Accident vasculaire cérébral et neuroplasticité

Stroke and neuroplasticity

Gilles Lafargue

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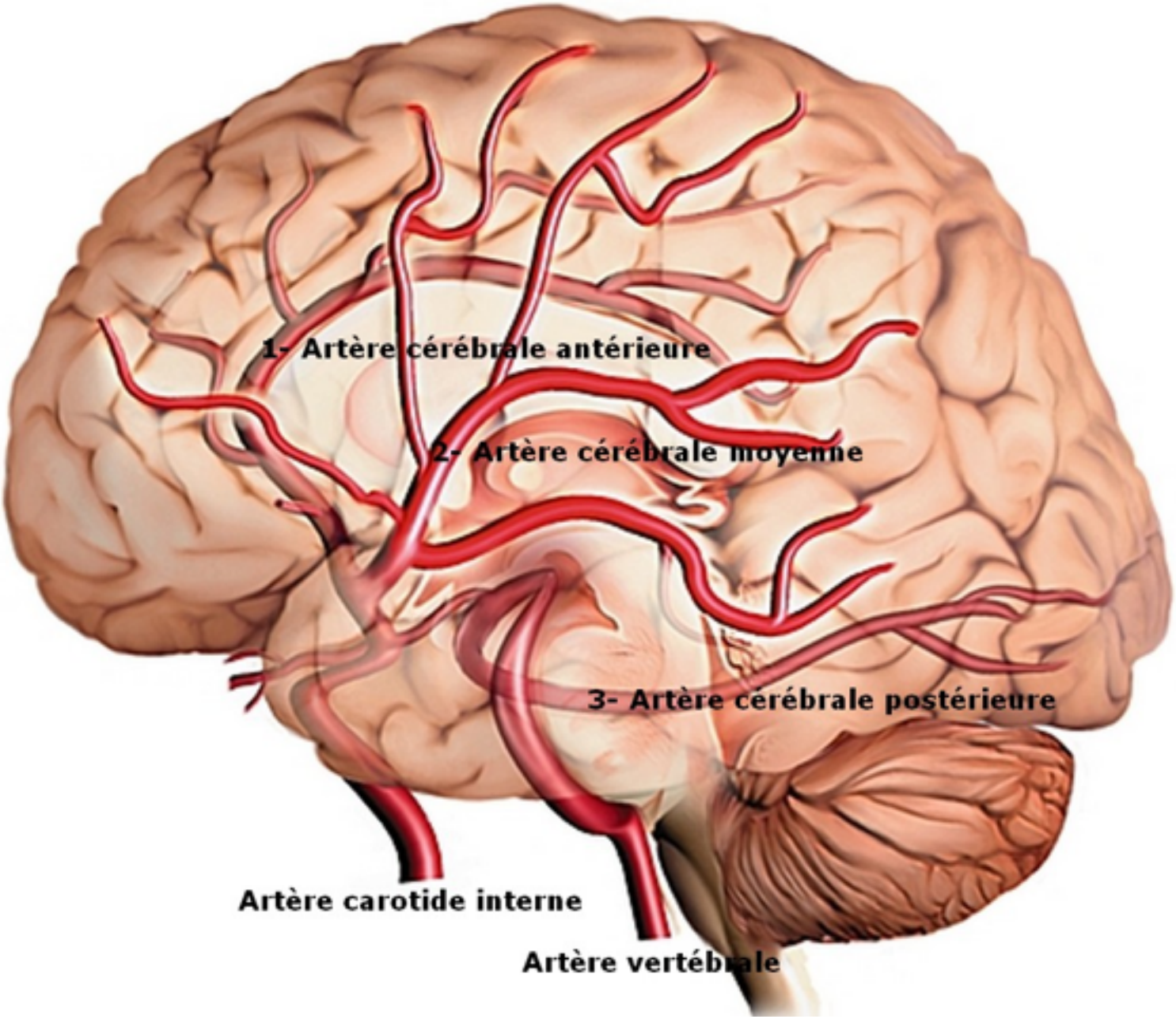
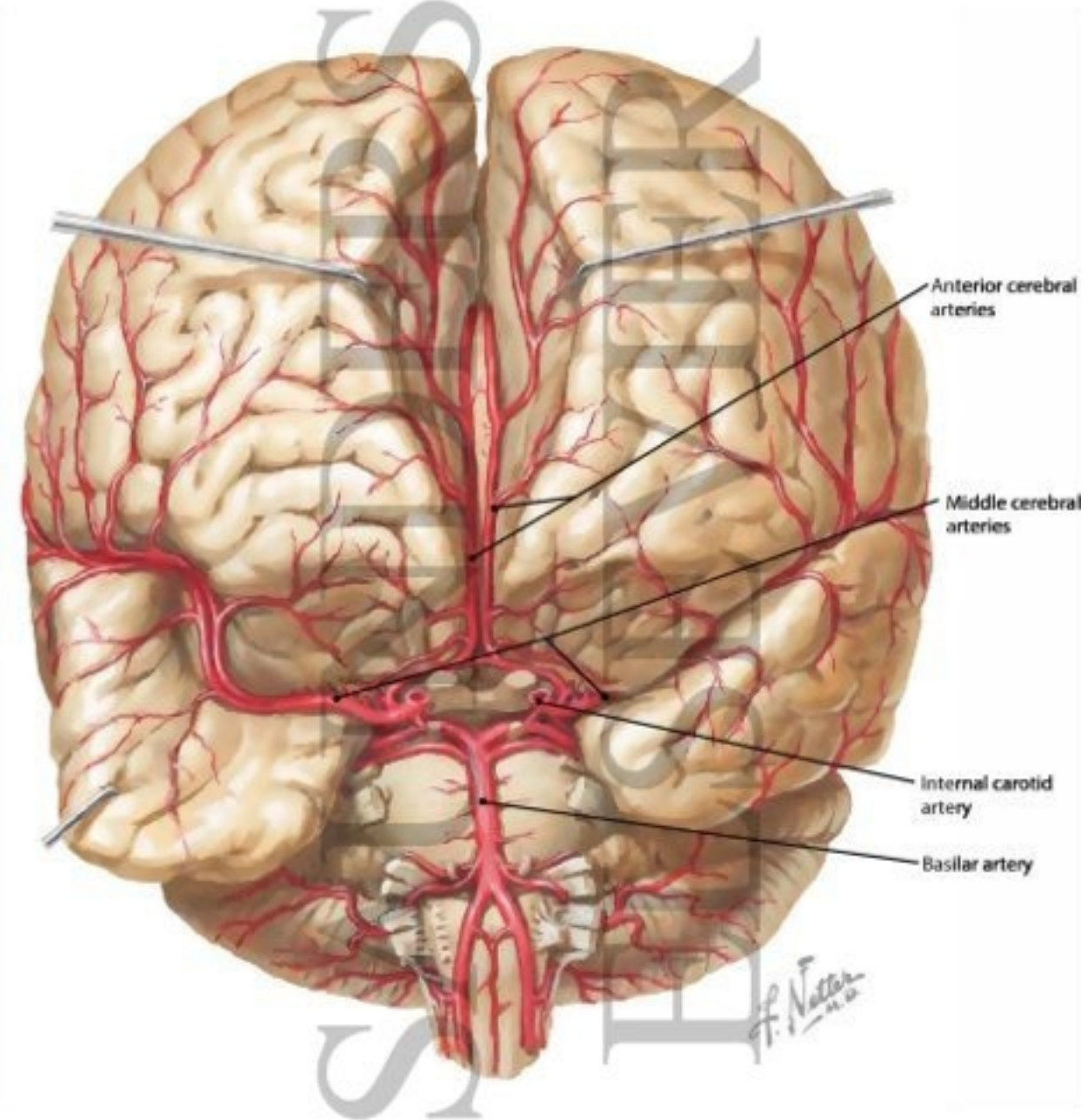
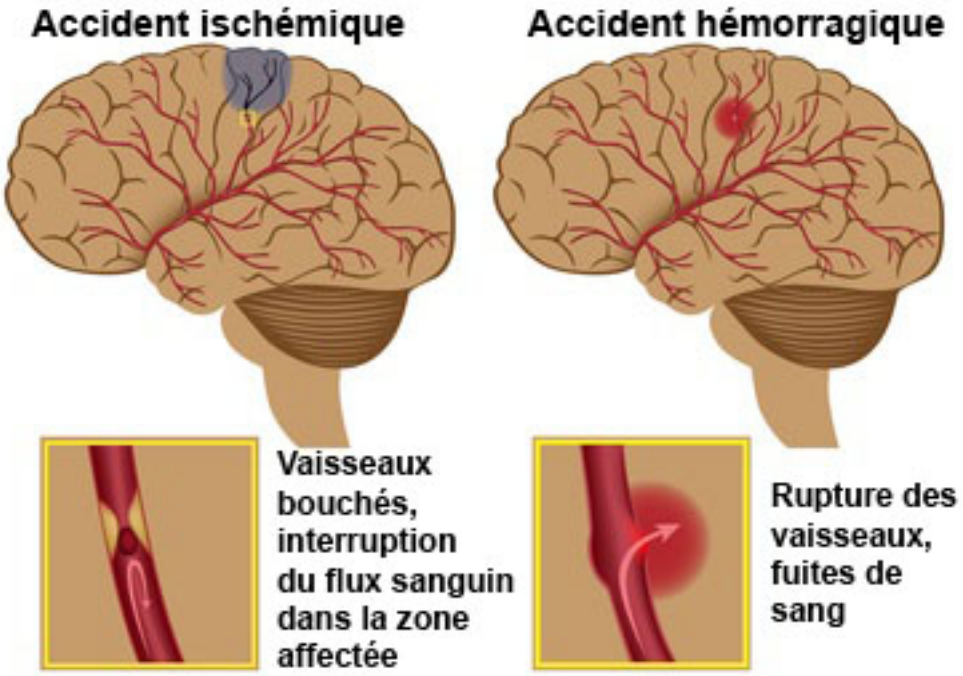
Le vascularisation du cerveau

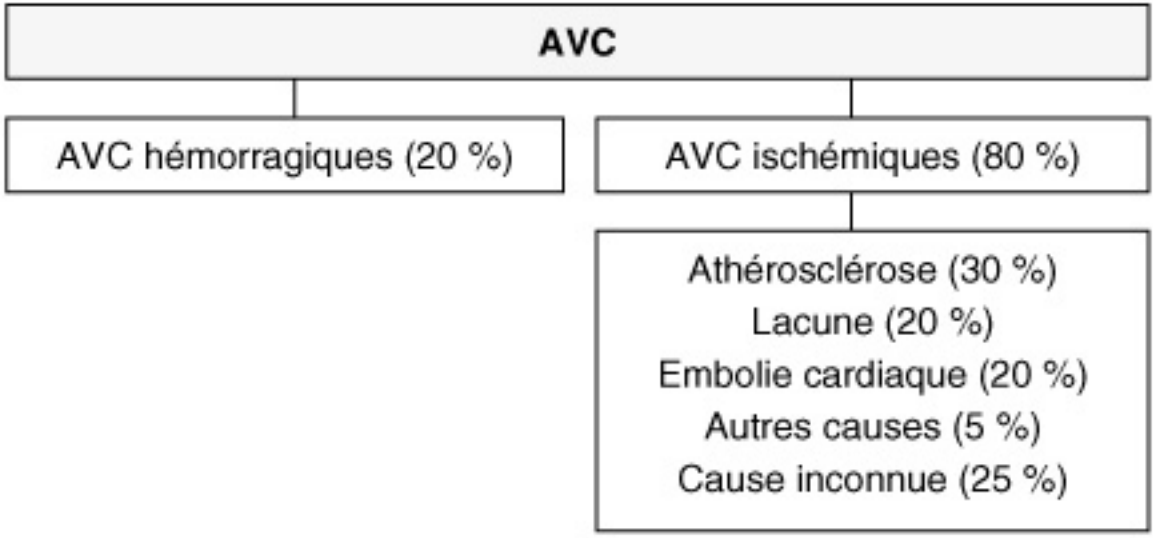

1- Artère cérébrale antérieure
2- Artère cérébrale moyenne
3- Artère cérébrale postérieure
Artère carotide interne
Artère vertébrale

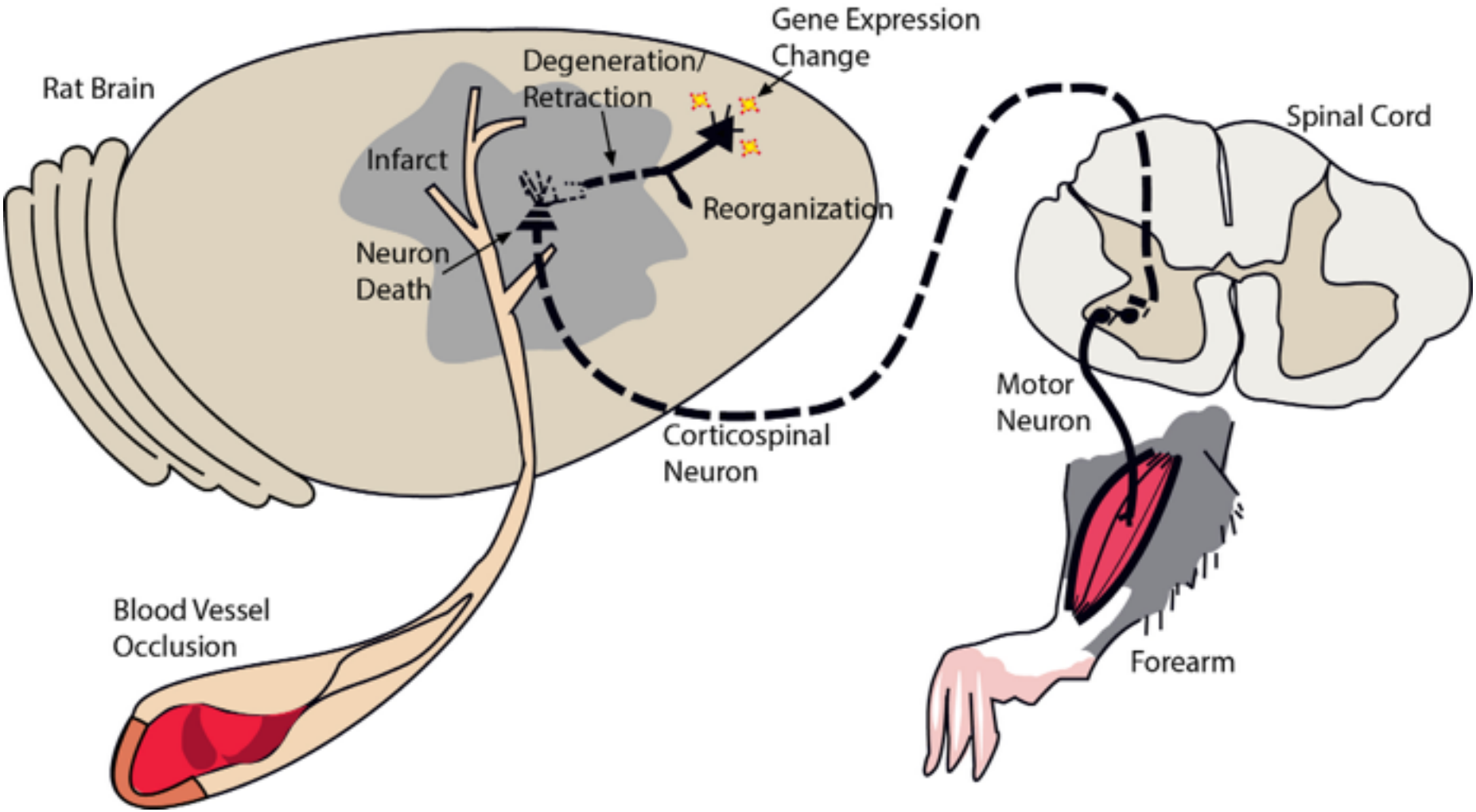


L’accident vasculaire cérébral (AVC)

