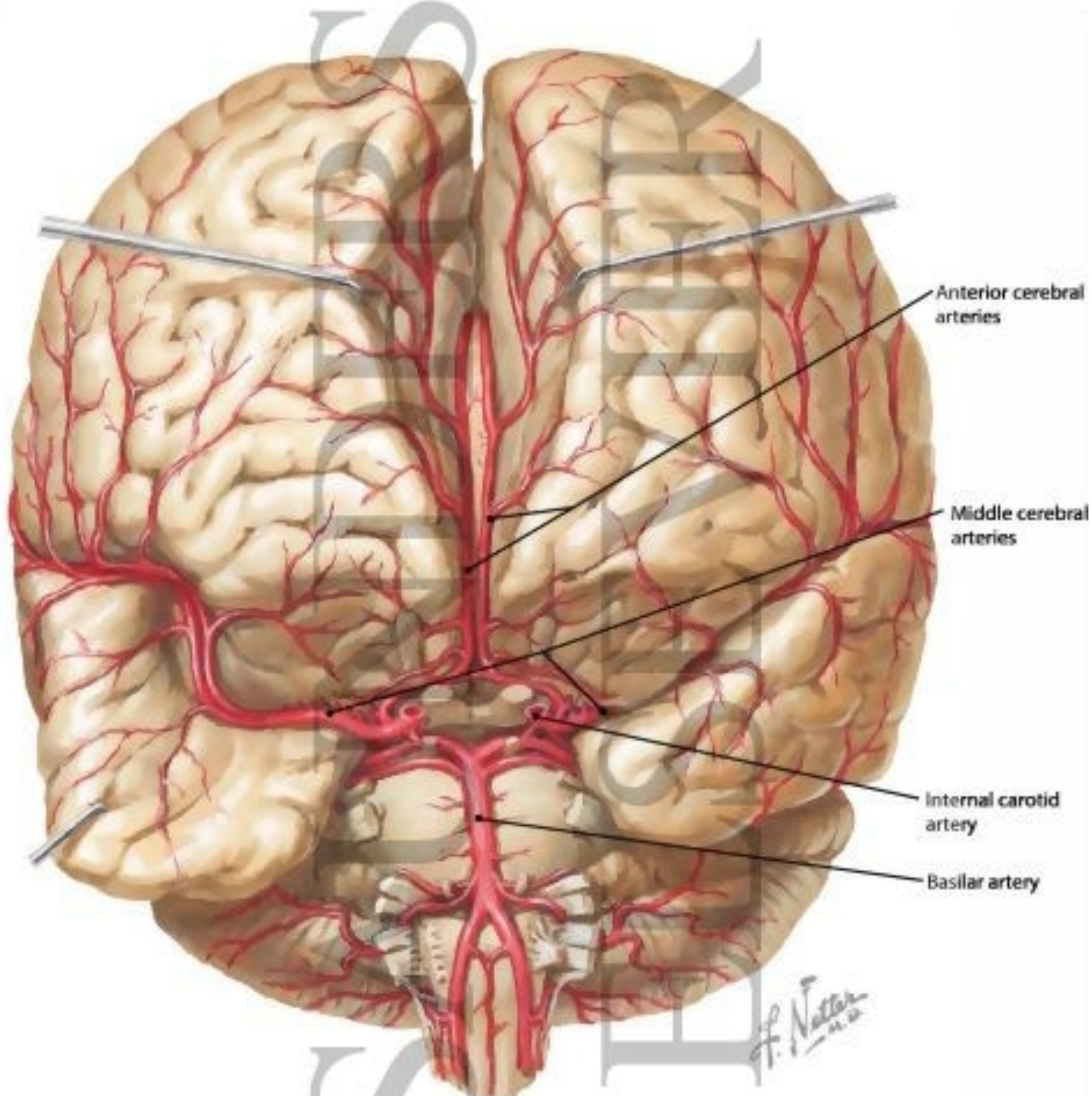

Taub et al. ***Nature Neuroscience reviews***, 2002, 3, 228-236.

# Changements structurels

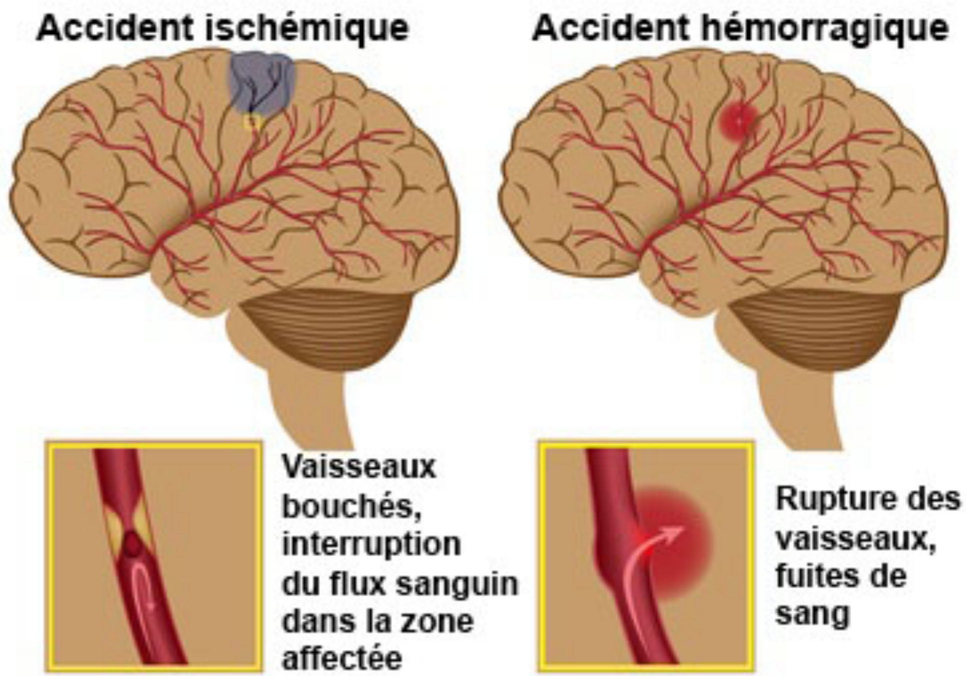


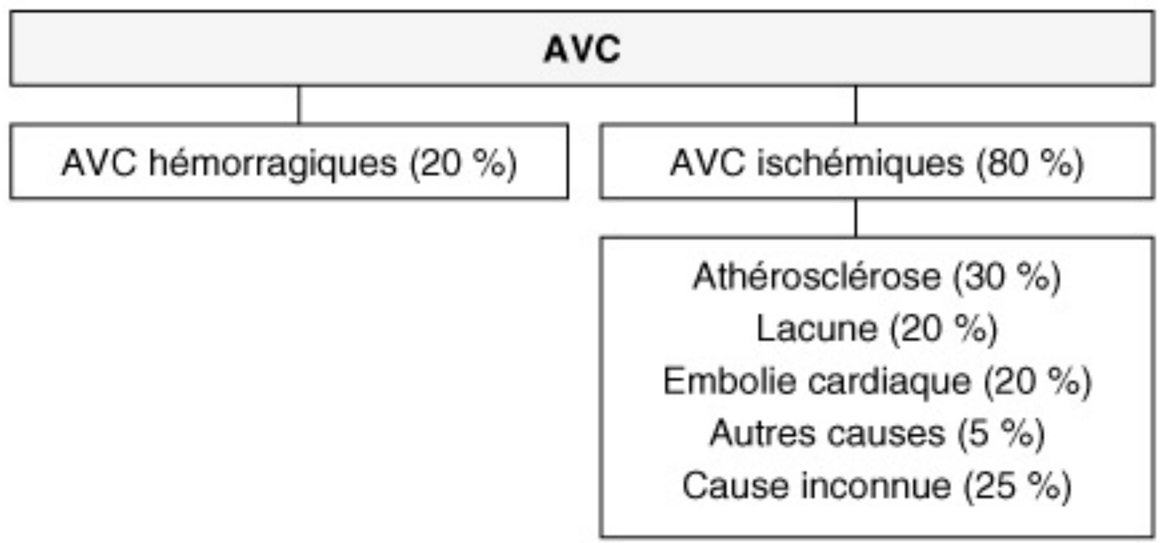
# L’accident vasculaire cérébral (AVC)

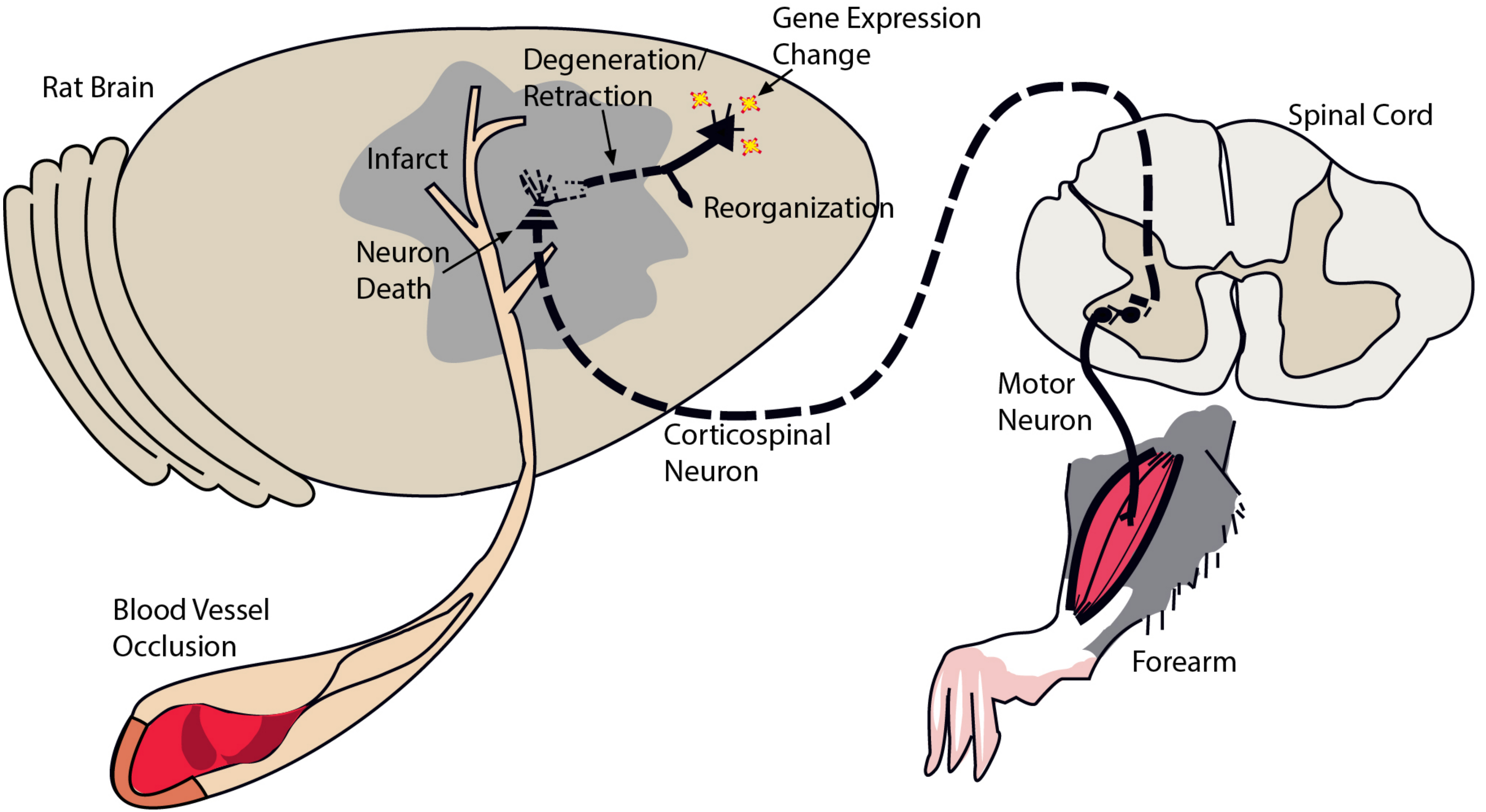

1- Artère cérébrale antérieure
2- Artère cérébrale moyenne
3- Artère cérébrale postérieure
Artère carotide interne
Artère vertébrale


Anterior cerebral
arteries
Middle cerebral
arteries
Internal carotid
artery
Basilar artery
F. Netter

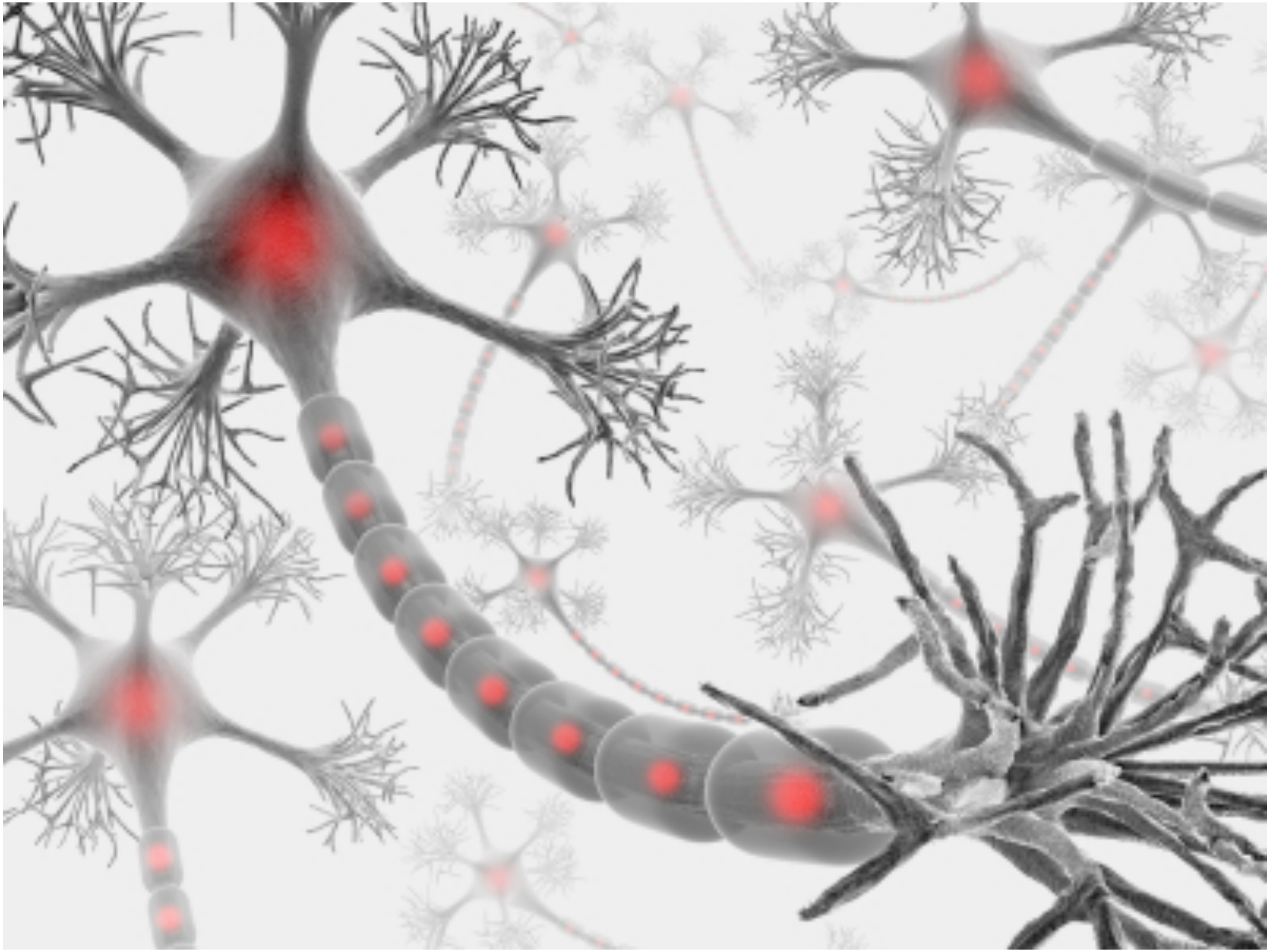
# AVC: accident vasculaire cérébral




AVC
AVC hémorragiques (20 %)
AVC ischémiques (80 %)
Athérosclérose (30 %)
Lacune (20 %)
Embolie cardiaque (20 %)
Autres causes (5 %)
Cause inconnue (25 %)