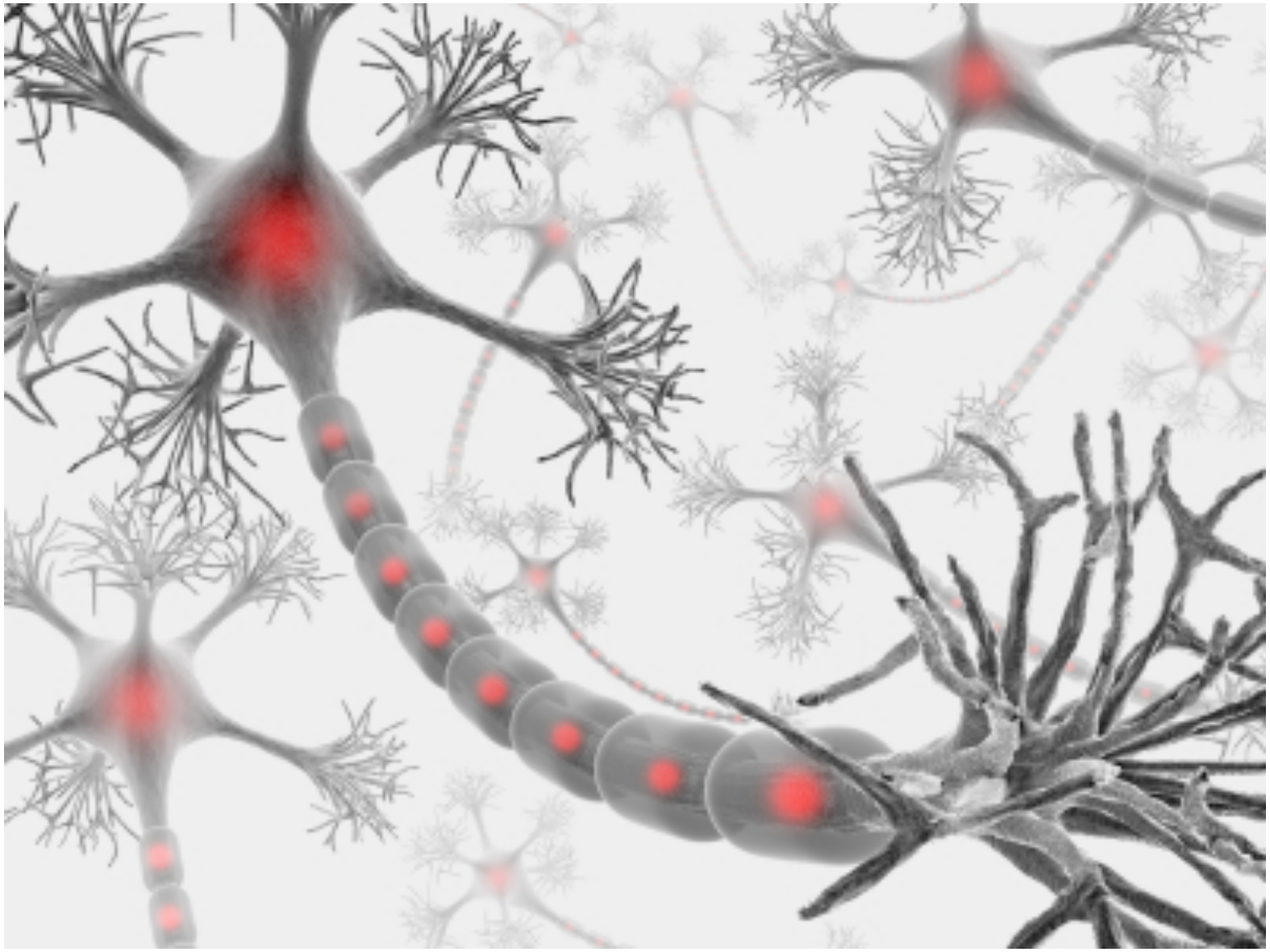
AVC: accident vasculaire cérébral




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

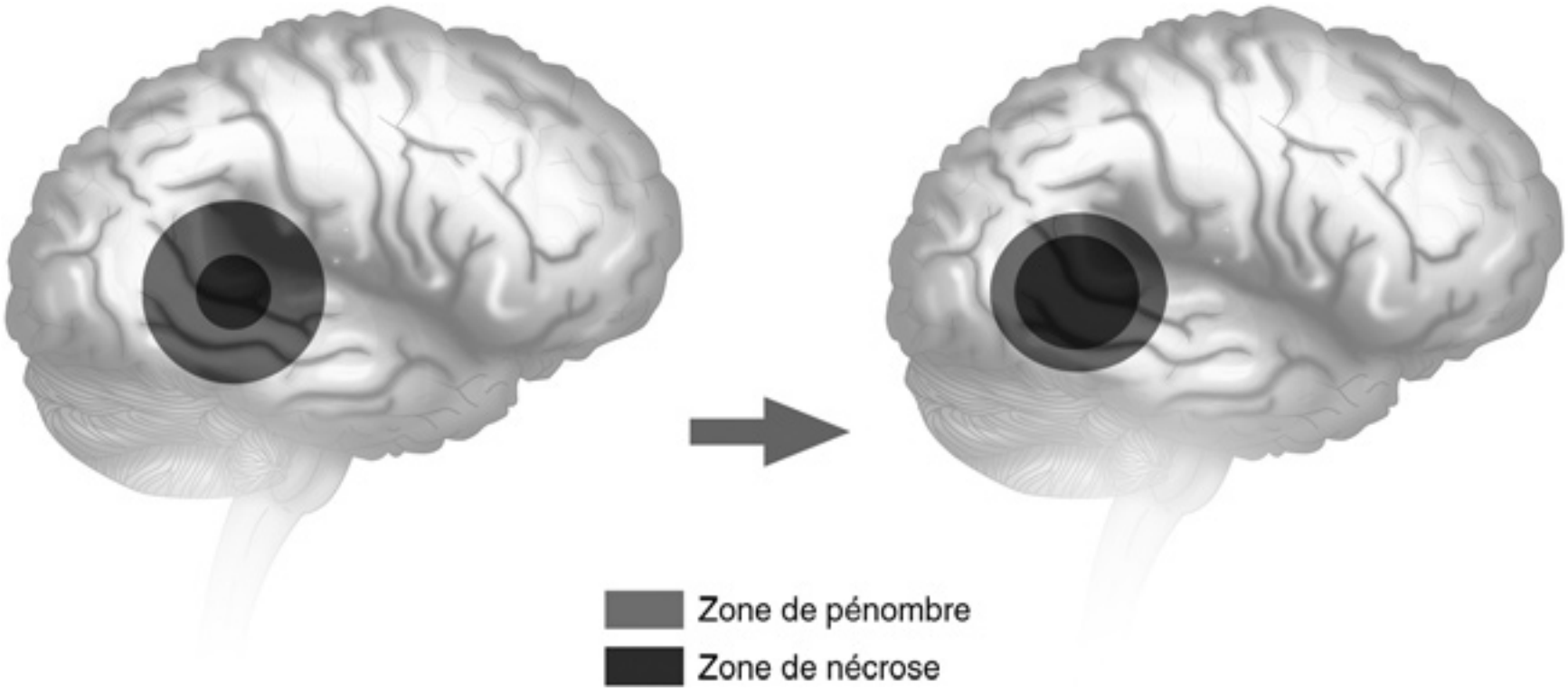


Gene expression changes of interconnected spared cortical neurons 7 days after ischemic infarct of the primary motor cortex in the rat. **Mol Cell Biochem. 2012;369(1-2):267-86**



“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)."

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

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 **restitution of the ischemic penumbra**, **resolution of diaschisis**, and **brain reorganization**.”

La récupération spontanée

La levée du diaschisis

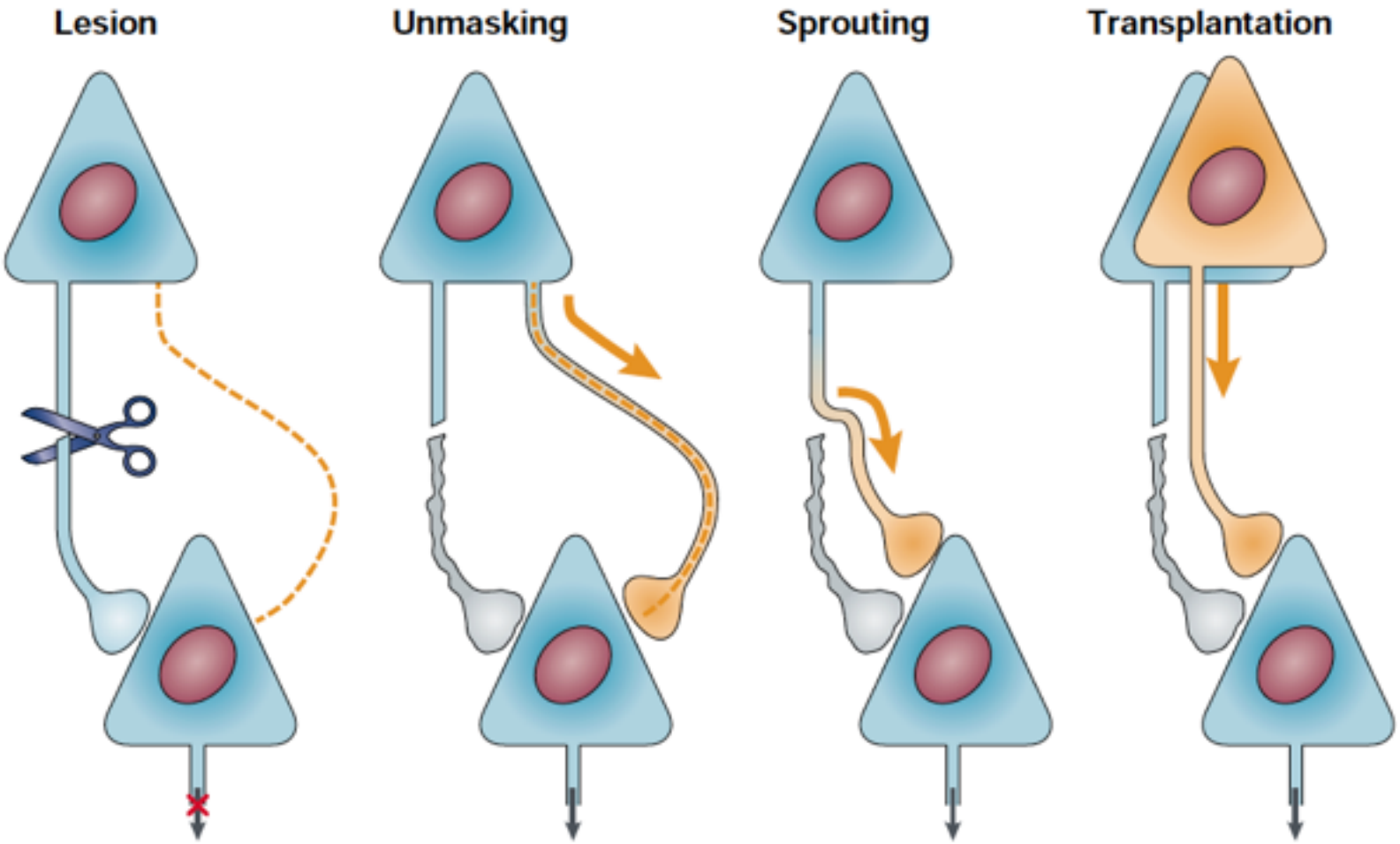
- Une partie de la récupération, au moins initiale, correspond à une reprise fonctionnelle des connexions inhibées mais restées anatomiquement intactes (“levée du diaschisis”)
  - Le diaschisis peut être considéré comme une déafférentation ; la levée du diaschisis correspond à une réafférentation des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

- Les modalités de la réafférentation sont multiples et se mettent en jeu très rapidement après la lésion
  - au niveau synaptique, lorsque 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

Les différentes formes de plasticité neurale

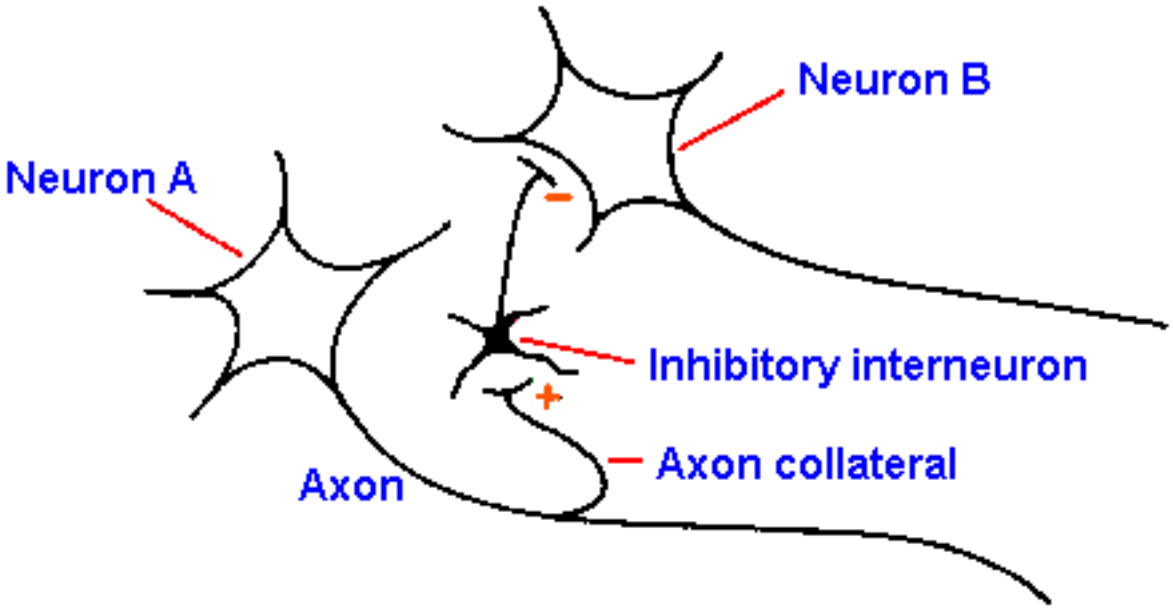


Taub et al. ***Nature Neuroscience reviews***, 2002, 3, 228-236.

Les différentes formes de plasticité neurale

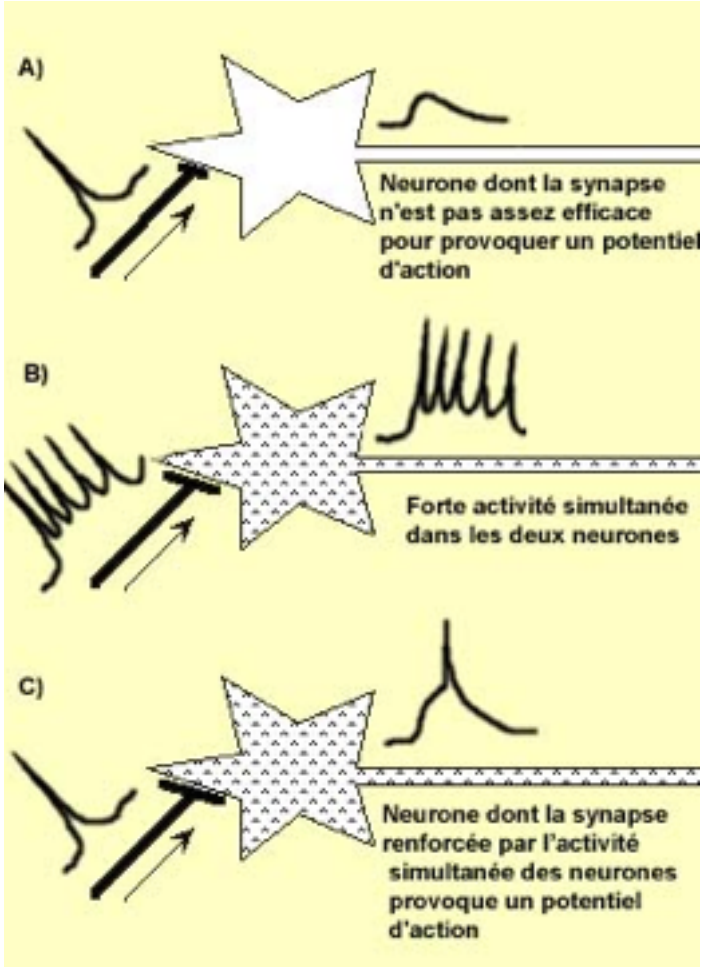
Démasquage de synapses inactives

Changements des effets modulateurs de connexions latérales



Les différentes formes de plasticité neurale

renforcement / affaiblissement synaptique

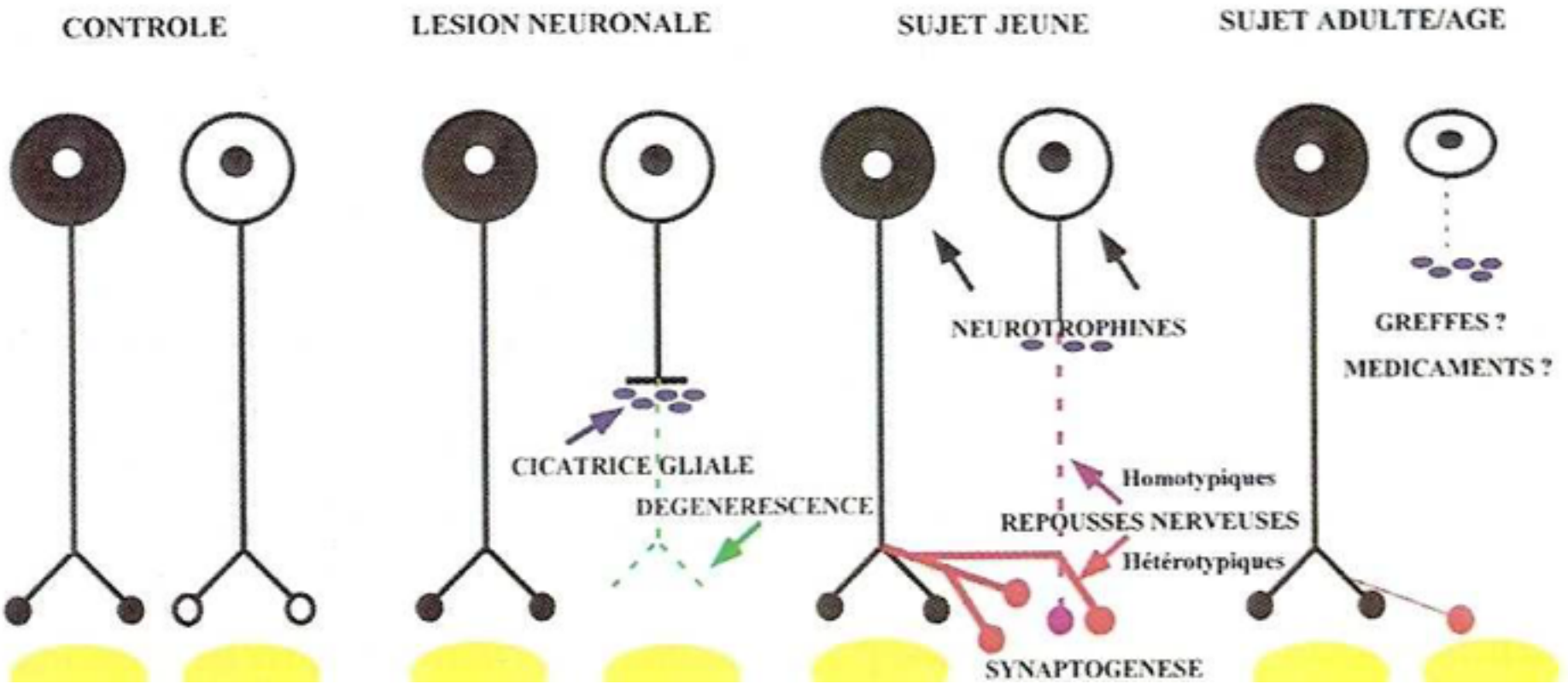


la loi de Hebb (1949)

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

Les différentes formes de plasticité neurale

La synaptogénèse



Les différentes formes de plasticité neurale

La synaptogénèse

- La recherche animale a montré qu'une forme de récupération structurelle était possible
  - Au niveau du réseau de neurones, les connexions perdues en aval de la lésion peuvent être remplacées par une prolifération des afférences restantes et qui partagent le même champ synaptique (les sites synaptiques restés vacants suite à une lésion ne restent jamais vides).

Evidence for stroke-induced neurogenesis in the human brain

Kunlin Jin*†, Xiaomei Wang†‡, Lin Xie*, Xiao Ou Mao*, Wei Zhu‡, Yin Wang§, Jianfeng Shen¶, Ying Mao‡, Surita Banwait*, and David A. Greenberg*‖

*Buck Institute for Age Research, Novato, CA 94945; Departments of ‡Neurosurgery and §Neuropathology, Huashan Hospital, Fudan University, Shanghai 200040, China; and ¶Department of Neurosurgery, First Affiliated Hospital, Zhejiang Medical University, Zhejiang 310031, China

Edited by Solomon H. Snyder, Johns Hopkins University School of Medicine, Baltimore, MD, and approved July 10, 2006 (received for review May 9, 2006)

Experimental stroke in rodents stimulates neurogenesis and migration of newborn neurons from their sites of origin into ischemic brain regions. We report that in patients with stroke, cells that express markers associated with newborn neurons are present in the ischemic penumbra surrounding cerebral cortical infarcts, where these cells are preferentially localized in the vicinity of blood vessels. These findings suggest that stroke-induced compensatory neurogenesis may occur in the human brain, where it could contribute to postischemic recovery and represent a target for stroke therapy.

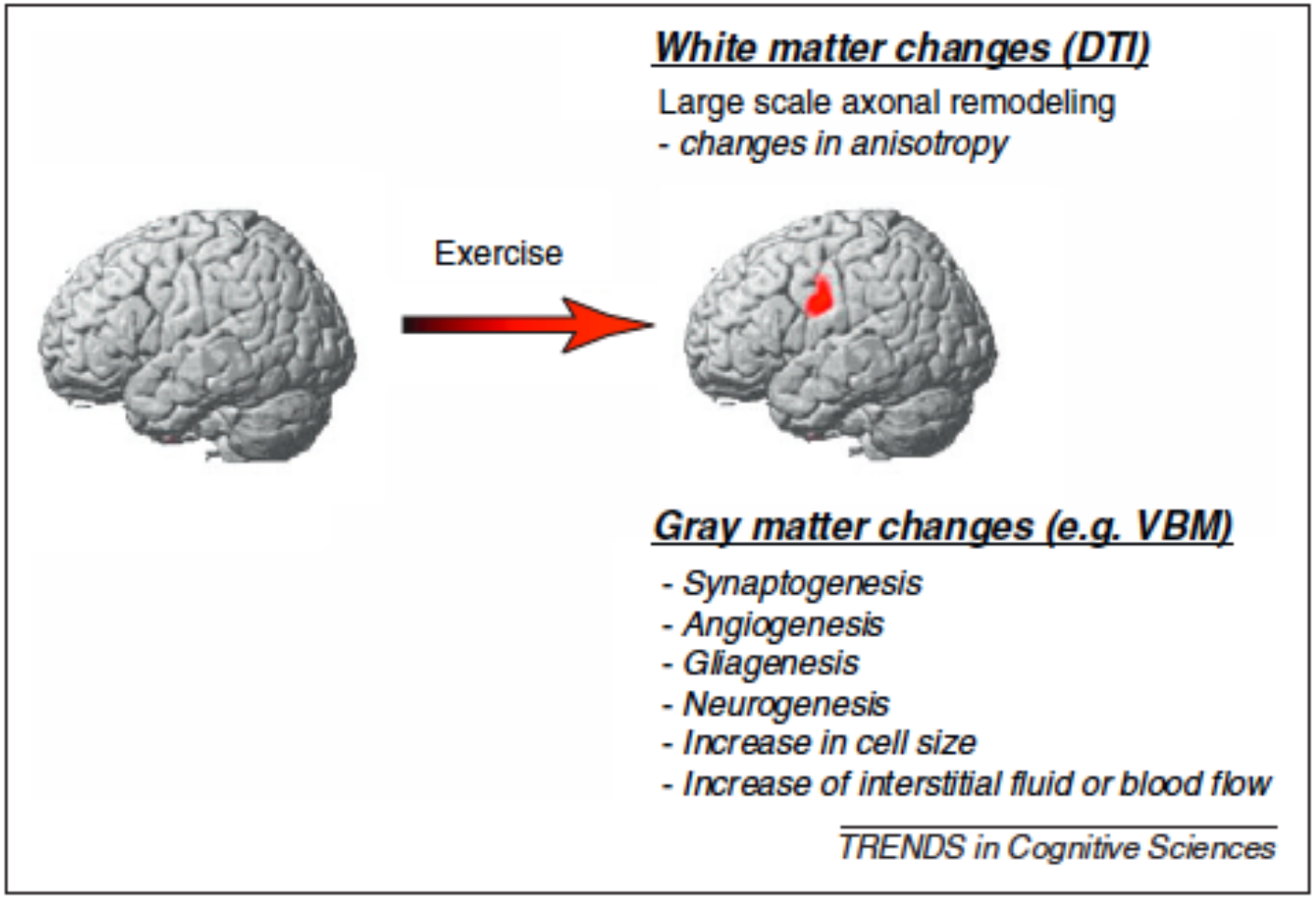
penumbra. Moreover, DCX (Fig. 2*c*), βIII tubulin (Fig. 2*d*), and TUC-4 (Fig. 2*e*) were detected in cells that also expressed Ki-67, and multiple immature neuronal markers were expressed in a given cell (Fig. 2*f*), confirming that these were newborn neurons. Consistent with this interpretation, some Ki-67/DCX-positive cells exhibited a migratory phenotype consisting of an elongated cellular profile with a leading edge and trailing nucleus (Fig. 2*g*).

In the hippocampal dentate gyrus (which, together with the subventricular zone, accounts for most neurogenesis in the adult brain), new neurons arise in proximity to blood vessels, which are thought to provide a "vascular niche" that supports their pro-

Huttner, H., Bergmann, O., Salehpour, M., Rácz, A., Tatarishvili, J. et al. (2014)
The age and genomic integrity of neurons after cortical stroke in humans.
Nature Neuroscience

"The present data uncover that, contrary to some experimental studies in animal models**, <u>the adult human neocortex is incapable of regenerating neurons, even in response to stroke</u>**."

Les principes de la plasticité neurale



“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.”