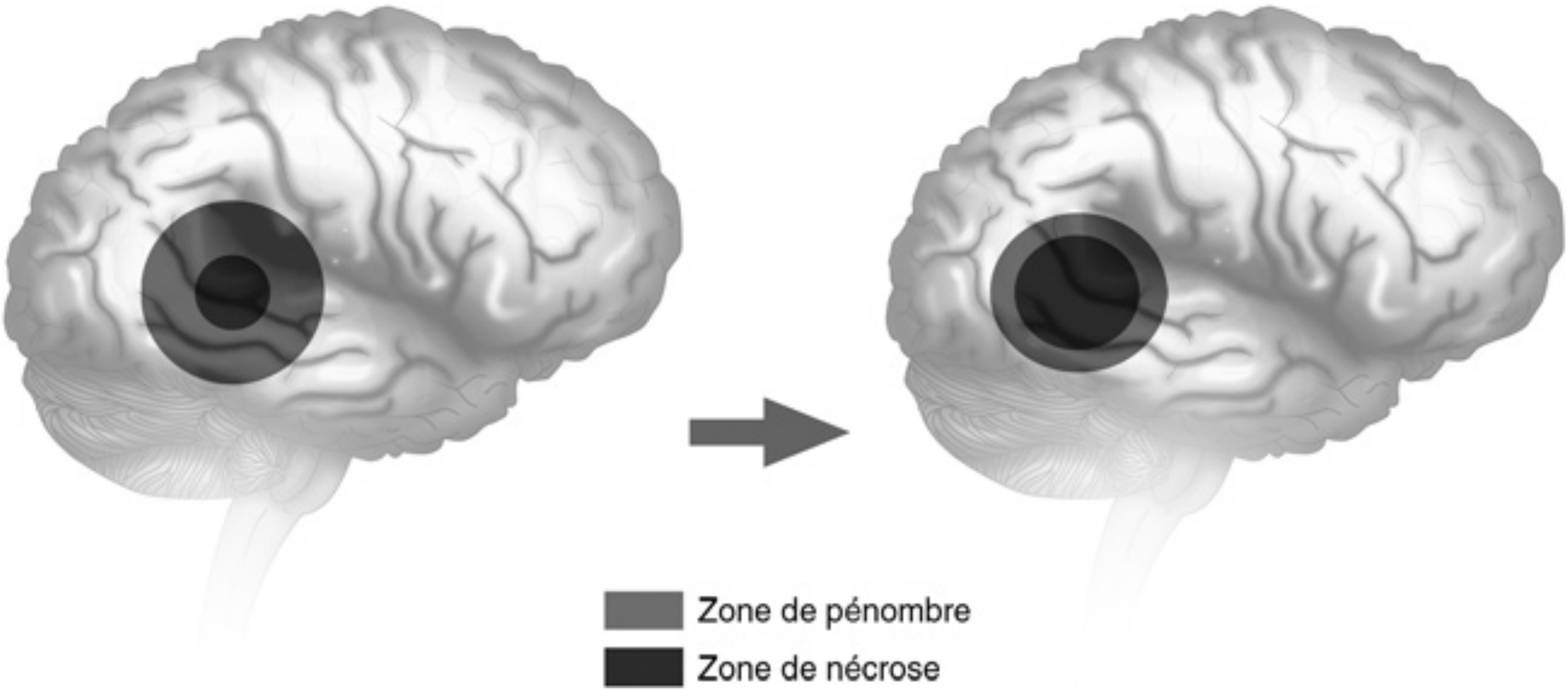



Gene expression changes of interconnected spared cortical neurons 7 days after ischemic infarct of the primary motor cortex in the rat. **Mol Cell Biochem. 2012;369(1-2):267-86**



"Jusqu'à cette dernière décennie, le dogme, selon lequel toute lésion cérébrale chez l'homme adulte était irréversible et ne pouvait pas être réparée, a prévalu aussi bien dans les facultés de médecine que dans la chambre du patient. Pourtant, cette vue statique de l'organisation cérébrale est en contradiction avec de nombreuses observations : après un accident vasculaire cérébral (AVC), les patients peuvent s'améliorer spontanément dans les trois premiers mois puis de manière plus lente dans l'année qui suit."

Deroide et al. (2010). Plasticité cérébrale : de la théorie à la pratique dans le traitement de l'accident vasculaire cérébral. ***La revue de médecine interne***


Zone de pénombre
Zone de nécrose

# **Effet à distance** - Diaschisis

Par exemple, baisse de l'excitabilité dans les zones normalement activées par la zone lésée.

- cortex cérébral controlatéral (via le corps calleux) ou le cervelet controlatéral (via les pédoncules cérébelleux).

The Monakow concept of diaschisis: origins and perspectives. Finger et al. ***Arch Neurol***, 2004 61:283-8.

“In patients who survive stroke, there is invariably some degree of functional recovery, ranging from minimal to complete (Twitchell, 1951).”

"Future studies should focus on understanding the mechanisms that define the **critical time window of functional recovery after stroke**. Better understanding of the different time frames for mechanisms that contribute to functional recovery such as plasticity, a gradual reversal of diaschisis, and behavioral mechanisms that allow compensation strategies may have a significant impact on rehabilitation management of patients."

modern neuroimaging has shown that many complex functions rely on the coordinated activity of distant regions connected by long-range fibers coursing through the cerebral white matter. Damage either to cortical areas or to underlying connections has far-reaching consequences on distant regions (Baron et al. 1981) through either **diaschisis** (i.e., dysfunction of a distant region connected to the damaged area) (Monakow 1897, 1914; Carrera and Tononi 2014) or **disconnection** (i.e., dysfunction of 2 intact areas connected by a damaged tract) (Wernicke 1874; Geschwind 1965a,b; Catani and ffytche 2005).


- Geschwind N, Kaplan E. 1962. A human cerebral deconnection syndrome. A preliminary report. Neurology. 12:675–685.

# La récupération /compensation après un AVC

# What Do Motor “Recovery” and “Compensation” Mean in Patients Following Stroke?

**Mindy F. Levin, PhD, PT** mindy.levin@mcgill.ca
**Jeffrey A. Kleim, PhD**
**Steven L. Wolf, PhD, PT, FAPTA, FAHA**

## Abstract

There is a lack of consistency among researchers and clinicians in the use of terminology that describes changes in motor ability following neurological injury. Specifically, the terms and definitions of *motor compensation* and *motor recovery* have been used in different ways, which is a potential barrier to interdisciplinary communication. This Point of View describes the problem and offers a solution in the form of definitions of compensation and recovery at the neuronal, motor performance, and functional levels within the framework of the International Classification of Functioning model.

# La récupération spontanée

“there is a process of spontaneous recovery that is maximally expressed in the first 4 weeks post-stroke and then tapers off over 6 months. Several mechanisms are likely for this spontaneous recovery, including <u>restitution of the ischemic penumbra, resolution of diaschisis, and brain reorganization.”</u>

# La récupération spontanée

## La levée du diaschisis

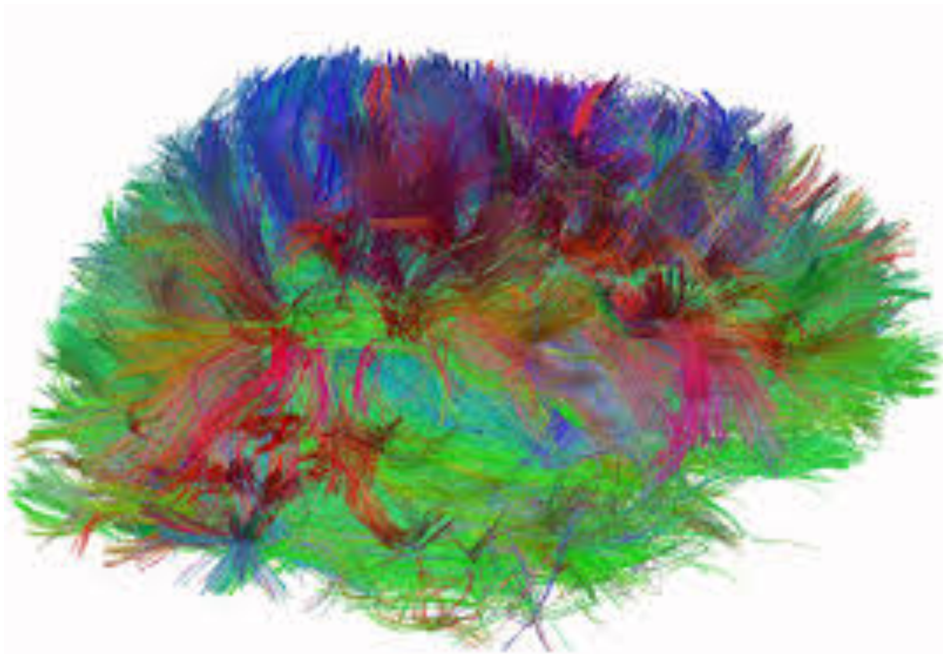
- Une partie de la récupération, au moins initiale, correspond à une reprise fonctionnelle des connexions inhibées mais restées anatomiquement intactes (“levée du diaschisis”)
  - Le diaschisis peut être considéré comme une déafférentation ; la levée du diaschisis correspond à une réafférentation des neurones cibles

- Les modalités de la réafférentation sont multiples et se mettent en jeu très rapidement après la lésion
  - au niveau synaptique, lorsqu’un neurones est privé d’une partie de ses afférences on observe un changement fonctionnel qui conduit à augmenter sa sensibilités à d’autres afférences conservées

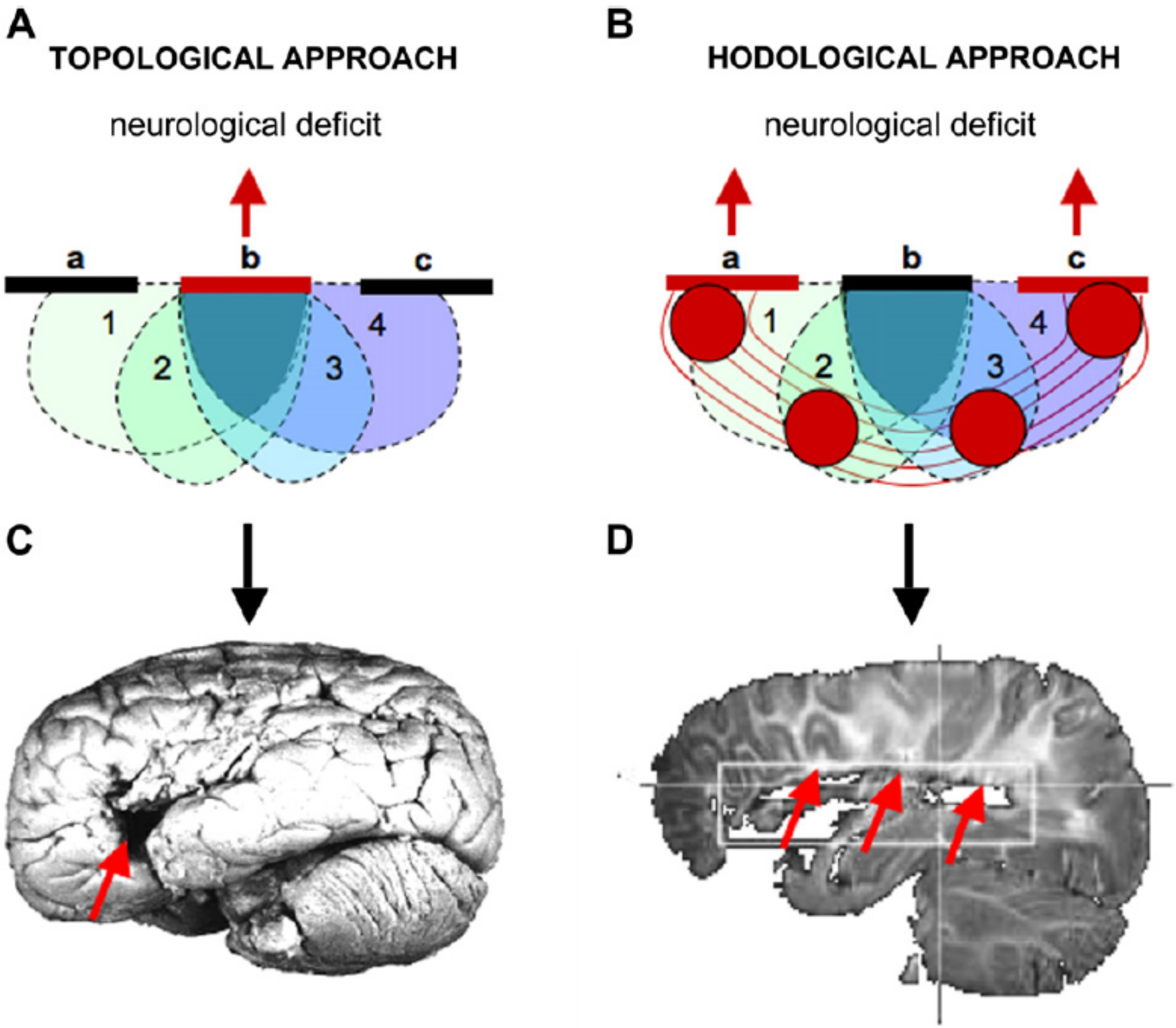
# La récupération spontanée

- Recherche animale
  - Nombreux processus biochimiques et cellulaires déclenchés par l'AVC… prennent place rapidement (minutes / heures) – pas seulement dans le voisinage de la lésion mais aussi dans des régions à distance et dans l'hémisphère controlatéral
    - Ces processus conduisent à la formation de nouvelles synapses et au bourgeonnement d'axones pour se reconnecter au tissus préservé