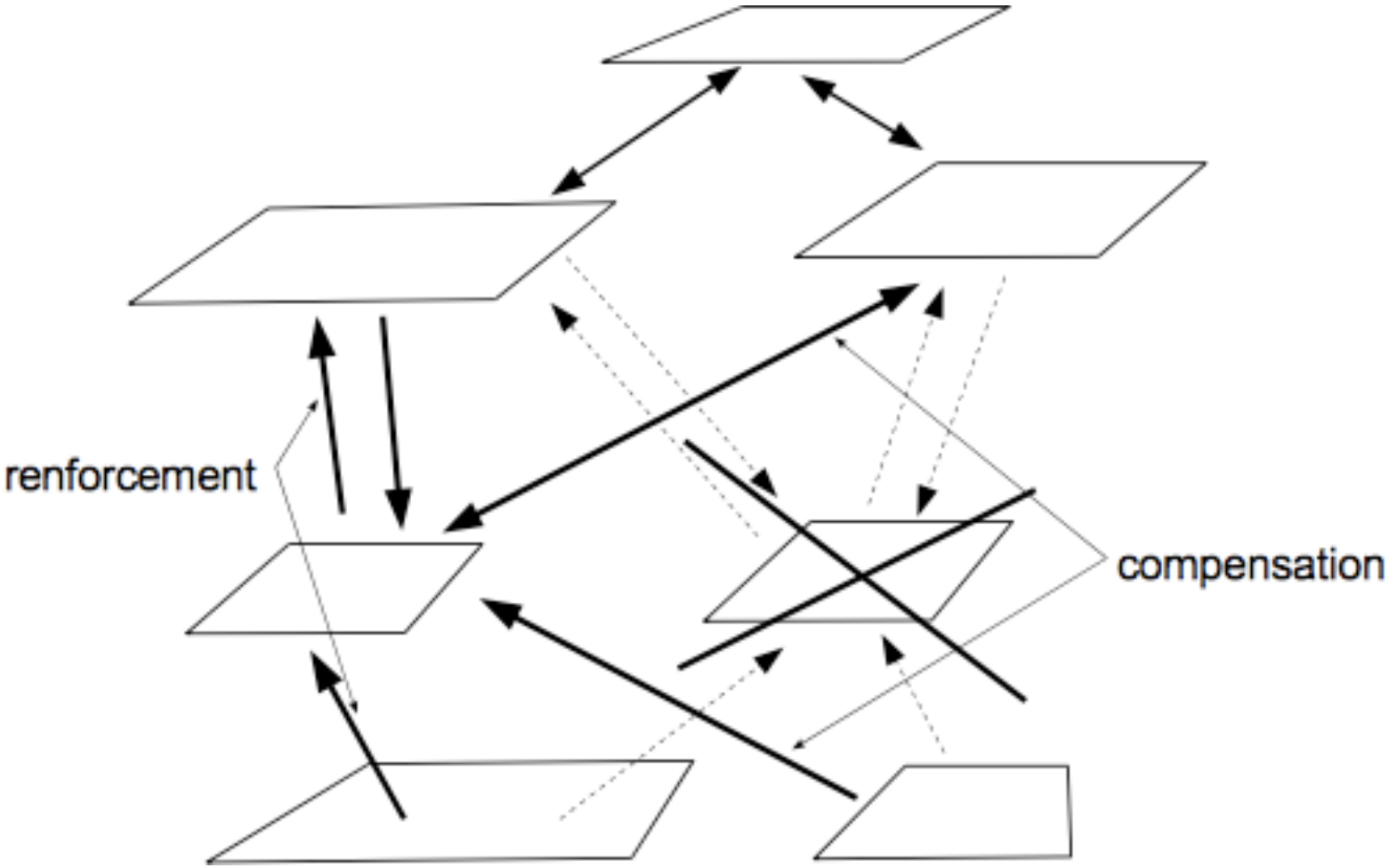
Les principes de la plasticité neurale

Le réentraînement

« Quelques soient les mécanismes en jeu dans la réorganisation neuronale il paraît évident que la sollicitation constante et systématique par le réentrainement systématique est essentielle pour ouvrir une voie inhibée, reconstruire un circuit interrompu, stabilisé un circuit nouveau, définir et mobiliser un nouvel ensemble neuronal »

Jeannerod et Hecaen

Les principes de la plasticité neurale



Les principes de la plasticité neurale

La vicariance fonctionnelle -

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'HD. Par TMS, on peut observer une extension considérable de la carte motrice à cet endroit

Les principes de la plasticité neurale

Augmentation du volume des faisceaux de substance blanche

Published in final edited form as:
Ann N Y Acad Sci. 2009 July ; 1169: 385–394. doi:10.1111/j.1749-6632.2009.04587.x.

Evidence for Plasticity in White Matter Tracts of Chronic Aphasic Patients Undergoing Intense Intonation-based Speech Therapy

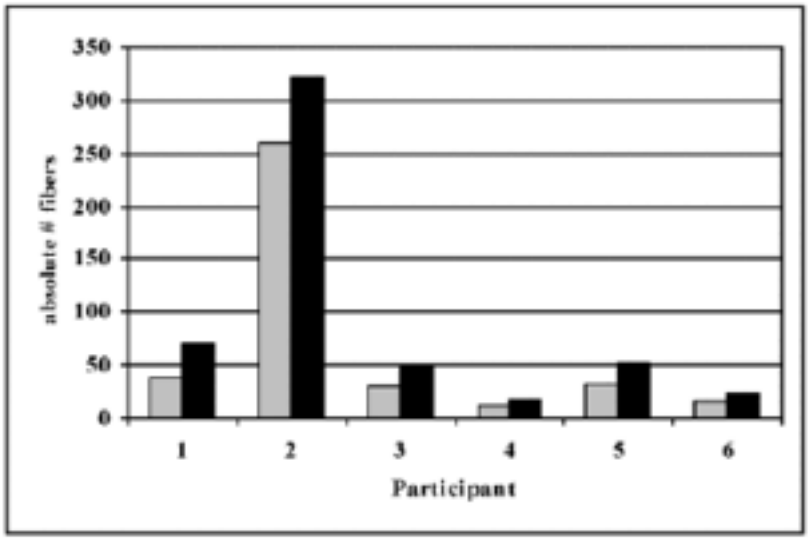
Gottfried Schlaug, **Sarah Marchina**, and **Andrea Norton**
Dept. of Neurology, Music, Stroke Recovery, and Neuroimaging Laboratories, Beth Israel Deaconess Medical Center and Harvard Medical School, Boston, MA 02215

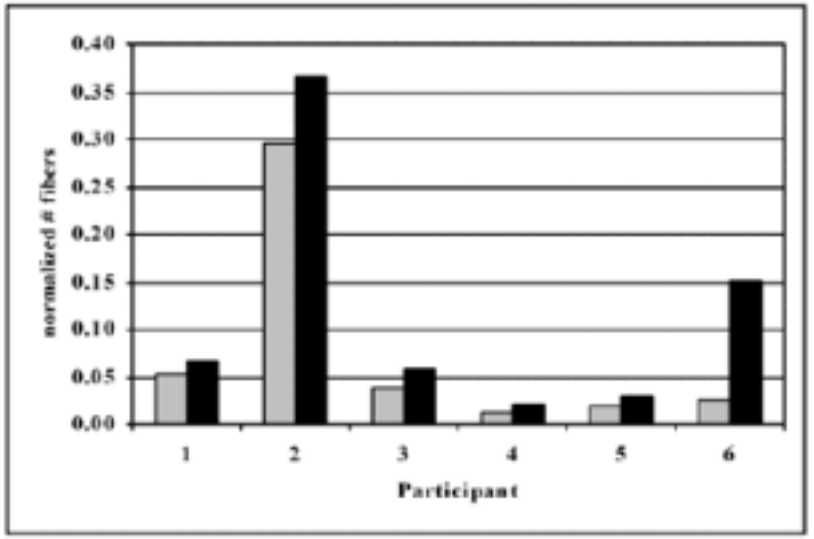
Abstract

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.

Les principes de la plasticité neurale

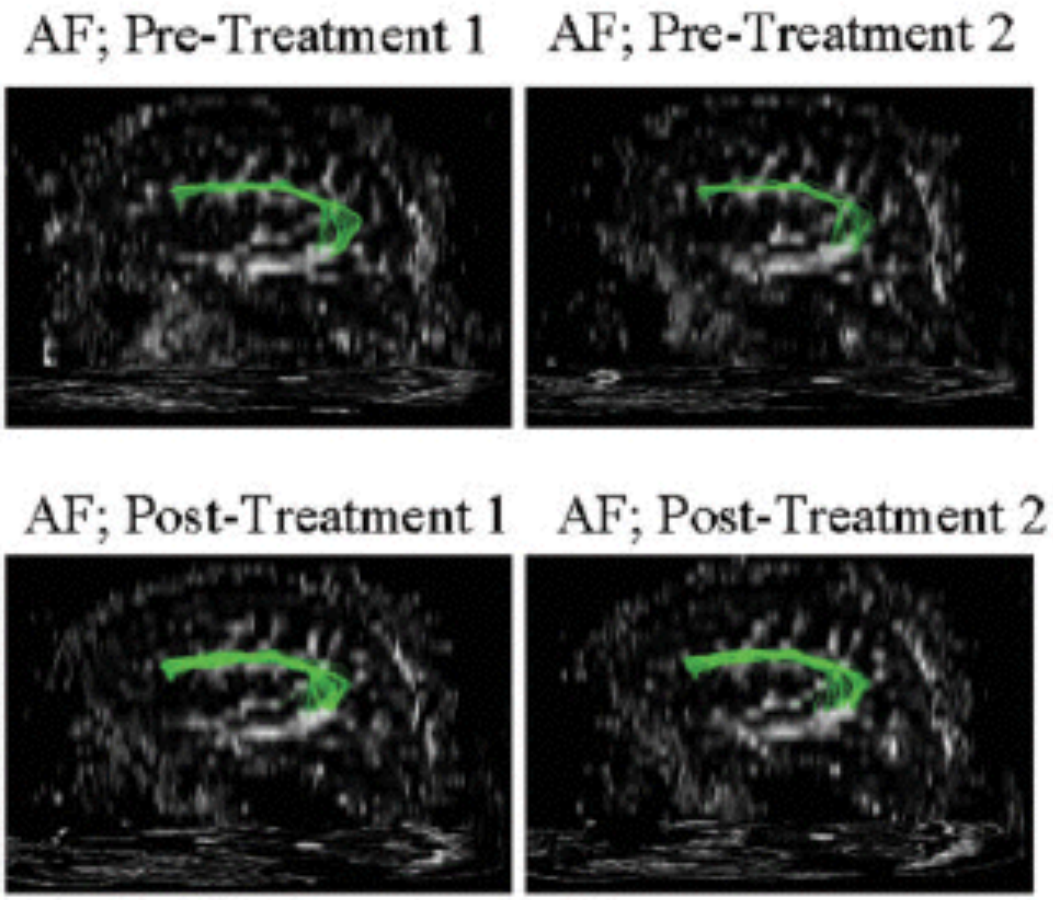
Augmentation du volume des faisceaux de substance blanche





Les principes de la plasticité neurale

Augmentation du volume des faisceaux de substance blanche



Les principes de la plasticité neurale

Réorganisation des cartes motrices corticales

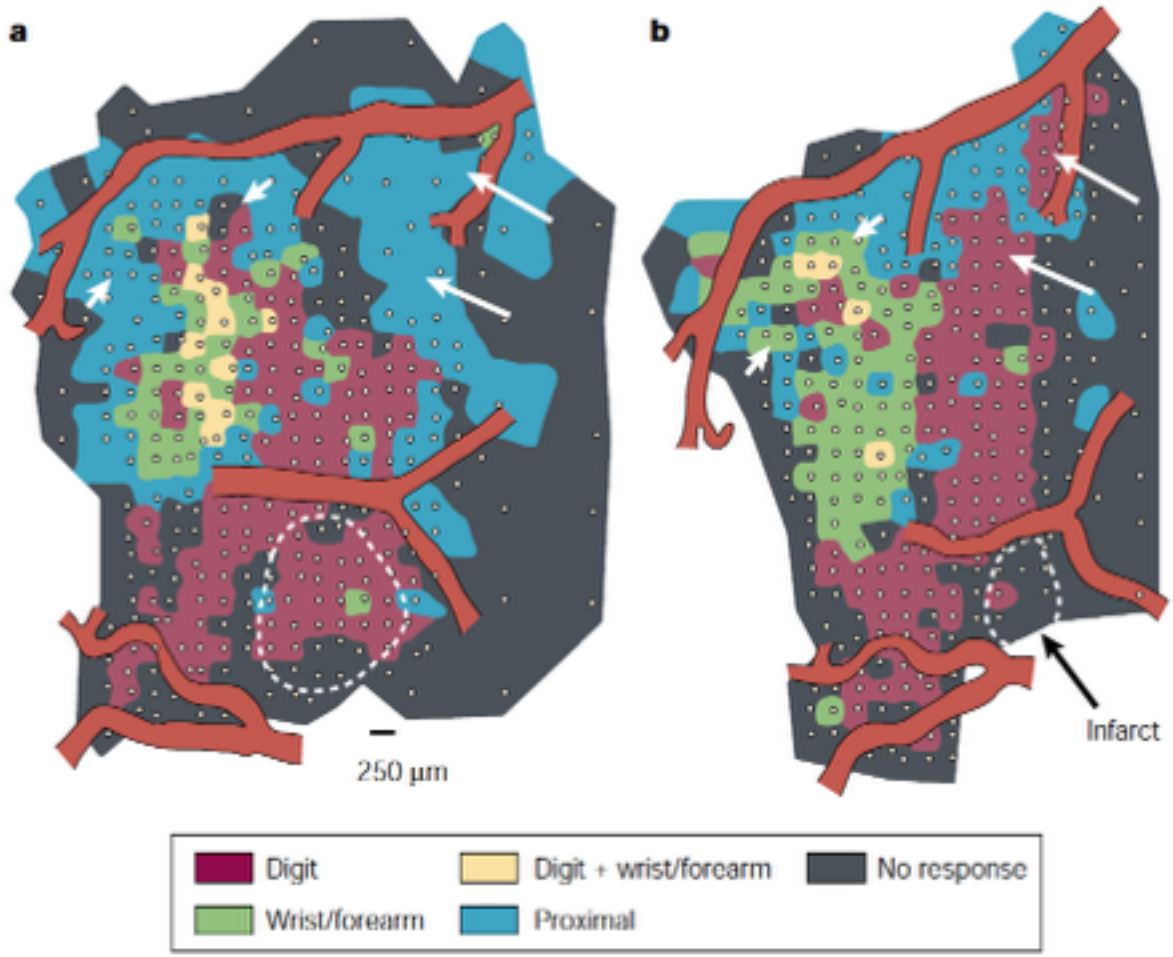
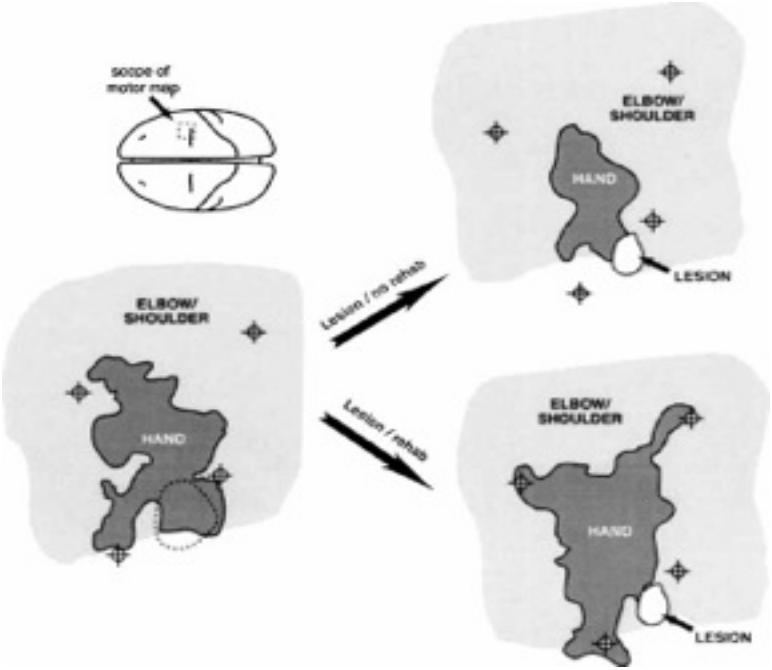


Figure 4 | **Reorganization in the motor cortex of a monkey after rehabilitative therapy.** **a** | Before infarct. **b** | After infarct and rehabilitative therapy. Note the large increase in the cortical representation of the wrist/forearm after therapy. Adapted with permission from REF 51 © 1996 American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

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.

OPINION

The musician's brain as a model of neuroplasticity

Thomas F. Münte, Eckart Altenmüller and Lutz Jäncke

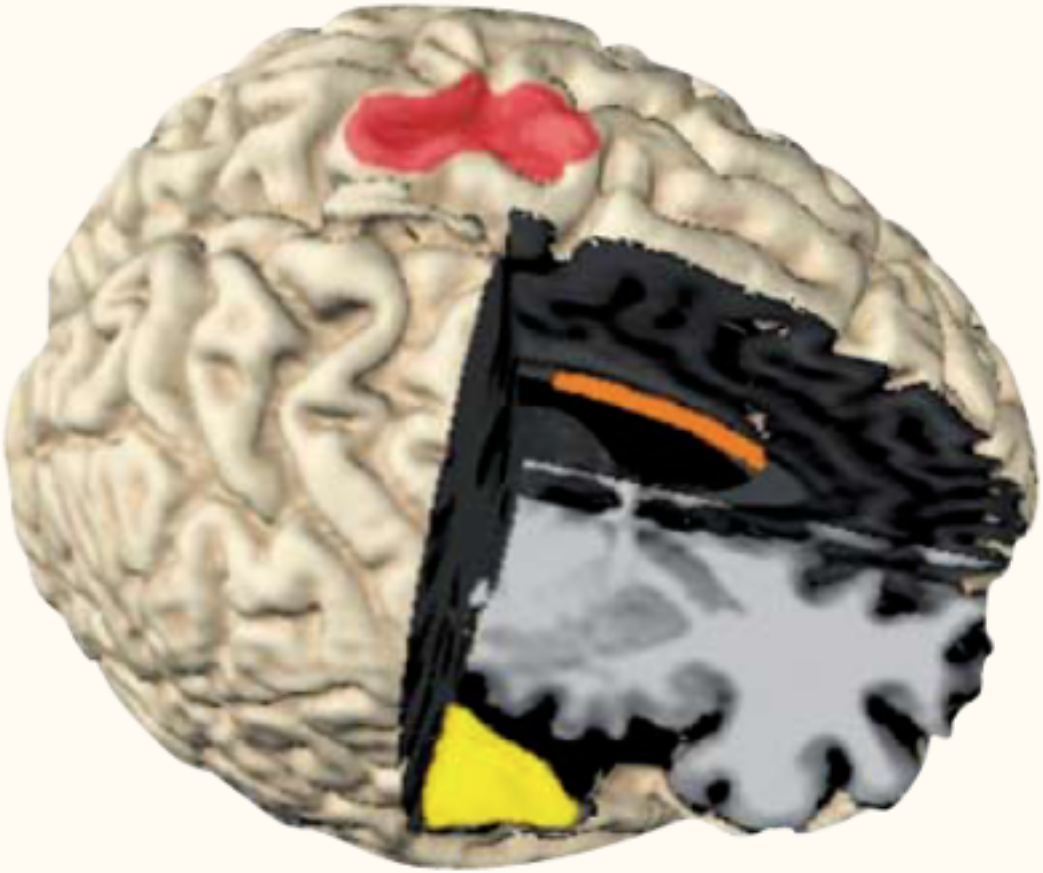
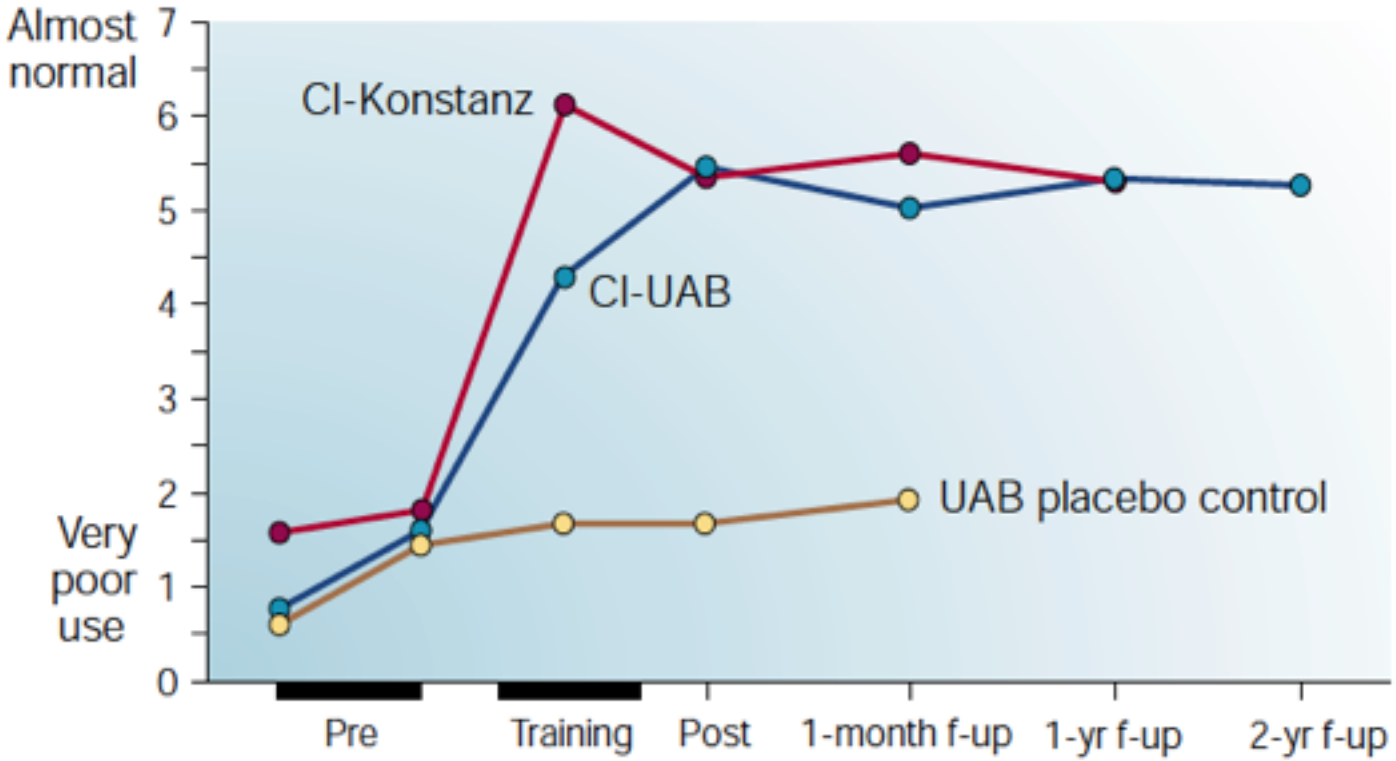
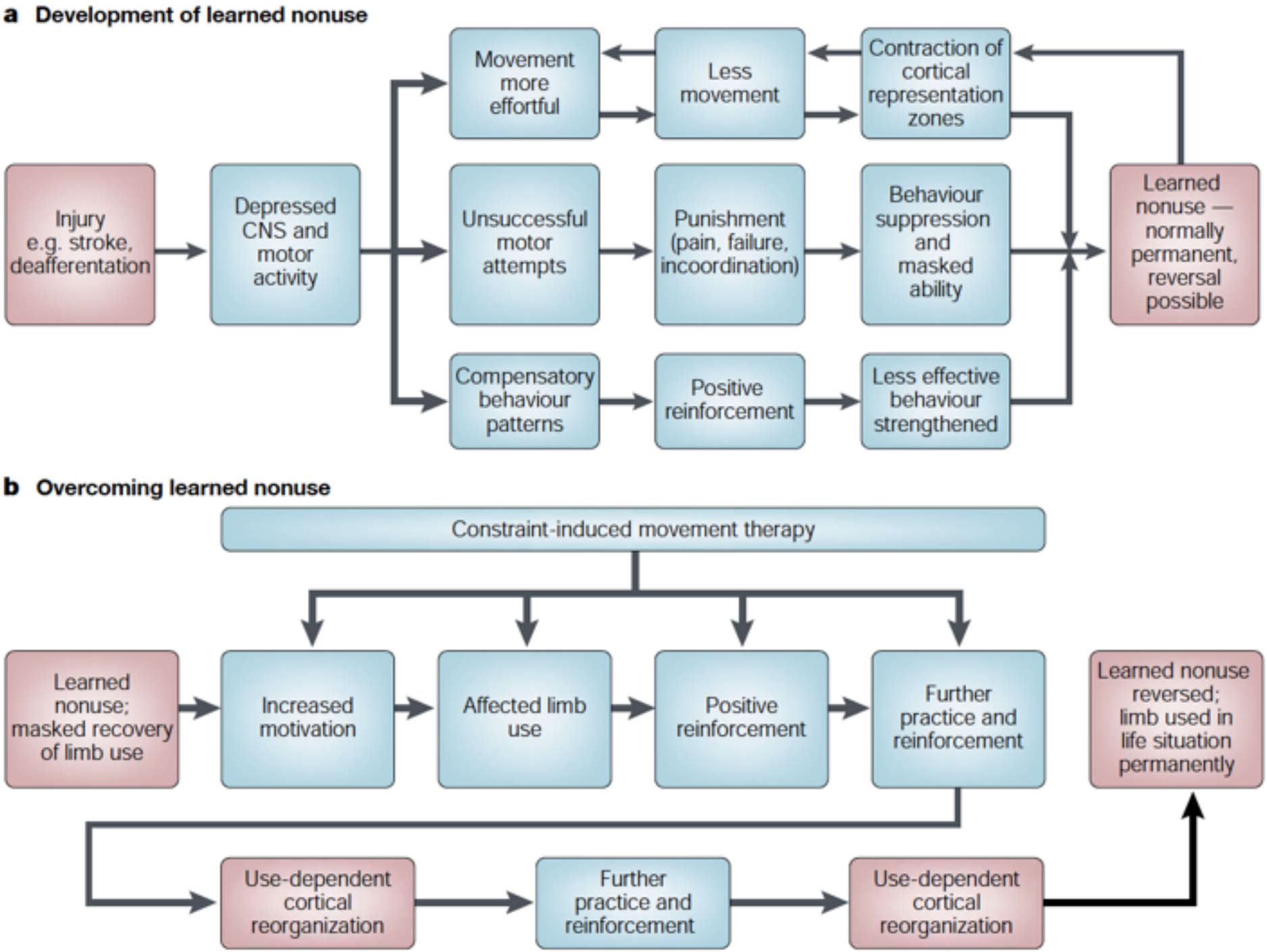


Figure 2 | **Structural changes in the brains of musicians.** Some of the brain areas that have been found to be enlarged in musicians in morphometric studies based on structural magnetic resonance imaging. Red, primary motor cortex; yellow, planum temporale; orange, anterior part of the corpus callosum.

La restauration par changement de stratégie


Almost normal
7
6
5
4
3
2
1
0
Very poor use
CI-Konstanz
CI-UAB
UAB placebo control
Pre
Training
Post
1-month f-up
1-yr f-up
2-yr f-up


a Development of learned nonuse
Injury e.g. stroke, deafferentation
Depressed CNS and motor activity
Movement more effortful
Less movement
Contraction of cortical representation zones
Unsuccessful motor attempts
Punishment (pain, failure, incoordination)
Behaviour suppression and masked ability
Compensatory behaviour patterns
Positive reinforcement
Less effective behaviour strengthened
Learned nonuse — normally permanent, reversal possible
b Overcoming learned nonuse
Constraint-induced movement therapy
Learned nonuse; masked recovery of limb use
Increased motivation
Affected limb use
Positive reinforcement
Further practice and reinforcement
Learned nonuse reversed; limb used in life situation permanently
Use-dependent cortical reorganization
Further practice and reinforcement
Use-dependent cortical reorganization

OPEN

Citation: Transl Psychiatry (2014) 4, e351; doi:10.1038/tp.2013.128

www.nature.com/tp

ORIGINAL ARTICLE

Social interaction plays a critical role in neurogenesis and recovery after stroke

VR Venna[1], Y Xu[1], SJ Doran[1], A Patrizz[1] and LD McCullough[1,2,3]

Stroke survivors often experience social isolation. Social interaction improves quality of life and decreases mortality after stroke. Male mice (20–25 g; C57BL/6N), all initially pair housed, were subjected to middle cerebral artery occlusion (MCAO). Mice were subsequently assigned into one of three housing conditions: (1) Isolated (SI); (2) Paired with their original cage mate who was also subjected to stroke (stroke partner (PH-SP)); or (3) Paired with their original cage mate who underwent sham surgery (healthy partner (PH-HP)). Infarct analysis was performed 72 h after stroke and chronic survival was assessed at day 30. Immediate post-stroke isolation led to a significant increase in infarct size and mortality. Interestingly, mice paired with a healthy partner had significantly lower mortality than mice paired with a stroke partner, despite equivalent infarct damage. To control for changes in infarct size induced by immediate post-stroke isolation, additional cohorts were assessed that remained pair housed for three days after stroke prior to randomization. Levels of brain-derived neurotrophic factor (BDNF) were assessed at 90 days and cell proliferation (in cohorts injected with 5-bromo-2′-deoxyuridine, BrdU) was evaluated at 8 and 90 days after stroke. All mice in the delayed housing protocol had equivalent infarct volumes (SI, PH-HP and PH-SP). Mice paired with a healthy partner showed enhanced behavioral recovery compared with either isolated mice or mice paired with a stroke partner. Behavioral improvements paralleled changes in BDNF levels and neurogenesis. These findings suggest that the social environment has an important role in recovery after ischemic brain injury.