# Approche "en réseau" de la récupération après un AVC



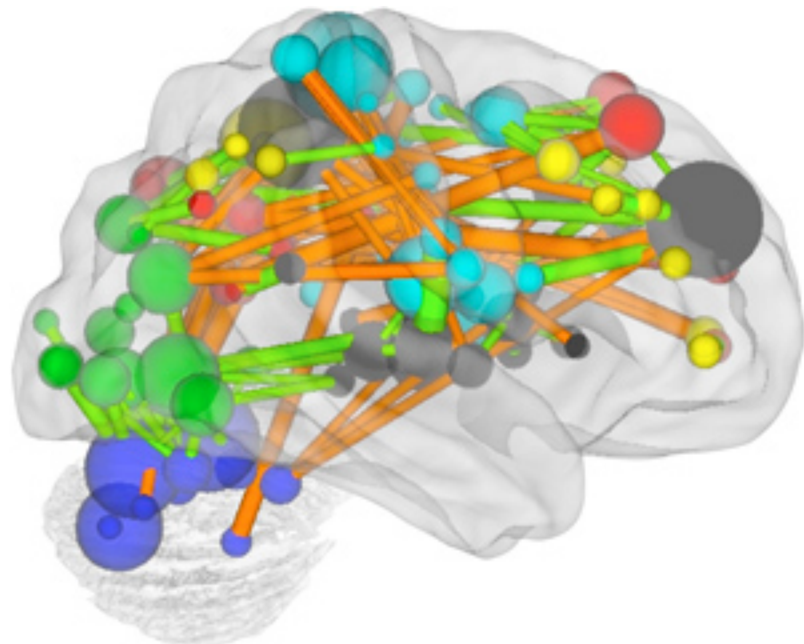
# Approche “en réseau” de la récupération après un AVC



# Approche “en réseau” de la récupération après un AVC

En neuroimagerie, **la connectivité fonctionnelle** entre les régions cérébrales peut être mesurée au cours d'une tâche particulière ou pendant le repos (en l'absence d'une tâche structurée). Pendant le repos, les participants doivent rester allongés et immobiles dans le scanner sans penser à quelque chose de particulier (tout en restant éveillés).

# Approche “en réseau” de la récupération après un AVC



# Approche “en réseau” de la récupération après un AVC

## Connectivity-based approaches in stroke and recovery of function

*Christian Grefkes, Gereon R Fink*

*Lancet Neurol* 2014; 13: 206–16

Department of Neurology, University Hospital Cologne, Köln, Germany (Prof C Grefkes PhD, Prof G R Fink PhD); Neuromodulation and Neurorehabilitation, Max Planck Institute for Neurological Research, Köln, Germany (C Grefkes); and Cognitive Neuroscience,

After focal damage, cerebral networks reorganise their structural and functional anatomy to compensate for both the lesion itself and remote effects. Novel developments in the analysis of functional neuroimaging data enable us to assess in vivo the specific contributions of individual brain areas to recovery of function and the effect of treatment on cortical reorganisation. Connectivity analyses can be used to investigate the effect of stroke on cerebral networks, and help us to understand why some patients make a better recovery than others. This systems-level view also provides insights into how neuromodulatory interventions might target pathological network configurations associated with incomplete recovery. In the future, such analyses of connectivity could help to optimise treatment regimens based on the individual network pathology underlying a particular neurological deficit, thereby opening the way for stratification of patients based on the possible response to an intervention.

# Approche "en réseau" de la récupération après un AVC

"..recent developments in computational neuroscience enable us to **move beyond the mere localisation of brain activity.** In particular, they allow us **to consider the dynamics within an ensemble or an entire network of areas sustaining a particular cognitive process or behaviour.**"

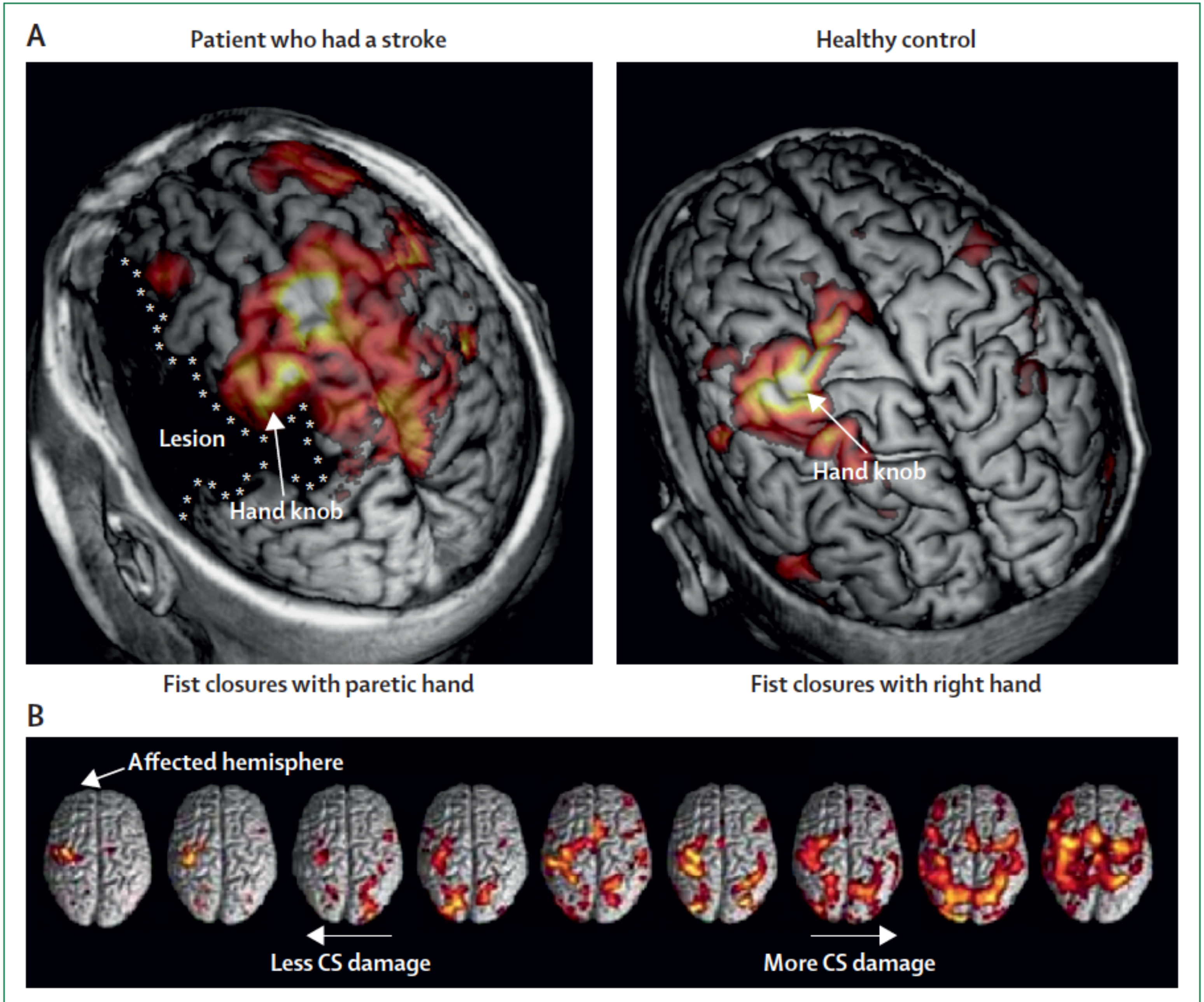
# Approche "en réseau" de la récupération après un AVC

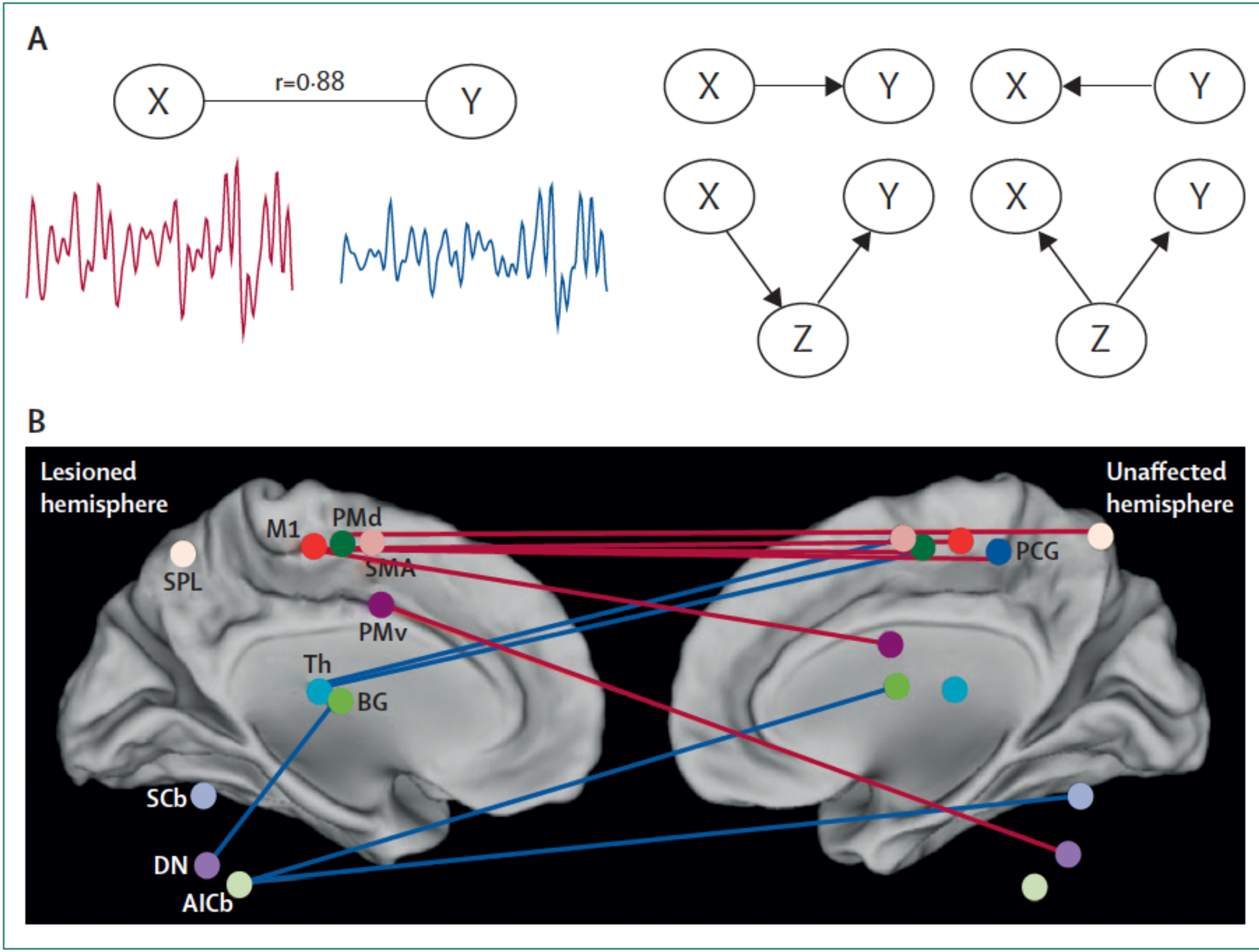
"..the exact functional role that brain regions such as the contralesional M1 have during recovery seems to be complex. Most likely, time since stroke, severity of deficit at baseline, lesion size, location, and other biological factors (eg, age of the patient) all contribute to interindividual differences."

Functional connectivity analyses based on resting-state fMRI have identified stroke-induced disturbances of the functional network architecture in both animals and patients (figure 2B). For example, **resting-state measurements in rats recovering from induced stroke showed that impaired sensorimotor performance was associated with a loss of interhemispheric connectivity between sensorimotor regions, <u>whereas recovery of function weeks after stroke was paralleled by normalisation of interhemispheric connectivity.</u>**

**Similar effects have been reported in fMRI studies of stroke in human beings.**

**white arrows; asterisks delineate lesion region**




A
X
r=0·88
Y
X
Y
X
Y
X
Y
Z
X
Y
Z
B
Lesioned hemisphere
Unaffected hemisphere
M1
PMd
SMA
SPL
PMv
Th
BG
SCb
DN
AICb
PCG

"Consistently, transient down regulation of contralesional M1 excitability has been used to improve motor function of the paretic hand, suggesting an inhibitory role of this area for functional recovery."

# Thérapies et neuroplasticité

# Les principes de la plasticité neurale

*Réorganisation des cartes motrices corticales*

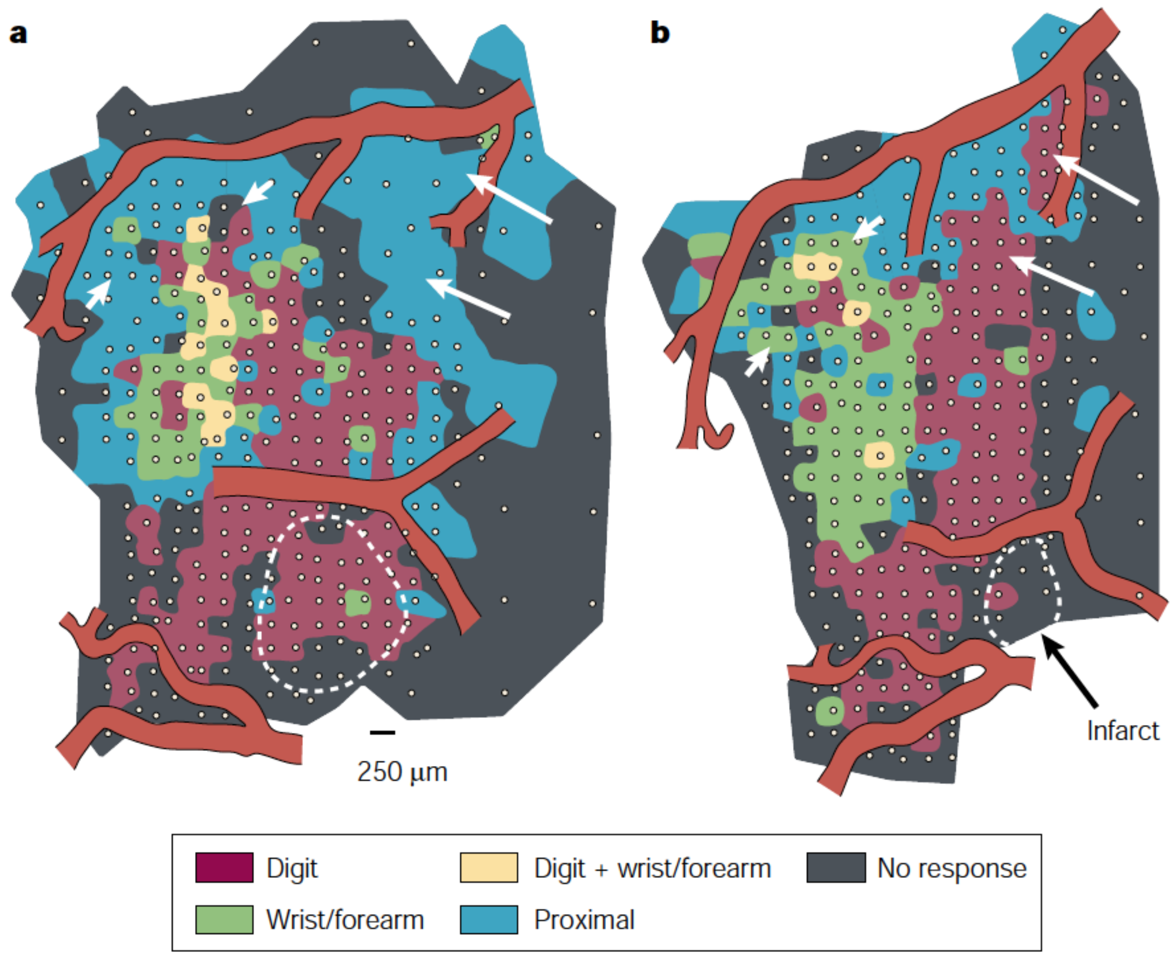
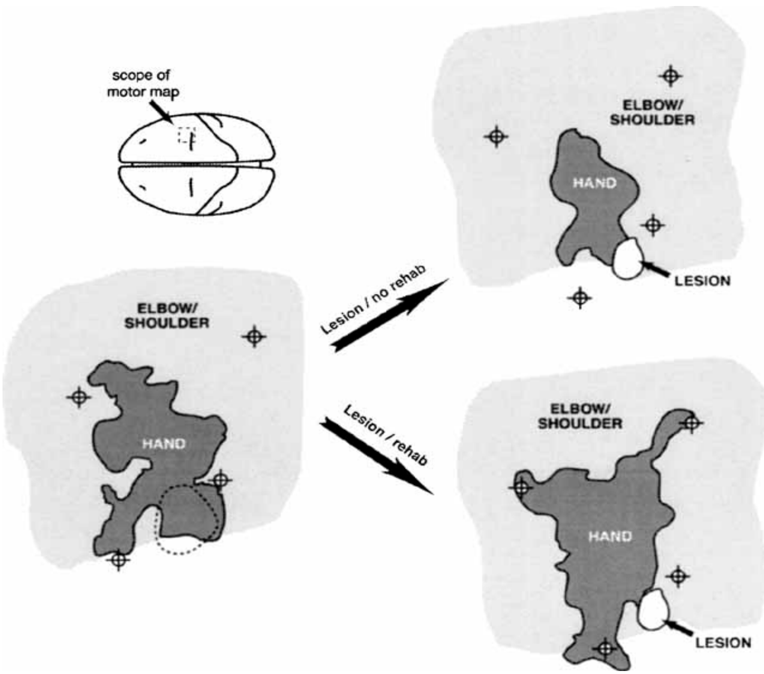



Figure 4 | **Reorganization in the motor cortex of a monkey after rehabilitative therapy.** **a** | Before infarct. **b** | After infarct and rehabilitative therapy. Note the large increase in the cortical representation of the wrist/forearm after therapy. Adapted with permission from REF. 51 © 1996 American Association for the Advancement of Science.

# Les principes de la plasticité neurale

*Réorganisation des cartes motrices corticales*




Plasticité **adaptative** de la carte motrice de la main après lésion corticale – Effet de la réhabilitation


- Nudo RJ, Wise BM, SiFuentes F, Milliken GW. Neural substrates for the effects of rehabilitative training on motor recovery after ischemic infarct. *Science* 1996;**272**: 1791-1794.
- Adapté: Nudo et al. Role of adaptive plasticity in recovery of function after damage to motor cortex. Muscle Nerve. 2001 Aug;24(8):1000-19.

# Recovery of Swallowing After Dysphagic Stroke Relates to Functional Reorganization in the Intact Motor Cortex

SHAHEEN HAMDY,*,‡ QASIM AZIZ,* JOHN C. ROTHWELL,‡ MAXINE POWER,§ KRISHNA D. SINGH,‖ DAVID A. NICHOLSON,¶ RAYMOND C. TALLIS,# and DAVID G. THOMPSON*
Departments of *Gastroenterology, §Speech and Language Therapy, ¶Radiology, and #Geriatric Medicine, Hope Hospital, University of Manchester, Salford; ‖Department of Psychology, Royal Holloway College, University of London, Egham, Surrey; and ‡Medical Research Council Human Movement and Balance Unit, Institute of Neurology, London, England

La **commande volontaire de déglutition** dépend d'une **zone restreinte du cortex moteur qui est normalement bilatérale avec dominance du cortex droit.**

Après un AVC dans cette région, la récupération est liée à la prise en charge de la fonction par l'aire correspondante de l'HG. Par TMS, on peut observer une extension considérable de la carte motrice à cet endroit

Neuron, Vol. 34, 831–840, May 30, 2002, 

# Driving Plasticity in Human Adult Motor Cortex Is Associated with Improved Motor Function after Brain Injury


## Summary

Changes in somatosensory input can remodel human cortical motor organization, yet the input characteristics that promote reorganization and their functional significance have not been explored. Here we show with transcranial magnetic stimulation that sensory-driven reorganization of human motor cortex is highly dependent upon the frequency, intensity, and duration of stimulus applied. Those patterns of input associated with enhanced excitability (5 Hz, 75% maximal tolerated intensity for 10 min) induce stronger cortical activation to fMRI. When applied to acutely dysphagic stroke patients, swallowing corticobulbar excitability is increased mainly in the undamaged hemisphere, being strongly correlated with an improvement in swallowing function. Thus, input to the human adult brain can be programmed to promote beneficial changes in neuroplasticity and function after cerebral injury.

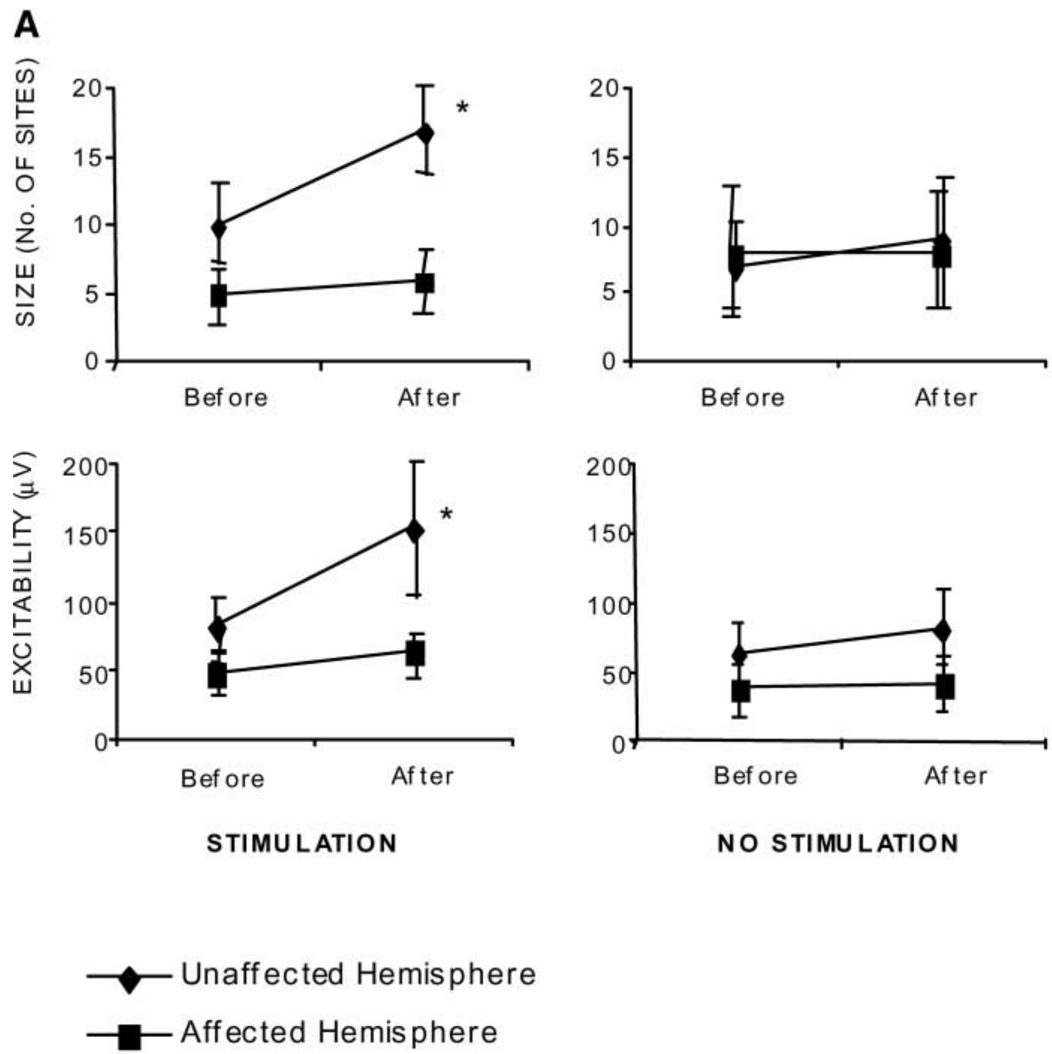



**Figure 4. Changes in the Organization of the Cortical Projection to Swallowing Muscles and Swallowing Function after Pharyngeal or No Stimulation in 16 Acutely Dysphagic Stroke Patients**

**A marked increase in pharyngeal corticobulbar excitability and topographic representation occurs in the undamaged hemisphere (closed diamond) compared to the affected hemisphere (closed square) in patients receiving pharyngeal stimulation (A). This is mirrored by the changes to swallowing (with stimulation [black] versus without stimulation [gray] with a functionally beneficial reduction in PTT, SRT, and aspiration [B]). PTT = pharyngeal transit time, SRT = swallowing response time, ASP = aspiration. (*$p < 0.05$, **$p < 0.01$).**

*Future Neurol*. 2010 September ; 5(5): 657–665.

# From singing to speaking: facilitating recovery from nonfluent aphasia

**Gottfried Schlaug**[1,†], **Andrea Norton**[1], **Sarah Marchina**[1], **Lauryn Zipse**[1], and **Catherine Y Wan**[1]

[1] Department of Neurology, Music, Neuroimaging & Stroke Recovery Laboratories, Beth Israel Deaconess Medical Center & Harvard Medical School, 330 Brookline Avenue, Boston, MA 02215, USA

## Abstract

It has been reported for more than 100 years that patients with severe nonfluent aphasia are better at singing lyrics than they are at speaking the same words. This observation led to the development of melodic intonation therapy (MIT). However, the efficacy of this therapy has yet to be substantiated in a randomized controlled trial. Furthermore, its underlying neural mechanisms remain unclear. The two unique components of MIT are the intonation of words and simple phrases using a melodic contour that follows the prosody of speech and the rhythmic tapping of the left hand that accompanies the production of each syllable and serves as a catalyst for fluency. Research has shown that both components are capable of engaging fronto–temporal regions in the right hemisphere, thereby making MIT particularly well suited for patients with large left hemisphere lesions who also suffer from nonfluent aphasia. Recovery from aphasia can happen in two ways: either through the recruitment of perilesional brain regions in the affected hemisphere, with variable recruitment of right-hemispheric regions if the lesion is small, or through the recruitment of homologous language and speech-motor regions in the unaffected hemisphere if the lesion of the affected hemisphere is extensive. Treatment-associated neural changes in patients undergoing MIT indicate that the unique engagement of right-hemispheric structures (e.g., the superior temporal lobe, primary sensorimotor, premotor and inferior frontal gyrus regions) and changes in the connections across these brain regions may be responsible for its therapeutic effect.

Published in final edited form as:
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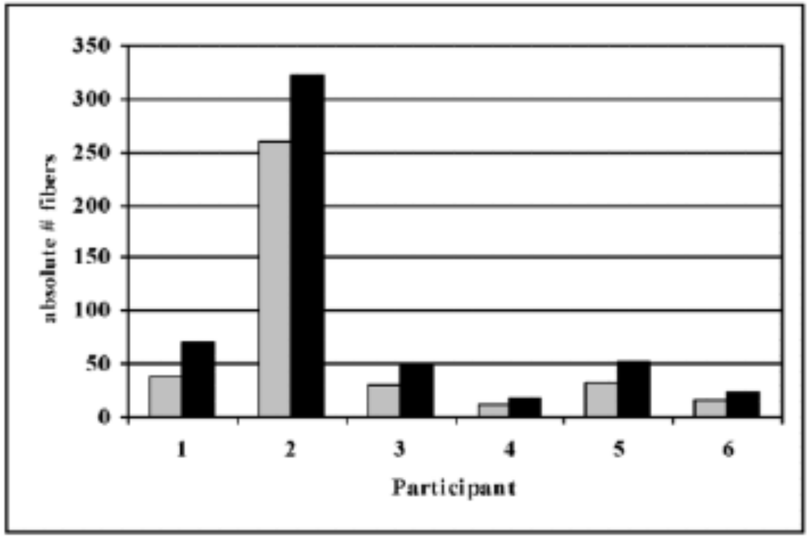
# Evidence for Plasticity in White Matter Tracts of Chronic Aphasic Patients Undergoing Intense Intonation-based Speech Therapy

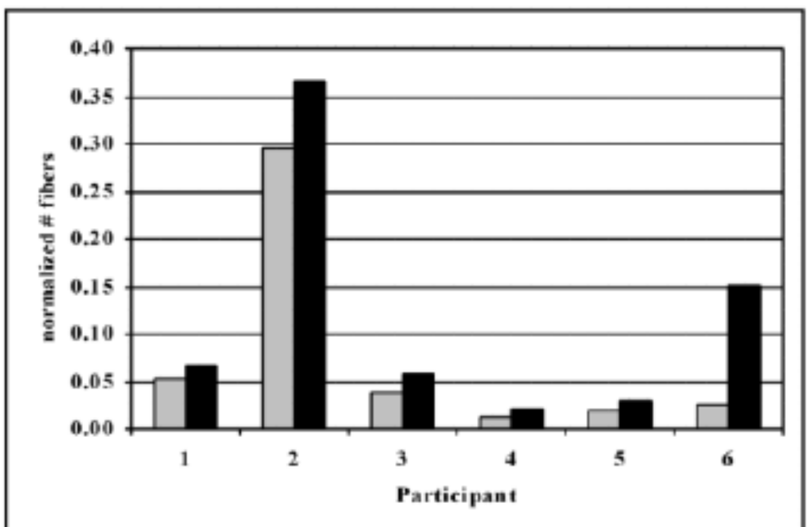
**Gottfried Schlaug**, **Sarah Marchina**, and **Andrea Norton**
Dept. of Neurology, Music, Stroke Recovery, and Neuroimaging Laboratories, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA 02215