Translational Psychiatry (2014) **4,** e351; doi:10.1038/tp.2013.128; published online 28 January 2014

Keywords: brain-derived neurotrophic factor; infarct; middle cerebral artery occlusion; neurogenesis; post-stroke recovery; social isolation

Mécanismes de la récupération de l'aphasie après un AVC

Rôle de la stimulation cérébrale non-invasive

Brain Lang. 2011 July ; 118(1-2): 40–50. doi:10.1016/j.bandl.2011.02.005.

Mechanisms of Aphasia Recovery After Stroke and the Role of Noninvasive Brain Stimulation

Roy H. Hamilton[1,2], **Evangelia G. Chrysikou**[3], and **Branch Coslett**[1,2]

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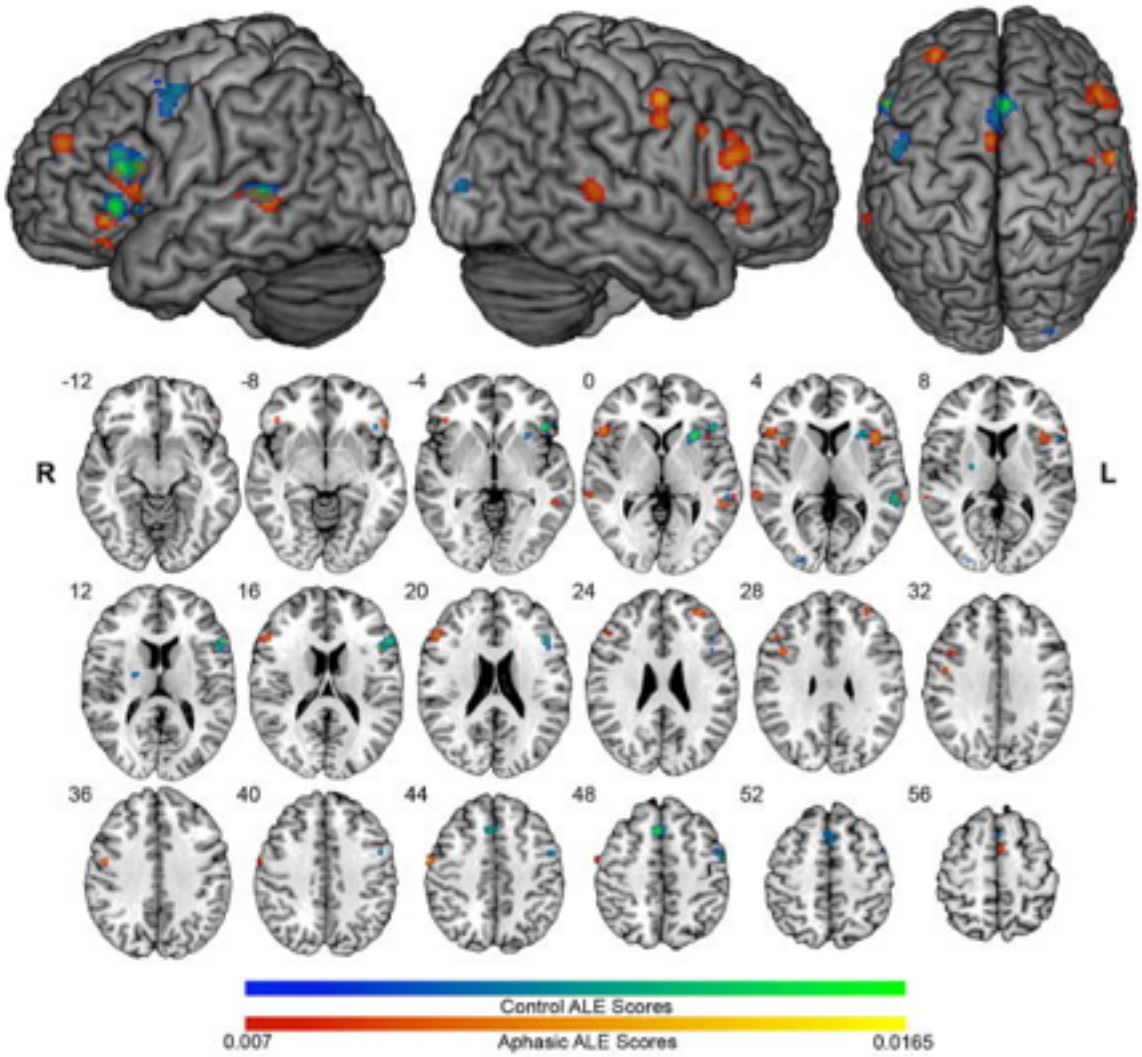
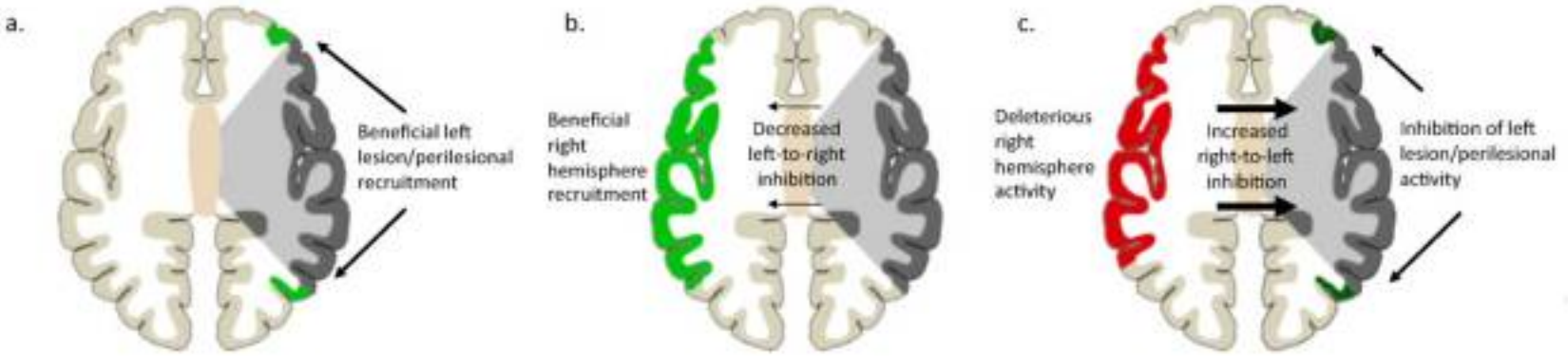
[3] University of Pennsylvania, Department of Psychology, Center for Cognitive Neuroscience, Philadelphia, PA

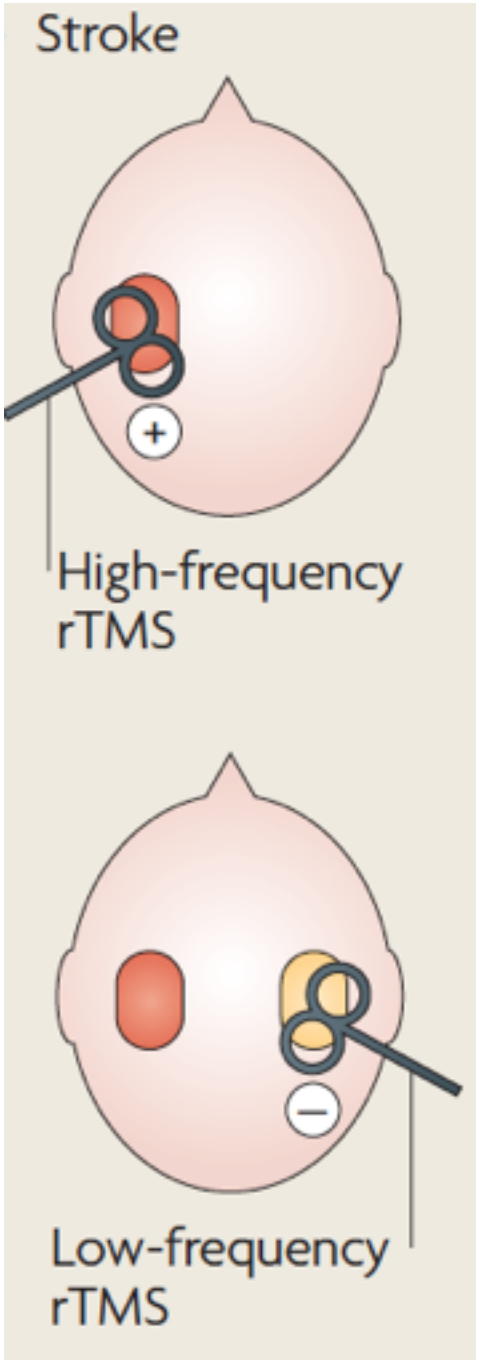
Abstract

One of the most frequent symptoms of unilateral stroke is aphasia, the impairment or loss of language functions. Over the past few years, behavioral and neuroimaging studies have shown that rehabilitation interventions can promote neuroplastic changes in aphasic patients that may be associated with the improvement of language functions. Following left-hemisphere strokes, the functional reorganization of language in aphasic patients has been proposed to involve both intrahemispheric interactions between damaged left-hemisphere and perilesional sites and transcallosal interhemispheric interactions between the lesioned left-hemisphere language areas and homotopic regions in the right hemisphere. A growing body of evidence for such reorganization comes from studies using transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS), two safe and noninvasive procedures that can be applied clinically to modulate cortical excitability during poststroke language recovery. We discuss a hierarchical model for the plastic changes in language representation that occur in the setting of dominant hemisphere stroke and aphasia. We further argue that TMS and tDCS are potentially promising tools for enhancing functional recovery of language and for further elucidating mechanisms of plasticity in patients with aphasia.



Turkel**t**aub et al.


a.
Beneficial left lesion/perilesional recruitment
b.
Beneficial right hemisphere recruitment
Decreased left-to-right inhibition
c.
Deleterious right hemisphere activity
Increased right-to-left inhibition
Inhibition of left lesion/perilesional activity


Stroke
+
High-frequency
rTMS
−
Low-frequency
rTMS

From: **Mechanisms Underlying Recovery of Motor Function After Stroke**

Arch Neurol. 2004;61(12):1844-1848. doi:10.1001/archneur.61.12.1844

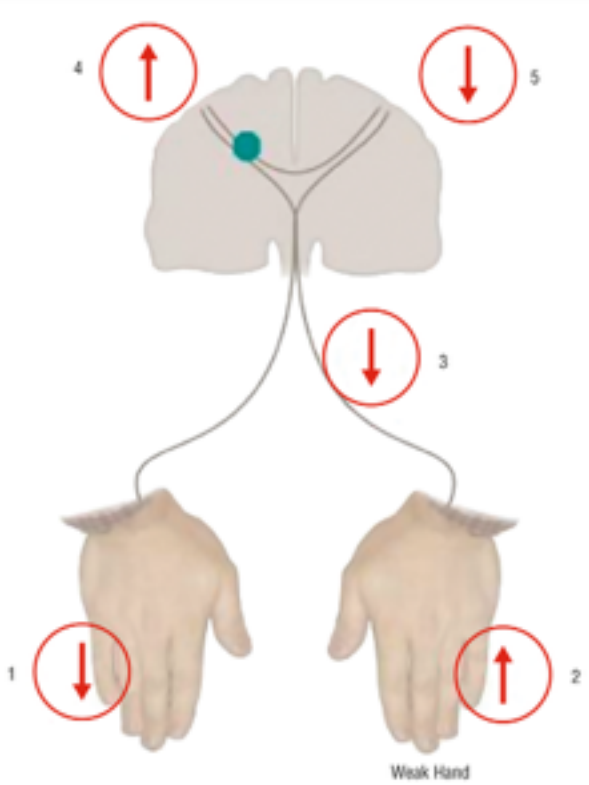


Figure Legend:

Diagram showing possible operational strategies to influence hand function (see “Possible Strategies to Enhance the Human Brain’s Response to Injury” section for details).

rTMS Studies in Aphasia

Study	N	Lesion Location	Time Since Stroke	Aphasia Type(s)	Location(s) Stimulated	Stimulation Parameters	Outcome Measures	Results
Naeser et al., 2005a	4	Large left frontotemporal cortical/ subcortical lesions (n=3); frontotemporal subcortical lesion with cortical sparing (n=1)	5–11 years	Broca's (n=2); anomic/conduction (n=1); global (n=1)	Right pars triangularis	1 Hz rTMS; 90/MT; 10 daily sessions over two weeks	Boston Naming Test (BNT), Boston Diagnostic Aphasia Examination (BDAE); Snodgrass and Vanderwart (S&V) picture naming	Improved accuracy and speeded reaction time for S&V items after 10 TMS sessions; improvement on BNT and Animal and Tool/ Implement subtests of BDAE 2 and 8 months after stimulation
Naeser et al., 2005b*	1	Left frontotemporal subcortical lesion with cortical sparing	6.5 years	Global	Best cortical region of interest (ROI) determined by stimulation of multiple left hemisphere targets; Right pars triangularis selected	1 Hz rTMS; 90/MT; 10 daily sessions over two weeks	BNT, BDAE, Cognitive Linguistic Quick Test (CLQT)	Improvements in BNT and Animal and Tool/ Implement subtests of BDAE as above; further improvement on BDAE and CLQT in speech therapy 1 year following stimulation
Martin et al., 2009	2	Subjects 1&2: Large left frontotemporal cortical/ subcortical lesions; Subject 2: Additional involvement of fibers under SMA, Wernicke's area, and posterior	1.5 and 10 years	Nonfluent	ROI determined by stimulation of multiple	1 Hz rTMS; 90/MT; 10 daily sessions over two weeks	BNT, BDAE, Cookie Theft Picture Description,	Subject 1: Improvement on BNT, BDAE, and Cookie Theft; new perilesional left frontal activation on fMRI 16 months post-TMS; Subject 2: No significant language improvement