## Abstract

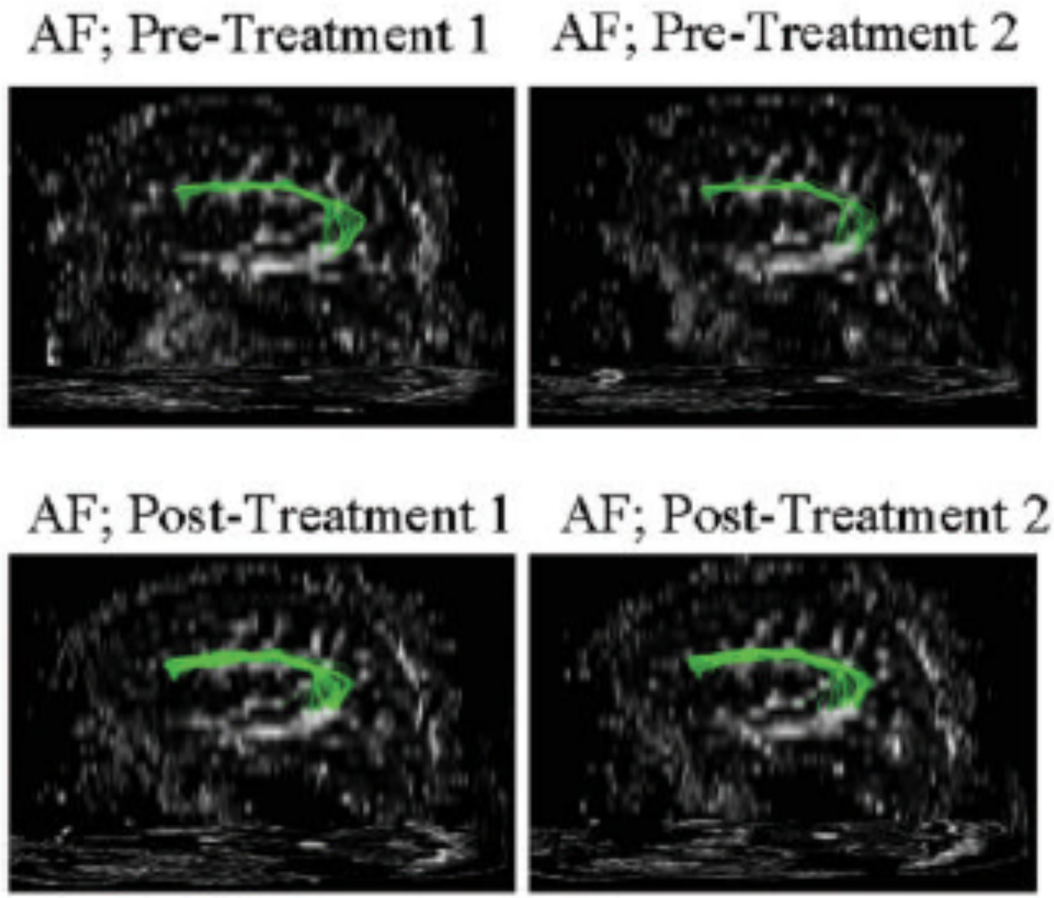
Recovery from aphasia can be achieved through recruitment of either peri-lesional brain regions in the affected hemisphere or homologous language regions in the non-lesional hemisphere. For patients with large left-hemisphere lesions, recovery through the right hemisphere may be the only possible path. The right hemisphere regions most likely to play a role in this recovery process are the superior temporal lobe (important for auditory feedback control), premotor regions/posterior inferior frontal gyrus (important for planning and sequencing of motor actions and for auditory-motor mapping) and the primary motor cortex (important for execution of vocal motor actions). These regions are connected reciprocally via a major fiber tract called the arcuate fasciculus (AF), but this tract is usually not as well developed in the non-dominant right hemisphere. We tested whether an intonation-based speech therapy (i.e., Melodic Intonation Therapy) which is typically administered in an intense fashion with 75–80 daily therapy sessions, would lead to changes in white matter tracts, particularly the AF. Using diffusion tensor imaging (DTI), we found a significant increase in the number of AF fibers and AF volume comparing post with pre-treatment assessments in 6 patients that could not be attributed to scan-to-scan variability. This suggests that intense, long-term Melodic Intonation Therapy leads to remodeling of the right AF and may provide an explanation for the sustained therapy effects that were seen in these 6 patients.



350
300
250
200
150
100
50
0
absolute # fibers
1
2
3
4
5
6
Participant

0,40
0,35
0,30
0,25
0,20
0,15
0,10
0,05
0,00
normalized # fibers
1
2
3
4
5
6
Participant


AF; Pre-Treatment 1
AF; Pre-Treatment 2
AF; Post-Treatment 1
AF; Post-Treatment 2

*Brain Lang*. 2014 September ; 136: 1–7. doi:10.1016/j.bandl.2014.03.011.

# Intensive therapy induces contralateral white matter changes in chronic stroke patients with Broca's aphasia

**Catherine Y. Wan**[#], **Xin Zheng**[#], **Sarah Marchina**, **Andrea Norton**, and **Gottfried Schlaug**
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[#] These authors contributed equally to this work.

## Abstract

Using a pre-post design, eleven chronic stroke patients with large left hemisphere lesions and nonfluent aphasia underwent diffusion tensor imaging and language testing before and after receiving 15 weeks of an intensive intonation-based speech therapy. This treated patient group was compared to an untreated patient group (n=9) scanned twice over a similar time period. Our results showed that the treated group, but not the untreated group, had reductions in fractional anisotropy in the white matter underlying the right inferior frontal gyrus (IFG, pars opercularis and pars triangularis), the right posterior superior temporal gyrus, and in the right posterior cingulum. Furthermore, we found that greater improvements in speech production were associated with greater reductions in FA in the right IFG (pars opercularis). Thus, our findings showed that an intensive rehabilitation program for patients with non-fluent aphasia led to structural changes in the right hemisphere, which correlated with improvements in speech production.

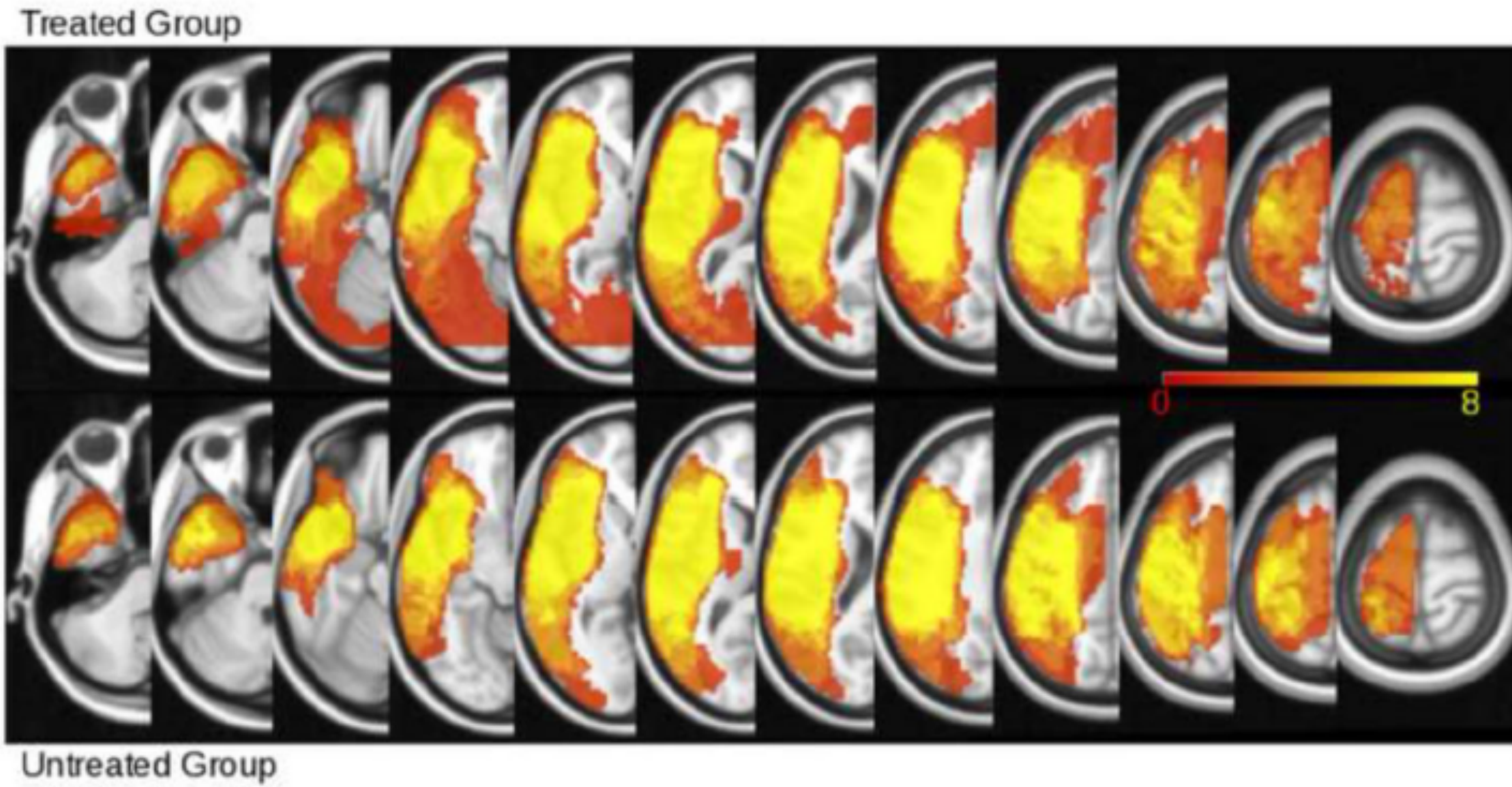


**Figure 1.**

Lesion density map in treated and untreated groups. Color bar indicates number of patients with lesions in a particular voxel.

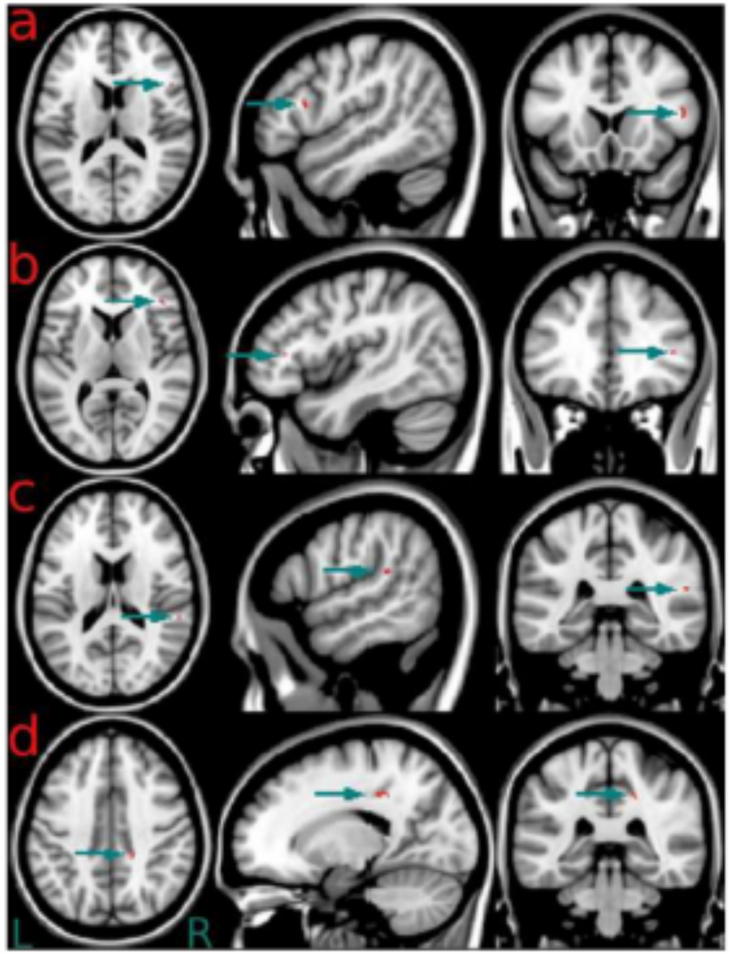


**Figure 2.**

Locations of significant clusters centered in the a) IFG, pars opercularis (MNI [50 17 13]), b) IFG, pars triangularis (MNI [44 33 8]), c) posterior superior temporal gyrus (MNI [57 −36 17]), d) posterior cingulum (MNI [18 −36 40]).

# Memory Training Impacts Short-Term Changes in Aging White Matter: A Longitudinal Diffusion Tensor Imaging Study

**Andreas Engvig,[1]* Anders M. Fjell,[1,2] Lars T. Westlye,[1] Torgeir Moberget,[1] Øyvind Sundseth,[2] Vivi Agnete Larsen,[1] and Kristine B. Walhovd[1,2]**

[1]*Center for the Study of Human Cognition, Department of Psychology, University of Oslo, Oslo, Norway*
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**Abstract:** A growing body of research indicates benefits of cognitive training in older adults, but the neuronal mechanisms underlying the effect of cognitive intervention remains largely unexplored. Neuroimaging methods are sensitive to subtle changes in brain structure and show potential for enhancing our understanding of both aging- and training-related neuronal plasticity. Specifically, studies using diffusion tensor imaging (DTI) suggest substantial changes in white matter (WM) in aging, but it is not known whether cognitive training might modulate these structural alterations. We used tract-based spatial statistics (TBSS) optimized for longitudinal analysis to delineate the effects of 8 weeks intensive memory training on WM microstructure. 41 participants (mean age 61 years) matched for age, sex and education were randomly assigned to an intervention or control group. All participants underwent MRI-scanning and neuropsychological assessments at the beginning and end of the study. Longitudinal analysis across groups revealed significant increase in frontal mean diffusivity (MD), indicating that DTI is sensitive to WM structural alterations over a 10-week interval. Further, group analysis demonstrated positive effects of training on the short-term changes. Participants in the training group showed a relative increase in fractional anisotropy (FA) compared with controls. Further, a significant relationship between memory improvement and change in FA was found, suggesting a possible functional significance of the reported changes. The training effect on FA seemed to be driven by a relative decrease in radial diffusivity, which might indicate a role for myelin-related processes in WM plasticity. *Hum Brain Mapp 33:2390–2406, 2012.* 

**Key words:** plasticity; white matter; memory; training; aging; DTI; FA; longitudinal

**TABLE I. Characteristics of completing participants at baseline ($n$ = 41)**

| | Intervention (11F/10M) | | Control (11F/9M) | | |
|---|---|---|---|---|---|
| | M | SD | M | SD | *P*-value* |
| Age | 61.7 | 9.4 | 60.3 | 9.1 | 0.64 |
| Education | 15.1 | 1.9 | 15.6 | 1.8 | 0.45 |
| IQ | 117.8 | 9.0 | 118.8 | 9.2 | 0.74 |
| MMSE | 29.0 | 1.0 | 29.1 | 0.9 | 0.63 |
| GDS | 1.7 | 1.9 | 1.5 | 2.2 | 0.75 |
| TMT A | 37.1 | 16.1 | 33.0 | 13.8 | 0.39 |
| TMT B | 81.6 | 35.3 | 70.7 | 32.7 | 0.31 |
| Digit-symbol | 65.2 | 15.6 | 67.7 | 14.1 | 0.61 |
| Rey-O, recall | 19.5 | 6.5 | 21.1 | 5.7 | 0.42 |
| CVLT, 1–5 total | 50.4 | 9.1 | 52.3 | 10.7 | 0.54 |
| CVLT, long delay | 11.8 | 2.3 | 11.9 | 3.6 | 0.93 |
| Re-test interval | 65.4 | 6.8 | 65.3 | 9.5 | 0.95 |

## Intervention

For the present study we developed a memory training program aimed at improving serial verbal recollection memory by implementing the mnemonic technique Method of loci (MoL) [Bower, 1970]. MoL involves learning to visualize a series of mental landmarks or loci (e.g., various rooms in one's house). These loci make up a route—the loci route. After acquisition of a loci route, the to-be-remembered information is linked to the various loci at the time of encoding. At test, the landmarks are mentally revisited in serial order, and the information associated with each locus is retrieved. This method is shown to substantially improve serial recall in older adults [Kliegl et al., 1990]. In the current intervention, each training week consisted of a 1-h classroom session and 4 days of homework exercises. The classroom sessions consisted of small groups lead by an instructor. Each session followed a basic structure: Review of homework and positive feedback; focus on weekly and overall course goals; presentation of new didactic information; individual in-class memory training; and homework assignments. In total, participants finished 40 exercises (in-class + homework), comprising roughly 25 min of training 5-days a week for 8 weeks. An extensive description of the intervention, including examples of in-class and homework exercises used in the memory training program has been published in [Engvig et al., 2010].

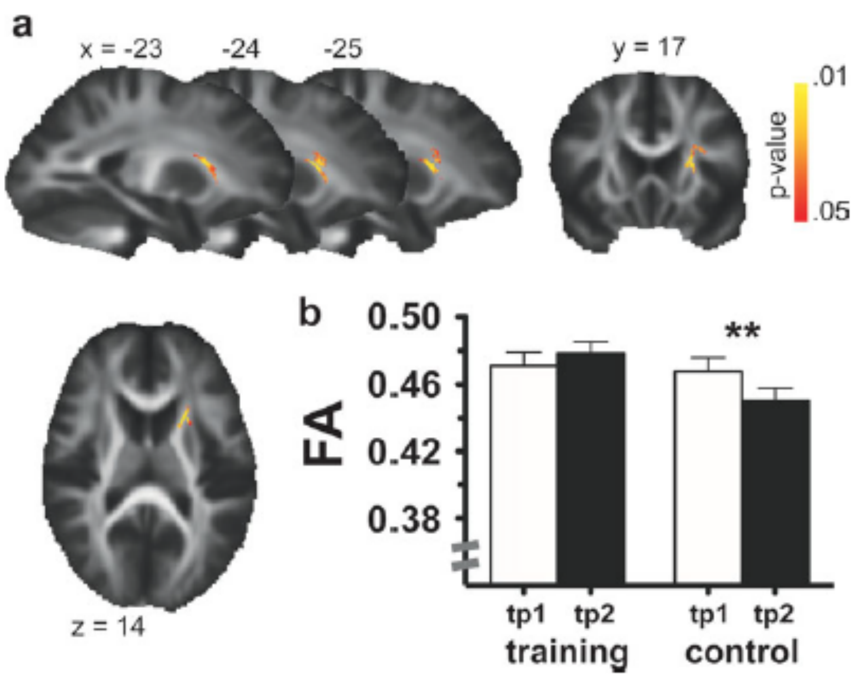


**Figure 6.**

Impact of memory training on left anterior WM. (**a**) Changes in FA in the left anterior hemisphere in response to cognitive intervention. The effects were estimated by comparing the training and control groups by means of voxel-wise general linear models (group × time interaction). The results are shown on the mean FA image of all participants. The sections are displayed in radiological convention and numbers denote the Montreal Neurological Institute XYZ-coordinates. Red-yellow areas indicate voxels with significant ($P < 0.05$, corrected) relative FA increases in trainers compared with controls. (**b**) Bar plots show mean FA (± 1 SEM) for the peak voxel at scan 1 and 2 for the control and training group. Asterisk (*) indicates $P < 0.05$ based on two-tailed paired samples *t* tests comparing FA at baseline and at the end of the study phase.

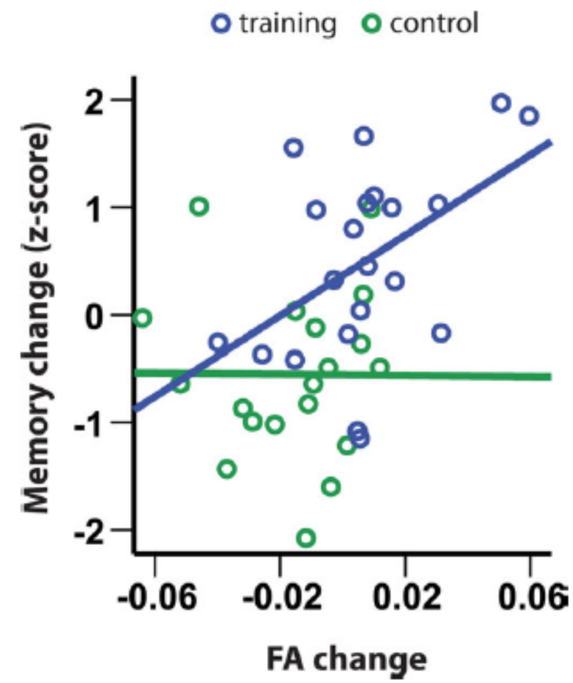


**Figure 7.**

FA change predicts memory change in the training, but not in the control group, respectively. Scatter plot showing verbal source memory change (Z-scores) as a function of FA change at the peak voxel in Figure 6a. Blue and green lines represent linear fit-lines for the training and control groups, respectively.

- “In sum, work on experience-dependent changes in animals suggests that **learning-related volume alterations might be related to synaptogenesis and changes in dendritic morphology**.”
- “In hippocampus, neurogenesis may also play a role. However, specific brain changes are unlikely to occur in isolation. Rather, plasticity of regional brain volume likely reflects a cascade of changes in dendritic branching, synapses, cell numbers, cell sizes, and capillaries.”

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ARTICLE

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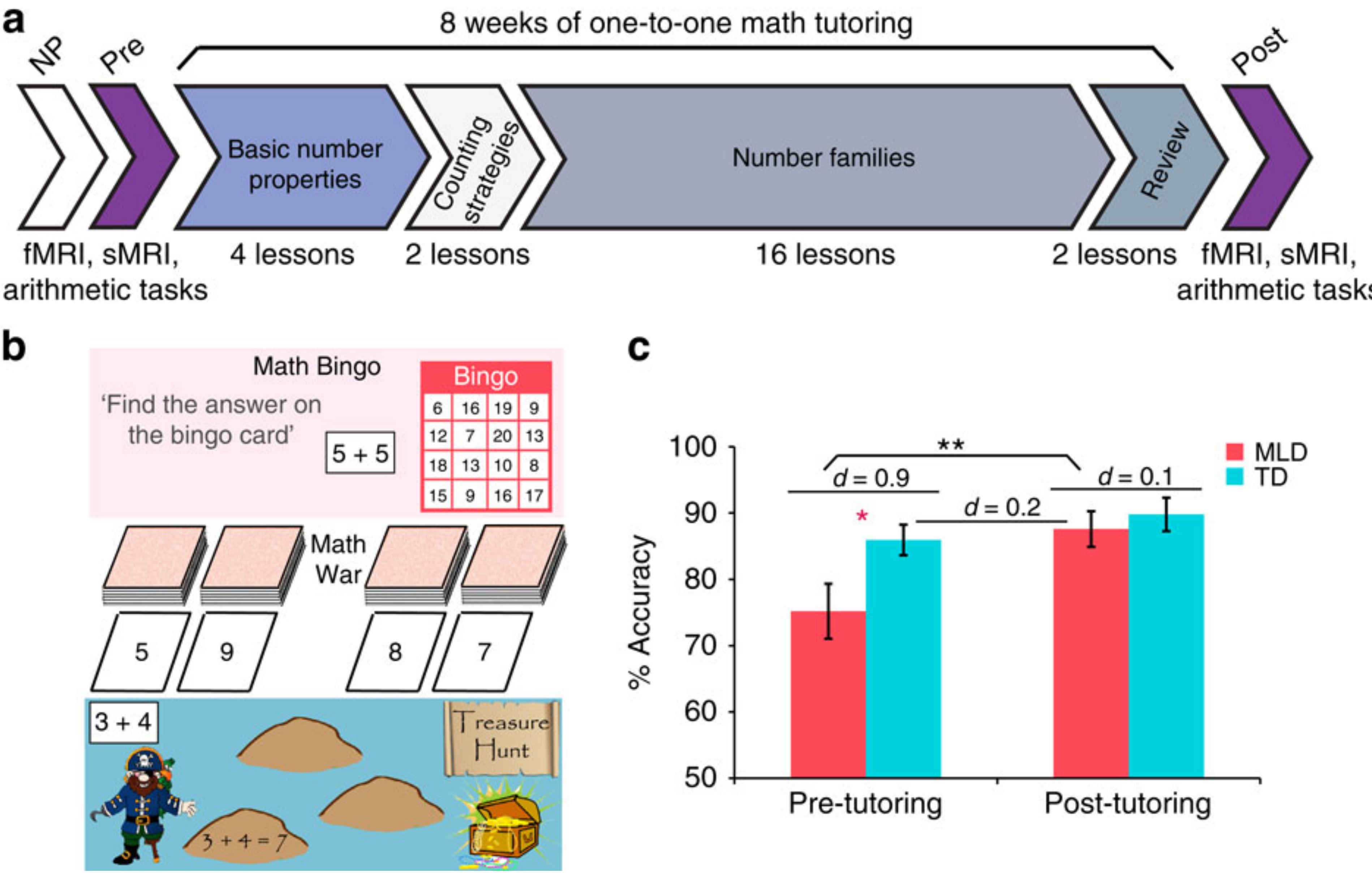
OPEN

# Cognitive tutoring induces widespread neuroplasticity and remediates brain function in children with mathematical learning disabilities

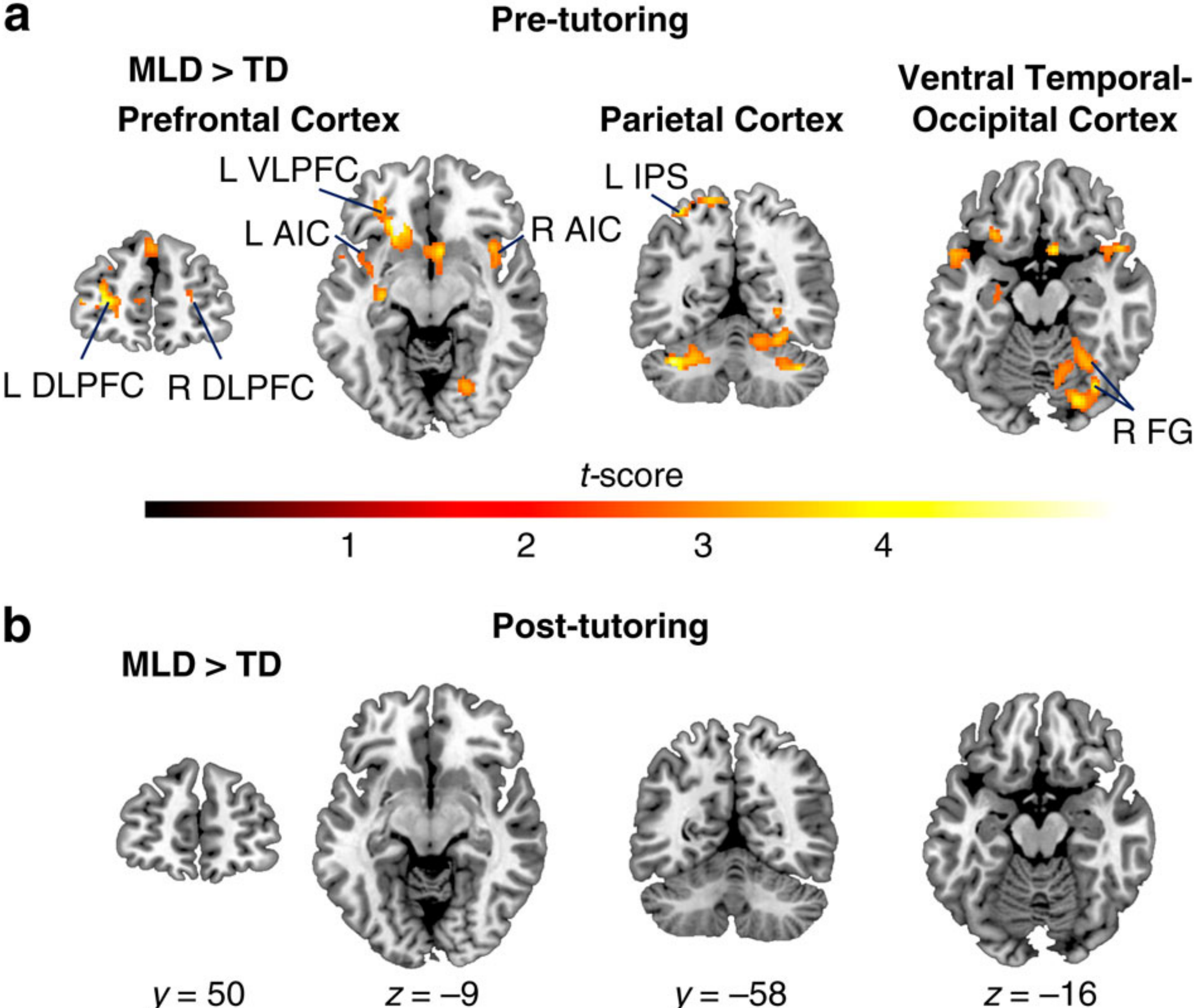
Teresa Iuculano[1], Miriam Rosenberg-Lee[1,*], Jennifer Richardson[1,*], Caitlin Tenison[1], Lynn Fuchs[2], Kaustubh Supekar[1] & Vinod Menon[1,3,4]