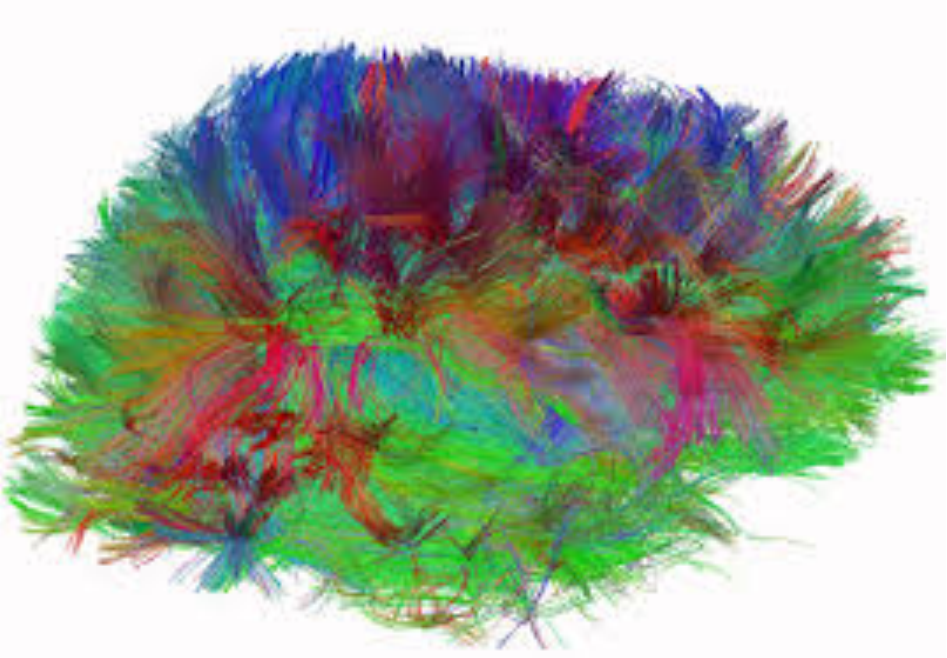
Study	N	Lesion Location	Time Since Stroke	Aphasia Type(s)	Location(s) Stimulated	Stimulation Parameters	Outcome Measures	Results
		middle frontal gyrus			targets; Right pars triangularis selected		fMRI during overt naming task	or fMRI changes
Naeser et al., 2010	1	Left temporal cortical/ subcortical lesion; minor involvement of left inferior frontal gyrus	2 years	Nonfluent	ROI determined by stimulation of multiple targets; Right pars triangularis selected	1 Hz rTMS; 90/MT; 10 daily sessions over two weeks; patient started on CPAP	BDAE, BNT	Increased phrase length, auditory comprehension, and naming persisting 3 months, 6 months, and 2.4 years after stimulation
Hamilton et al., 2010	1	Large left frontotemporal cortical/ subcortical lesion	7 years	Broca's	ROI determined by stimulation of multiple targets; Right pars triangularis selected	1 Hz rTMS; 90/MT; 10 daily sessions over two weeks	Western Aphasia Battery (WAB), BDAE, Cookie Theft Picture Description	Improved object and action naming and Cookie Theft. Persistent benefits at 2.6, and 10 months
Kakuda et al., 2010a	4	Left frontotemporal cortical lesion (n=2); frontal cortical lesion (n=1); left putamen (n=1)	5–28 years	Motor-dominant (impaired speech).	Site determined by fMRI activation during naming task: left frontal (n=2) and right frontal (n=2).	1 Hz rTMS; 90/MT; 10 sessions over six days	Japanese versions of WAB, Standard Language Test of Aphasia (SLTA), and Supplementary tests of SLTA (SLTA-ST)	Presumed improvement in WAB, SLTA, and SLTA-ST (no statistical analyses)
Kakuda et al., 2010b	2	Left MCA territory lesions	7 months and 8 months	Sensory-dominant (impaired comprehension)	Wernicke's area	1 Hz rTMS; 90/MT; 10 sessions over six days; daily language therapy	Token test, Japanese SLTA	Presumed improvement in scores on Token test and some subtests of SLTA that persisted at 3 months (no statistical analyses).
Barwood et al., 2010	12	Left MCA territory cortical/ subcortical lesions	2–6 years	Nonfluent	Right pars triangularis; subjects received real (n=6) or sham (n=6) stimulation	1 Hz rTMS; 90/MT; 10 daily sessions over 10 days	BDAE, Cookie Theft, BNT, S&V.	Improved naming and picture description among subjects receiving real TMS but not sham; persistent effects 2 months after real stimulation.

Study	N	Lesion Location	Time Since Stroke	Aphasia Type(s)	Location(s) Stimulated	Stimulation Parameters	Outcome Measures	Results
Weiduschat et al., 2010	10	Left posterior temporoparietal lesions (n=4);frontal cortical/ subcortical lesions (n=3); subcortical lesions (n=2); entire left MCA territory (n=1)	16 weeks	Wernicke's (n=5); Broca's (n=2); global (n=1); amnestic (n=1)	Right pars triangularis (study group, n=5), vertex (control control group, n=5)	1 Hz rTMS; 90/MT; 10 daily sessions over two weeks; Speech and language therapy after each TMS session	Aachen Aphasia Test (AAT), PET activation during verb generation task	Improved AAT scores 2 weeks after stimulation in study patients but not control group; PET activation toward right hemisphere in control but not in treatment group 2 weeks after stimulation compared to baseline; no relationship between laterality shift and clinical improvement.

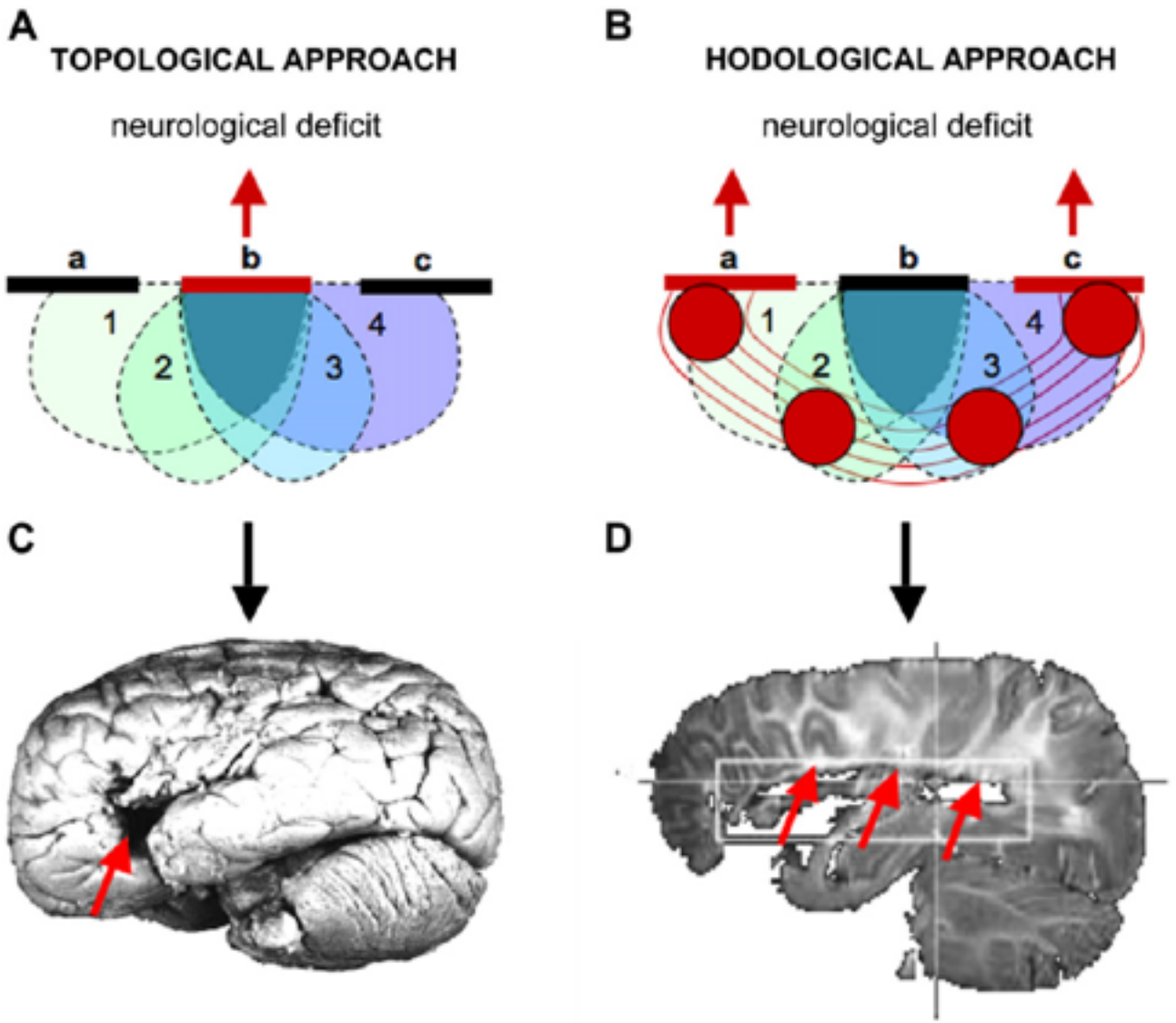
tDCS Studies in Aphasia

Study	N	N Lesion Location	Time Since Stroke	Aphasia Type(s)	Location(s) Stimulated	Stimulation Parameters	Outcome Measure	Results
Monti et al., 2008	8	Left frontal cortical/subcortical lesions (n=3); frontoparietal cortical/subcortical lesions (n=2); 8 frontotemporoparietal cortical/subcortical lesions (n=2); frontoparietal subcortical lesion	2–8 years	Broca's aphasia (n=4); global aphasia (n=4)	Broca's area; occipital lobe control site	Single session of anodal, cathodal, and sham tDCS over Broca's area at 1 mA for 20 min; cathodal and sham tDCS applied to occipital lobe in separate experiment	Picture naming	Improved picture naming accuracy immediately after cathodal tDCS of Broca's area but not anodal, sham, or occipital tDCS
Fiori et al., 2010	3	Left frontoparietal subcortical lesion (n=1); frontoparietal 3 cortical/subcortical lesion (n=1); large frontotemporoparietal cortical/subcortical lesion (n=1)	~2–6 years	Mild (n=1), moderate (n=1), and severe (n=1) nonfluent aphasia	Wernicke's area	5 consecutive daily sessions of anodal (1 mA for 20 min) or sham tDCS paired with language therapy	Picture naming	Improved naming accuracy and reaction time after 5 days of anodal but not sham tDCS. In 2 subjects, improvements persisted at 1 and 3 weeks after stimulation
Baker et al., 2010	10	Left temporoparietal lesions (n=4); frontotemporal lesions (n=3); frontotemporoparietal lesion (n=1); 10 temporoparietooccipital lesion (n=1); Lesion of entire MCA territory, medial frontal lobe, and basal ganglia (n=1)	~1–20 years	Anomic aphasia (n=6), Broca's aphasia (n=4)	tDCS localization guided to left hemisphere targets by fMRI activation during an overt naming task: premotor cortex (n=5), dorsolateral prefrontal cortex (n=2), anterior prefrontal cortex (n=1), pars triangularis (n=1), pars opercularis (n=1)	5 consecutive daily sessions of anodal (1 mA for 20 min) or sham tDCS paired with anomia therapy	Picture naming	Improved picture naming after anodal tDCS compared to sham stimulation; persistent benefits 1 week after treatment

Approche “en réseau” de la récupération après un AVC



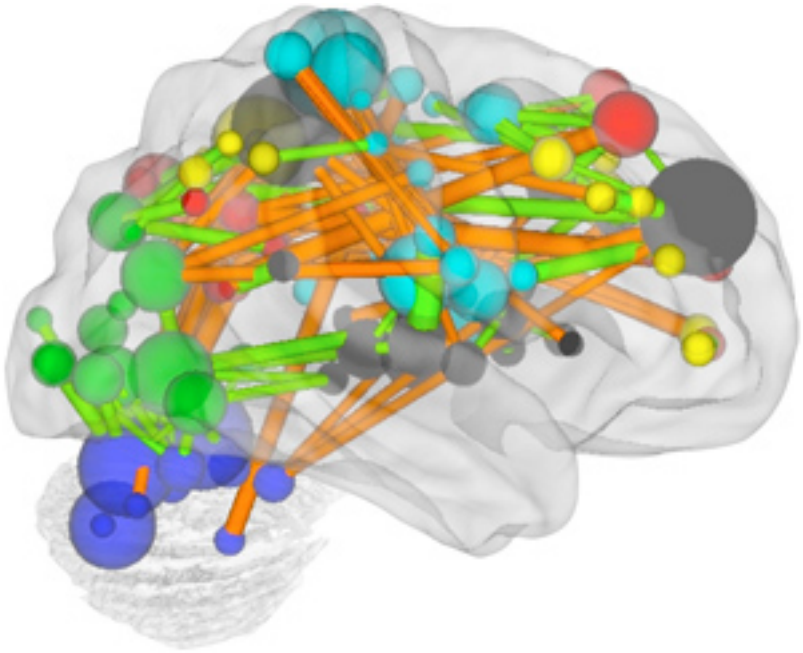
Approche “en réseau” de la récupération après un AVC



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

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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