- "Competency with numbers is essential in today's society; yet, up to 20% of children exhibitmoderate to severe mathematical learning disabilities (MLD). Behavioural intervention can be effective, but the neurobiological mechanisms underlying successful intervention are unknown. Here we demonstrate **that eight weeks of 1:1 cognitive tutoring** not only remediates poor performance in children with MLD, <u>but also induces widespread changes in brain activity. Neuroplasticity manifests as normalization of aberrant functional responses in a distributed network of parietal, prefrontal and ventral temporal–occipital areas that support successful numerical problem solving, and is correlated with performance gains. …</u>

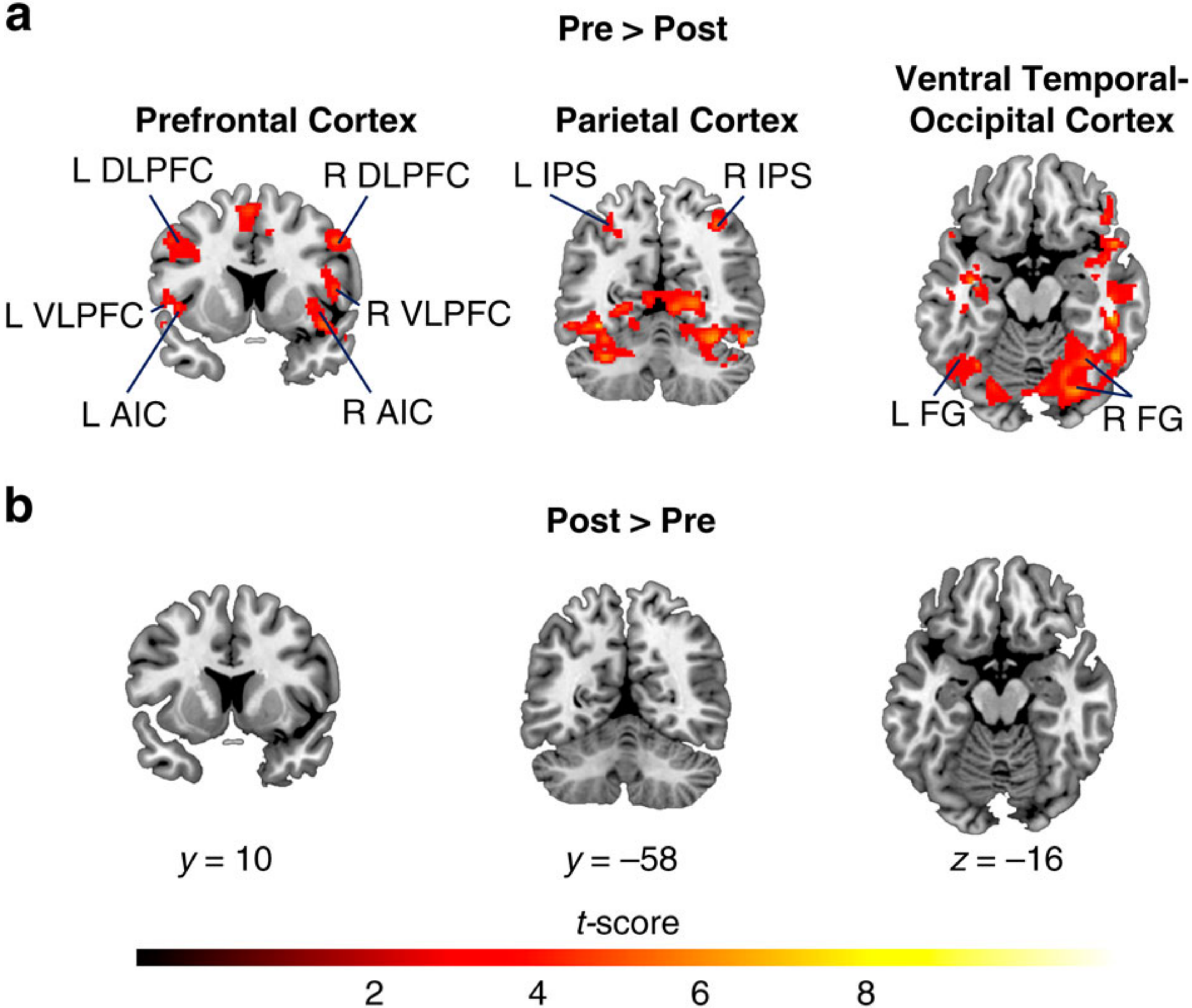
  Our study identifies functional brain mechanisms underlying effective intervention in children with MLD and provides novel metrics for assessing response to intervention."




**TD**: typically developing children



a
Pre-tutoring
MLD > TD
Prefrontal Cortex
Parietal Cortex
Ventral Temporal-
Occipital Cortex
L VLPFC
L AIC
R AIC
L IPS
L DLPFC
R DLPFC
R FG
t-score
1
2
3
4
b
Post-tutoring
MLD > TD
y = 50
z = –9
y = –58
z = –16


a
Pre > Post
Prefrontal Cortex
L DLPFC
R DLPFC
L VLPFC
R VLPFC
L AIC
R AIC
Parietal Cortex
L IPS
R IPS
Ventral Temporal-Occipital Cortex
L FG
R FG
b
Post > Pre
y = 10
y = –58
z = –16
t-score
2
4
6
8

OPEN ACCESS Freely available online

PLoS one

# Working Memory Training Using Mental Calculation Impacts Regional Gray Matter of the Frontal and Parietal Regions

Hikaru Takeuchi[1]*, Yasuyuki Taki[2], Yuko Sassa[2], Hiroshi Hashizume[2], Atsushi Sekiguchi[3], Ai Fukushima[3], Ryuta Kawashima[1,2,3]

1 Smart Ageing International Research Center, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan, 2 Division of Developmental Cognitive Neuroscience, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan, 3 Department of Functional Brain Imaging, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan

## Abstract

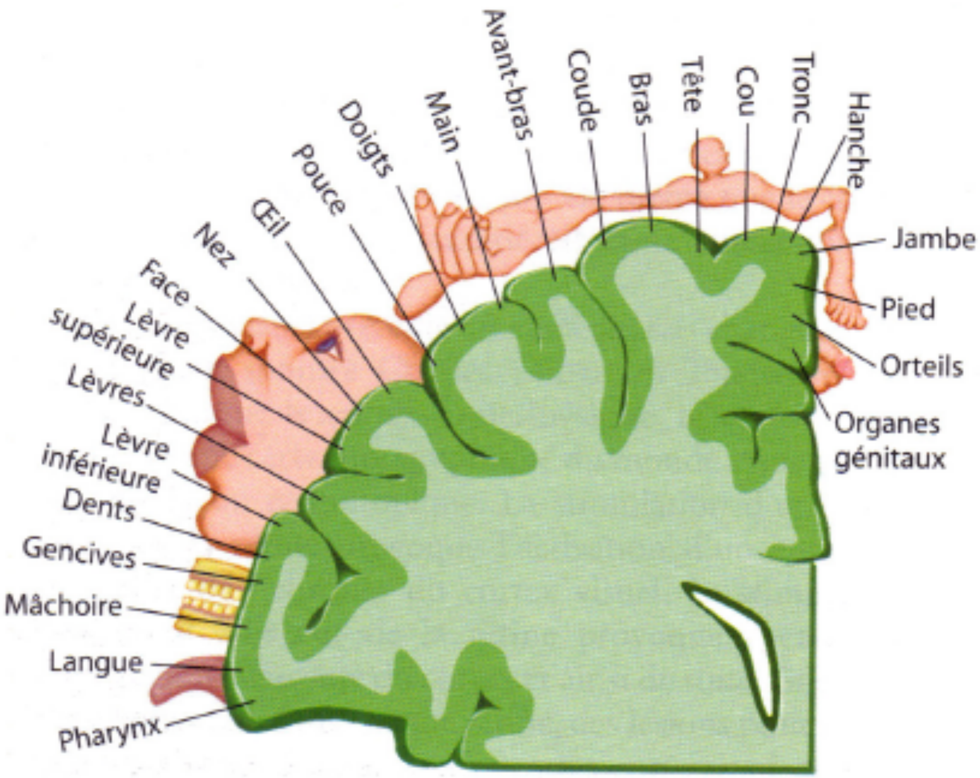
Training working memory (WM) improves performance on untrained cognitive tasks and alters functional activity. However, WM training's effects on gray matter morphology and a wide range of cognitive tasks are still unknown. We investigated this issue using voxel-based morphometry (VBM), various psychological measures, such as non-trained WM tasks and a creativity task, and intensive adaptive training of WM using mental calculations (IATWMMC), all of which are typical WM tasks. IATWMMC was associated with reduced regional gray matter volume in the bilateral fronto-parietal regions and the left superior temporal gyrus. It improved verbal letter span and complex arithmetic ability, but deteriorated creativity. These results confirm the training-induced plasticity in psychological mechanisms and the plasticity of gray matter structures in regions that have been assumed to be under strong genetic control.

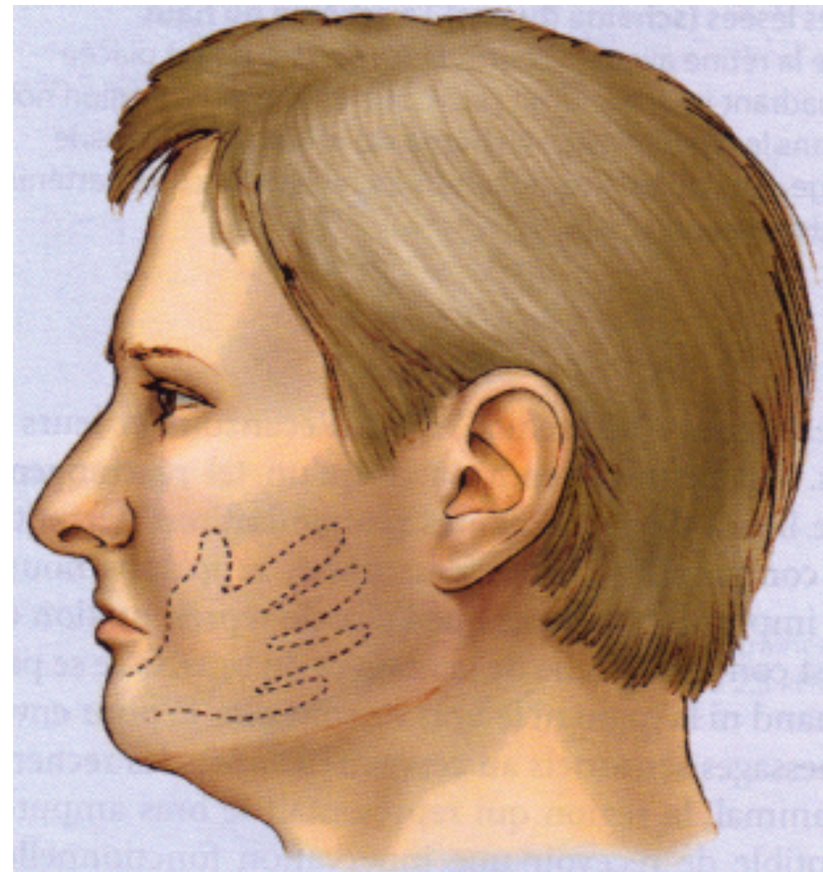
From: **Phantom Limbs and Neural Plasticity**

Arch Neurol. 2000;57(3):317-320. doi:10.1001/archneur.57.3.317


Figure Legend:

Points on the face of a patient that elicit precisely localized, modality-specific referral in the phantom limb 4 weeks after amputation of the left arm below the elbow. **Sensations were felt simultaneously on the face and phantom limb.**


Avant-bras
Coude
Bras
Tête
Cou
Tronc
Hanche
Main
Doigts
Pouce
Œil
Nez
Face
Lèvre supérieure
Lèvres
Lèvre inférieure
Dents
Gencives
Mâchoire
Langue
Pharynx
Jambe
Pied
Orteils
Organes génitaux



From: **Phantom Limbs and Neural Plasticity**

Arch Neurol. 2000;57(3):317-320. doi:10.1001/archneur.57.3.317

Figure Legend:

Mirror box used to provide visual feedback. Patient views the reflection of his own hand in the mirror.

# Mirror Therapy for Phantom Limb Pain

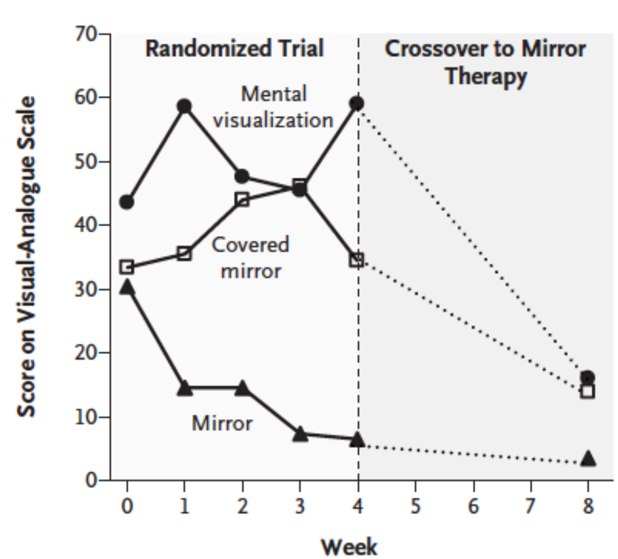



**Figure 1. Changes in Phantom Limb Pain, as Measured on a 100-mm Visual-Analogue Scale.**

The score on the visual-analogue scale ranges from 0 to 100, with higher scores indicating a greater severity of pain. The dotted lines represent the weeks during which patients in all three groups used to mirror therapy. Data points show medians.

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NeuroImage
NeuroImage 20 (2003) S107–S111
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# Illusory movements of the paralyzed limb restore motor cortex activity

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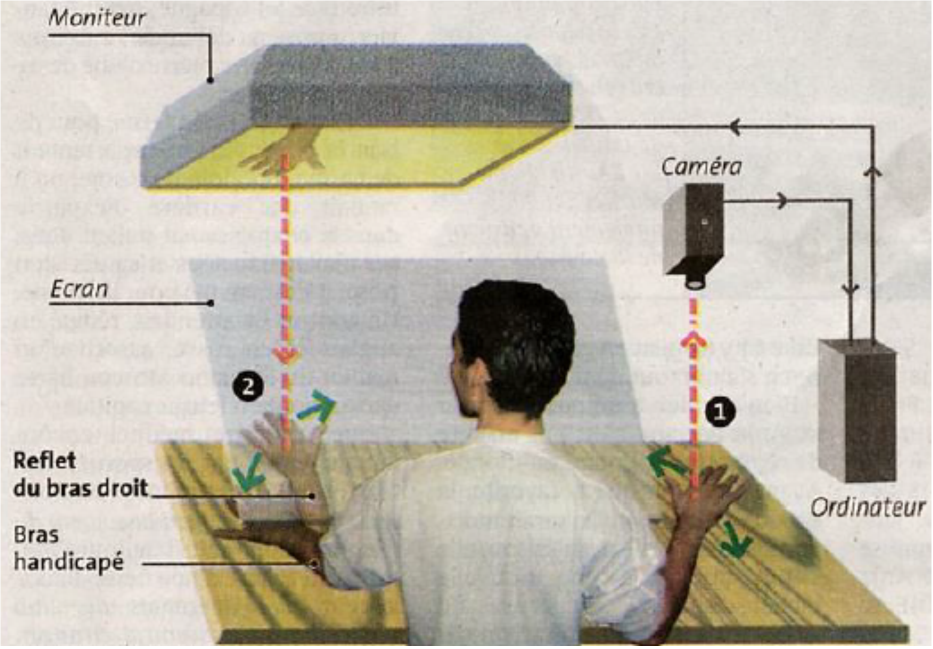
[a] Institut des Sciences Cognitives, CNRS, UMR 5015, Lyon, France
[b] Departement de Rehabilitation, Faculté de Médecine Jacques Lisfranc, Saint-Etienne, France

**Abstract**

In humans, limb amputation or brachial plexus avulsion (BPA) often results in phantom pain sensation. Actively observing movements made by a substitute of the injured limb can reduce phantom pain (V.S. Ramachandran and D. Rogers-Ramachandran, 1996, Proc. R. Soc. London B Biol. Sci. 263, 377–386). The neural basis of phantom limb sensation and its amelioration remains unclear. Here, we studied the effects of visuomotor training on motor cortex (M1) activity in three patients with BPA. Functional magnetic resonance imaging scans were obtained before and after an 8-week training program during which patients learned to match voluntary "movements" of the phantom limb with prerecorded movements of a virtual hand. Before training, phantom limb movements activated the contralateral premotor cortex. After training, two subjects showed increased activity in the contralateral primary motor area. This change was paralleled by a significant reduction in phantom pain. The third subject showed no increase in motor cortex activity and no improvement in phantom pain. We suggest that successful visuomotor training restores a coherent body image in the M1 region and, as a result, directly affects the experience of phantom pain sensation. Artificial visual feedback on the movements of the phantom limb may thus "fool" the brain and reestablish the original hand/arm cortical representation.


*Keywords:* Motor cortex; Motor plasticity; Brachial plexus avulsion; Illusory movements; fMRI


Moniteur
Caméra
Ecran
2
1
Reflet
du bras droit
Ordinateur
Bras
handicapé

- Subjects were asked to produce a hand movement with their phantom limb while watching the hand in the mirror.

- Sessions started with simple and slow movements, then the speed and complexity gradually increased dependent on the subject's report of his kinesthetic and pain sensations. Each subject completed 24 sessions, at a rate of 3 sessions per week, each session involving 100 move- ments. In patients with phantom pain, voluntary movement of the phantom limb is painful by itself. Thus, pain level was assessed before and after each session in two ways: first, subjects reported a percentage of pain relief ranging from 0 (no relief) to 100 (complete relief). Second, they marked on a 100-mm Visual Analogue Scale the average pain level (Price et al., 1983).

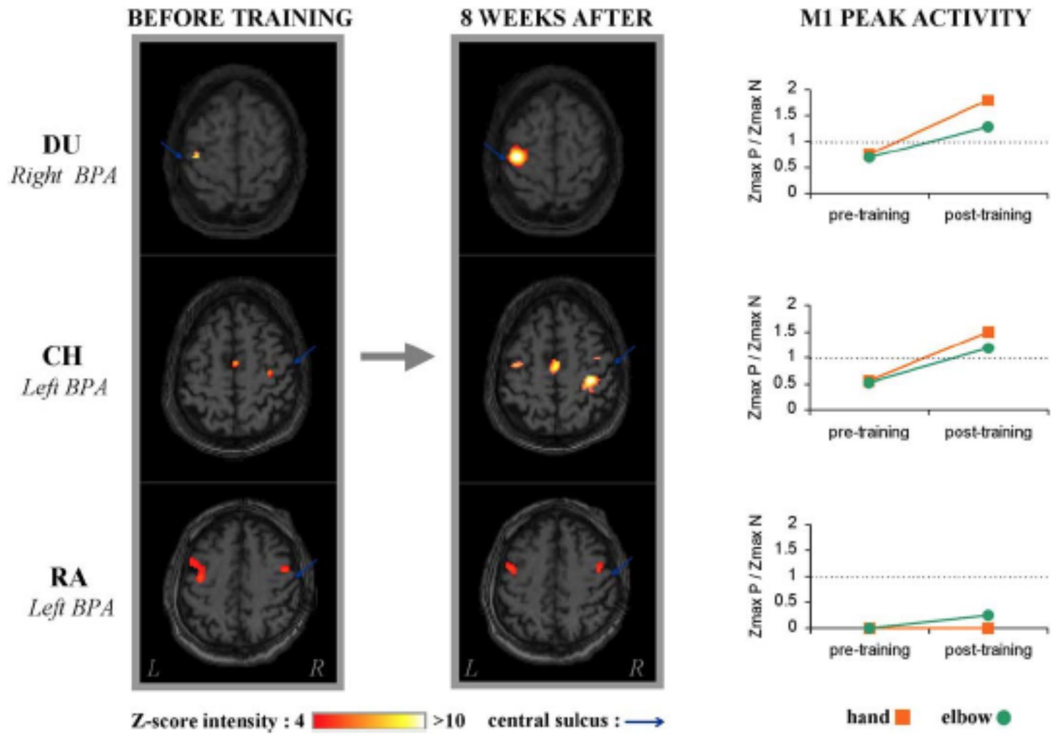



Fig. 2. Individual significant activations in motor regions (superimposed on individual anatomical MRI) for phantom hand "movements" before training (left) and after training (middle). The plots on the right illustrate the evolution of M1 activations ($Z_{max}$) by showing the ratio of maximal activity for the phantom limb (P) compared to the normal limb (N).

Table 1
Effect of visuomotor training on M1 activation and on mean pain level

| Subject | M1 activation[a] | | | | | | | | Pain[b] | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | Hand | | | | Elbow | | | | | | |
| | Z score | | Cluster size | | Z score | | Cluster size | | VAS | | |
| | Pre | Post | Pre | Post | Pre | Post | Pre | Post | Pre | Post | % Relief |
| DU | 5 | 11 | 1 | 104 | 7 | 12 | 46 | 348 | 7 | 1.5 | 80 |
| CH | 7 | 14 | 9 | 317 | 6 | 12 | 12 | 392 | 7 | 4 | 40 |
| RA | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 49 | 7 | 6 | 0 |

[a] Maximal Z score and cluster size in voxel.
[b] Pain evaluation as assessed by the Visual Analogue Scale (VAS) and the percentage relief scale.

# Some Neurobiological Aspects of Psychotherapy

## *A Review*

Deborah Y. Liggan, M.D.
Jerald Kay, M.D.

# Motor Imagery

## A Backdoor to the Motor System After Stroke?

Nikhil Sharma, MB, ChB, MRCP(UK); Valerie M. Pomeroy, PhD;
Jean-Claude Baron, MD, FRCP, FmedSci

***Background and Purpose***—Understanding brain plasticity after stroke is important in developing rehabilitation strategies. Active movement therapies show considerable promise but depend on motor performance, excluding many otherwise eligible patients. Motor imagery is widely used in sport to improve performance, which raises the possibility of applying it both as a rehabilitation method and to access the motor network independently of recovery. Specifically, whether the primary motor cortex (M1), considered a prime target of poststroke rehabilitation, is involved in motor imagery is unresolved.

***Summary of Review***—We review methodological considerations when applying motor imagery to healthy subjects and in patients with stroke, which may disrupt the motor imagery network. We then review firstly the motor imagery training literature focusing on upper-limb recovery, and secondly the functional imaging literature in healthy subjects and in patients with stroke.

***Conclusions***—The review highlights the difficulty in addressing cognitive screening and compliance in motor imagery studies, particularly with regards to patients with stroke. Despite this, the literature suggests the encouraging effect of motor imagery training on motor recovery after stroke. Based on the available literature in healthy volunteers, robust activation of the nonprimary motor structures, but only weak and inconsistent activation of M1, occurs during motor imagery. In patients with stroke, the cortical activation patterns are essentially unexplored as is the underlying mechanism of motor imagery training. Provided appropriate methodology is implemented, motor imagery may provide a valuable tool to access the motor network and improve outcome after stroke. (***Stroke*. 2006;37:1941-1952.**)

**TABLE 5. Functional Imaging Studies: Activation Patterns During the Motor Imagery Task vs Rest, Using Voxel-Based Whole-Brain Analysis**

| | M1 | | SMA | | Pre-SMA | | Ba6 | | GPo | | Ba 44/45/46 | | Ba 9,10,11 | | Sup.P | | Ant.Cing | | Inf.P | | Cb | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Study | C | I | C | I | C | I | C | I | C | I | C | I | C | I | C | I | C | I | C | I | C | I |
| Binkofski (2000)[92] | − | − | + | − | − | + | + | + | − | − | − | − | − | − | − | − | + | − | + | − | − | − |
| Gerardin (2000)[62] | − | − | − | − | − | − | + | + | + | + | + | + | − | + | + | + | − | − | + | − | − | − |
| Boecker (2001)[93] | − | − | − | − | − | − | + | + | + | − | − | − | − | + | − | − | − | − | + | − | − | + |
| Naito E (2002)[63] | − | − | + | − | − | − | + | − | − | − | − | − | − | − | − | − | − | − | + | − | − | + |
| Lacourse (2005)[94] | + | + | − | − | + | + | − | − | − | − | + | − | − | + | + | − | − | − | + | + | − | + |

M1 indicates primary motor cortex; SMA, supplementary motor cortex; Ba, brodman area; Sup.P, superior parietal lobe; Inf.P, inferior parietal lobe; Gpo, post central gyrus; CB, cerebellar; Ant.Cing, anterior cingulate.

BRIEF REPORT

# Using Motor Imagery in the Rehabilitation of Hemiparesis

*Jennifer A. Stevens, PhD, Mary Ellen Phillips Stoykov, MS, OTR/L*

ABSTRACT. Stevens JA, Phillips Stoykov ME. Using motor imagery in the rehabilitation of hemiparesis. Arch Phys Med Rehabil 2003;84:1090-2.

**Objective:** To examine the effectiveness of using motor imagery training in the rehabilitation of hemiparesis.

**Design:** A before-after trial with clinical and behavioral analyses of single cases.

**Setting:** Academic-affiliated rehabilitation hospital.

**Participants:** Two survivors of embolic middle cerebral artery stroke that resulted in chronic hemiparesis.

**Intervention:** A motor imagery training program consisting of imagined wrist movements (extension, pronation-supination) and mental simulations of reaching and object manipulation making use of a mirror box apparatus. Twelve 1-hour experimental sessions were delivered, 3 times a week for 4 consecutive weeks.

**Main Outcome Measures:** Two clinical assessments, grip strength, 4 wrist functionality measurements, and 3 timed performance tests. All outcome measures were recorded before training began, at 3 times during the intervention month, with 2 additional long-term measurements.

**Results:** Performance of the paretic limb improved after the imagery intervention, indicated by increases in assessment scores and functionality and decreases in movement times. The improvements over baseline performance remained stable over a 3-month period.

**Conclusions:** These results demonstrate the potential for using motor imagery as a cognitive strategy for functional recovery from hemiparesis. The intervention targets the cognitive level of action processing while its effects may be realized in overt behavioral performance.

# Brain repair after stroke—a novel neurological model

*Steven L. Small, Giovanni Buccino and Ana Solodkin*

**Abstract** | Following stroke, patients are commonly left with debilitating motor and speech impairments. This article reviews the state of the art in neurological repair for stroke and proposes a new model for the future. We suggest that stroke treatment—from the time of the ictus itself to living with the consequences—must be fundamentally neurological, from limiting the extent of injury at the outset, to repairing the consequent damage. Our model links brain and behaviour by targeting brain circuits, and we illustrate the model though action observation treatment, which aims to enhance brain network connectivity. The model is based on the assumptions that the mechanisms of neural repair inherently involve cellular and circuit plasticity, that brain plasticity is a synaptic phenomenon that is largely stimulus-dependent, and that brain repair required both physical and behavioural interventions that are tailored to reorganize specific brain circuits. We review current approaches to brain repair after stroke and present our new model, and discuss the biological foundations, rationales, and data to support our novel approach to upper-extremity and language rehabilitation. We believe that by enhancing plasticity at the level of brain network interactions, this neurological model for brain repair could ultimately lead to a cure for stroke.

Small, S. L. *et al. Nat. Rev. Neurol.* 9, 698–707 (2013); published online 12 November 2013; doi:10.1038/nrneurol.2013.222

**Figure 2** | Visual stimuli for action observation treatment. During action observation treatment, patients watch video sequences containing daily life hand and arm actions[124] (top panels) or leg and foot actions[132] (bottom panels) for 6 min, and then perform the action for 6 min, using the same movement and objects shown in the video clip. On each day of treatment, a 'unit' of three limb movements of increasing complexity is presented. In each video, the presented action is shown from three perspectives. A complete session consists of three or four such videos. Patients typically undergo 20 rehabilitation sessions over 20 consecutive weekdays. During both observation and execution, patients are instructed to focus on the goal of the action rather than on the movement *per se*.

We have recently developed a therapeutic approach, called IMITATE, which is based on matching observation and execution in speech, and is currently being tested in a clinical trial in patients with aphasia following stroke.  IMITATE therapy involves silent observation of audiovisually presented words and phrases that are spoken aloud by six talkers, followed by a period during which the participant orally repeats the stimuli. The clinical trial is a randomized single-blind controlled trial (the researcher, but not the participant, knows whether the participant is receiving IMITATE or a control therapy). **Treatment is provided intensively (90 min per day) for 6 weeks**, with weekly incremental increases in difficulty from monosyllabic words to disyllabic words, disyllabic sentences, and finally longer utterances, combined with progressively increasing rate of speech. Functional MRI scans are obtained before, during and after therapy.
Recent work in neural network computer models suggests that gradual incremental learning has theoretical advantages. We are currently analysing data from 19 patients with aphasia following left middle cerebral artery stroke, and have preliminary results showing sig- nificant improvement on an overall language score from pretreatment to post-treatment in the IMITATE group, but not in the control group.

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# Structural and Functional Neuroplasticity in Relation to Traumatic Stress

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