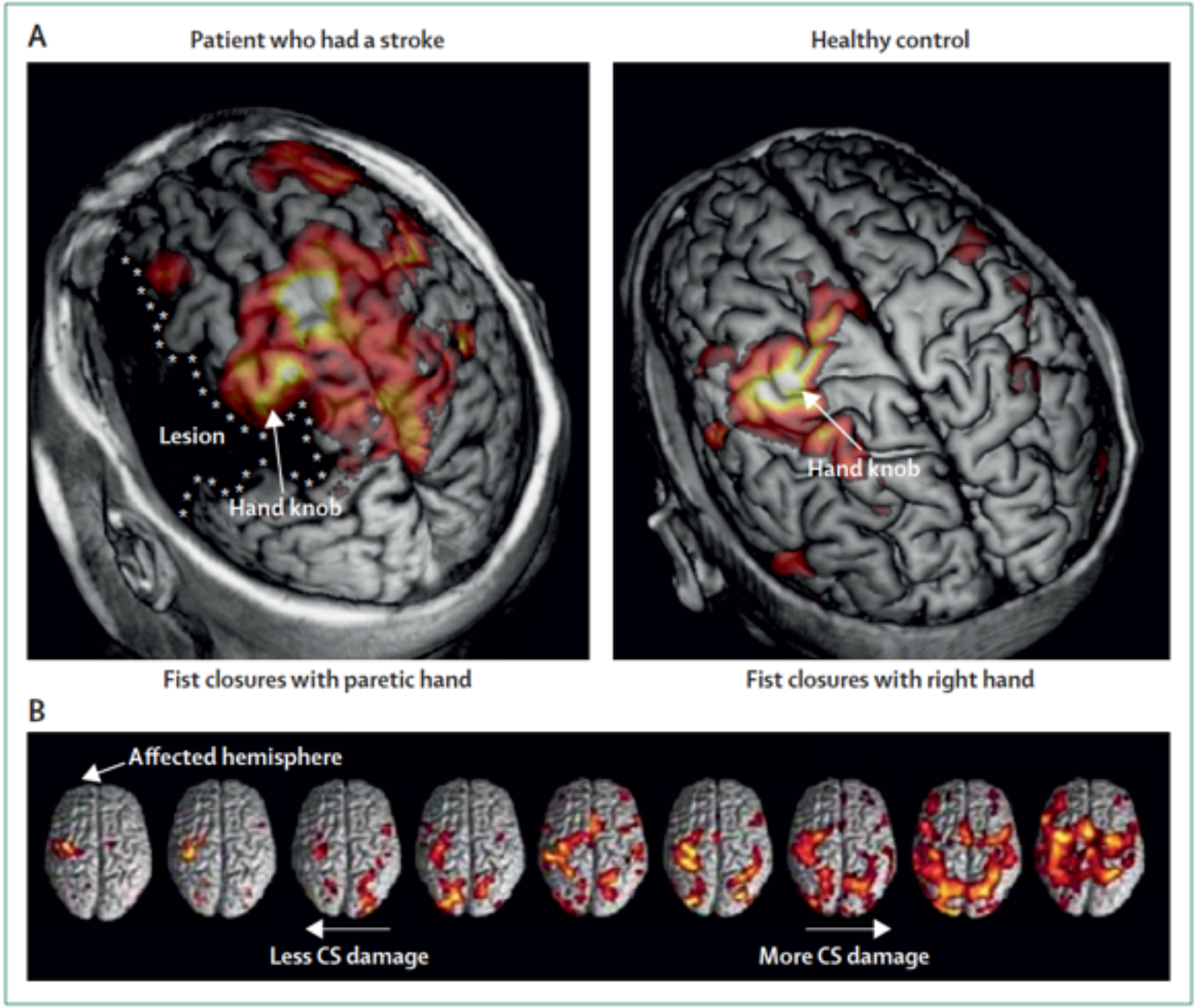
“..recent developments in computational neuroscience enable us to **move beyond the mere localisation of brain activity.** In particular, they allow us **to consider the dynamics within an ensemble or an entire network of areas sustaining a particular cognitive process or behaviour**.”

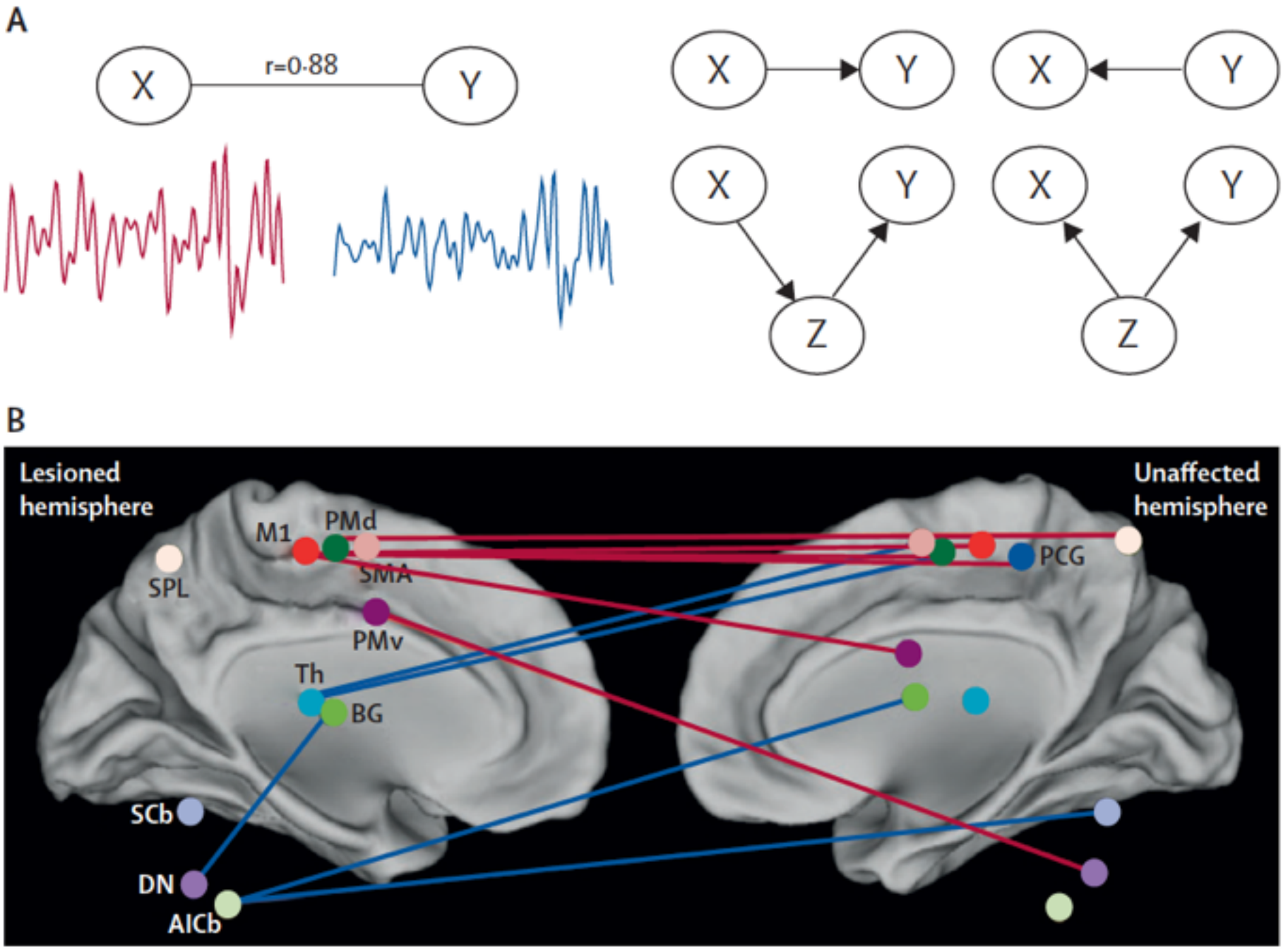
Approche “en réseau” de la récupération après un AVC

“..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, whereas recovery of function weeks after stroke was paralleled by normalisation of interhemispheric connectivity.**

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


A
Patient who had a stroke
Healthy control
Lesion
Hand knob
Hand knob
Fist closures with paretic hand
Fist closures with right hand
B
Affected hemisphere
Less CS damage
More CS damage


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
PCG
SCb
DN
AICb

“Consistently, transient downregulation 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.”

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BRAIN
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REVIEW ARTICLE

Reorganization of cerebral networks after stroke: new insights from neuroimaging with connectivity approaches

Christian Grefkes[1,2] and Gereon R. Fink[2,3]

The motor system comprises a network of cortical and subcortical areas interacting via excitatory and inhibitory circuits, thereby governing motor behaviour. The balance within the motor network may be critically disturbed after stroke when the lesion either directly affects any of these areas or damages-related white matter tracts. A growing body of evidence suggests that abnormal interactions among cortical regions remote from the ischaemic lesion might also contribute to the motor impairment after stroke. Here, we review recent studies employing models of functional and effective connectivity on neuroimaging data to investigate how stroke influences the interaction between motor areas and how changes in connectivity relate to impaired motor behaviour and functional recovery. Based on such data, we suggest that pathological intra- and inter-hemispheric interactions among key motor regions constitute an important pathophysiological aspect of motor impairment after subcortical stroke. We also demonstrate that therapeutic interventions, such as repetitive transcranial magnetic stimulation, which aims to interfere with abnormal cortical activity, may correct pathological connectivity not only at the stimulation site but also among distant brain regions. In summary, analyses of connectivity further our understanding of the pathophysiology underlying motor symptoms after stroke, and may thus help to design hypothesis-driven treatment strategies to promote recovery of motor function in patients.

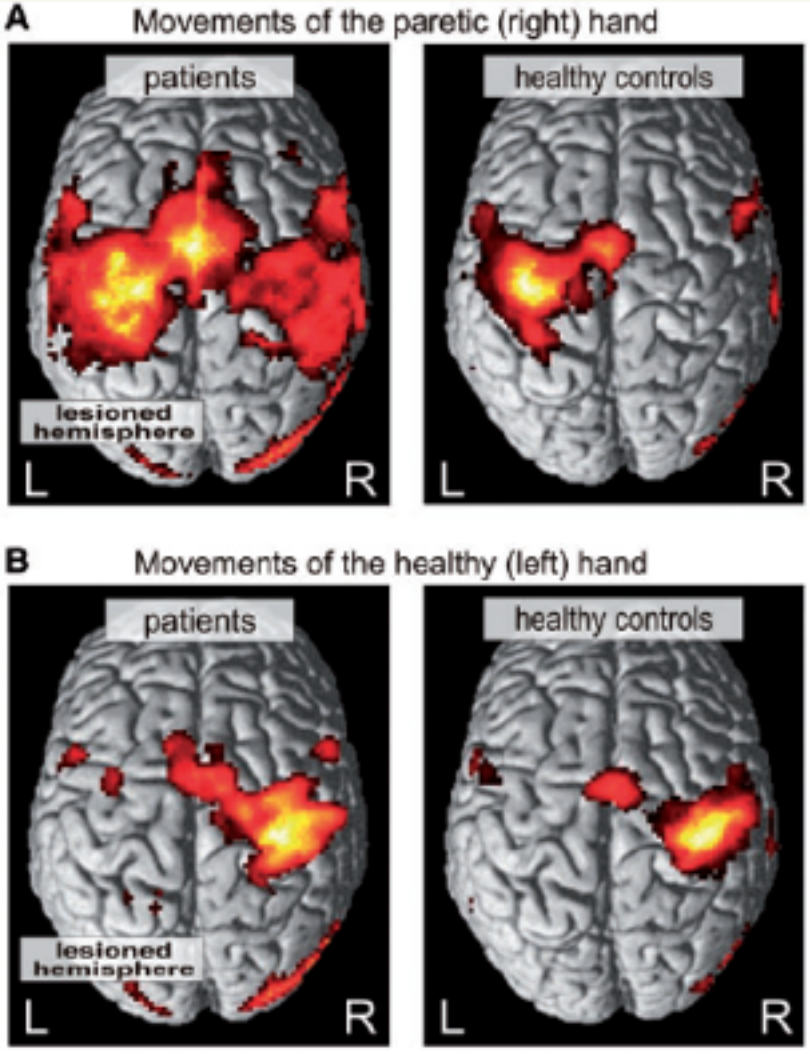
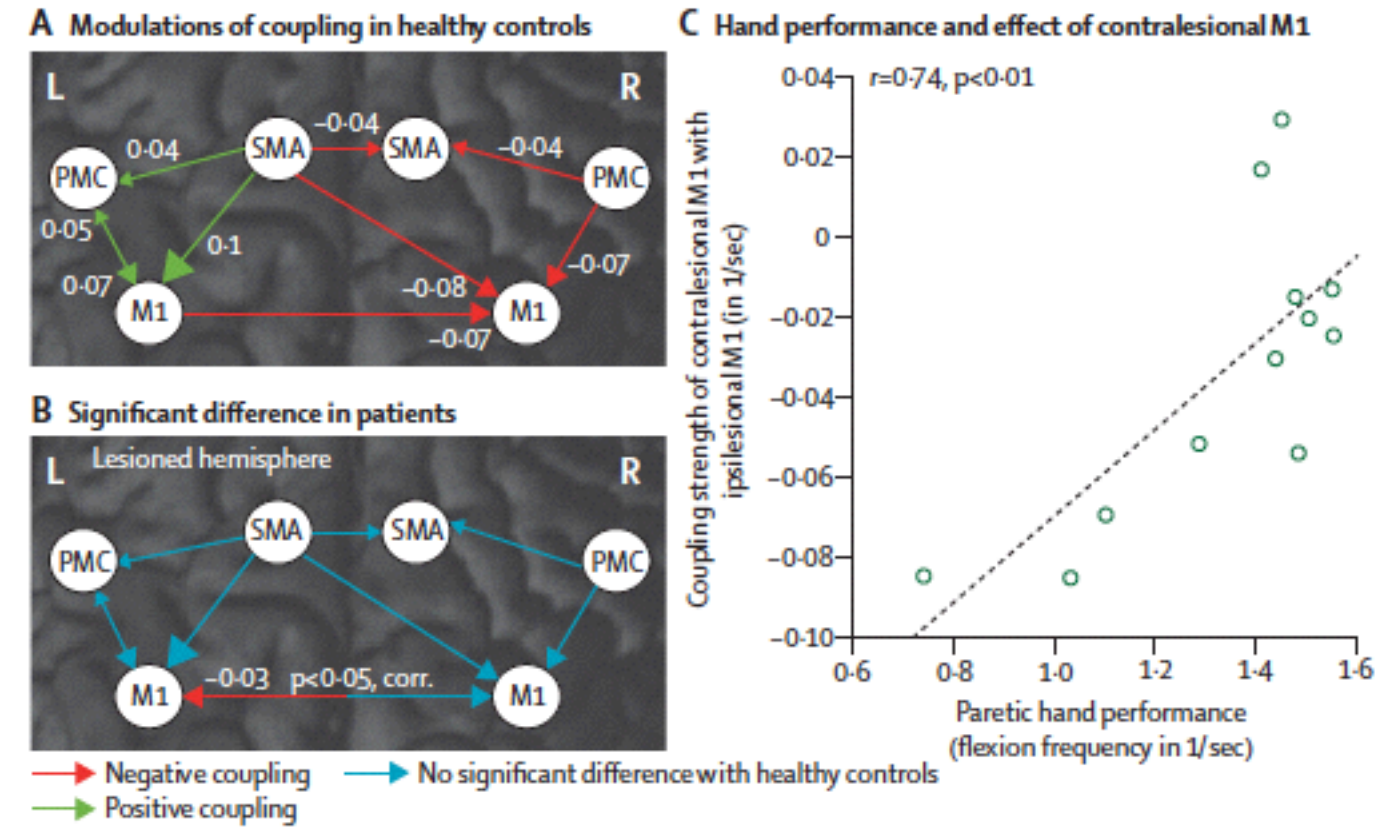
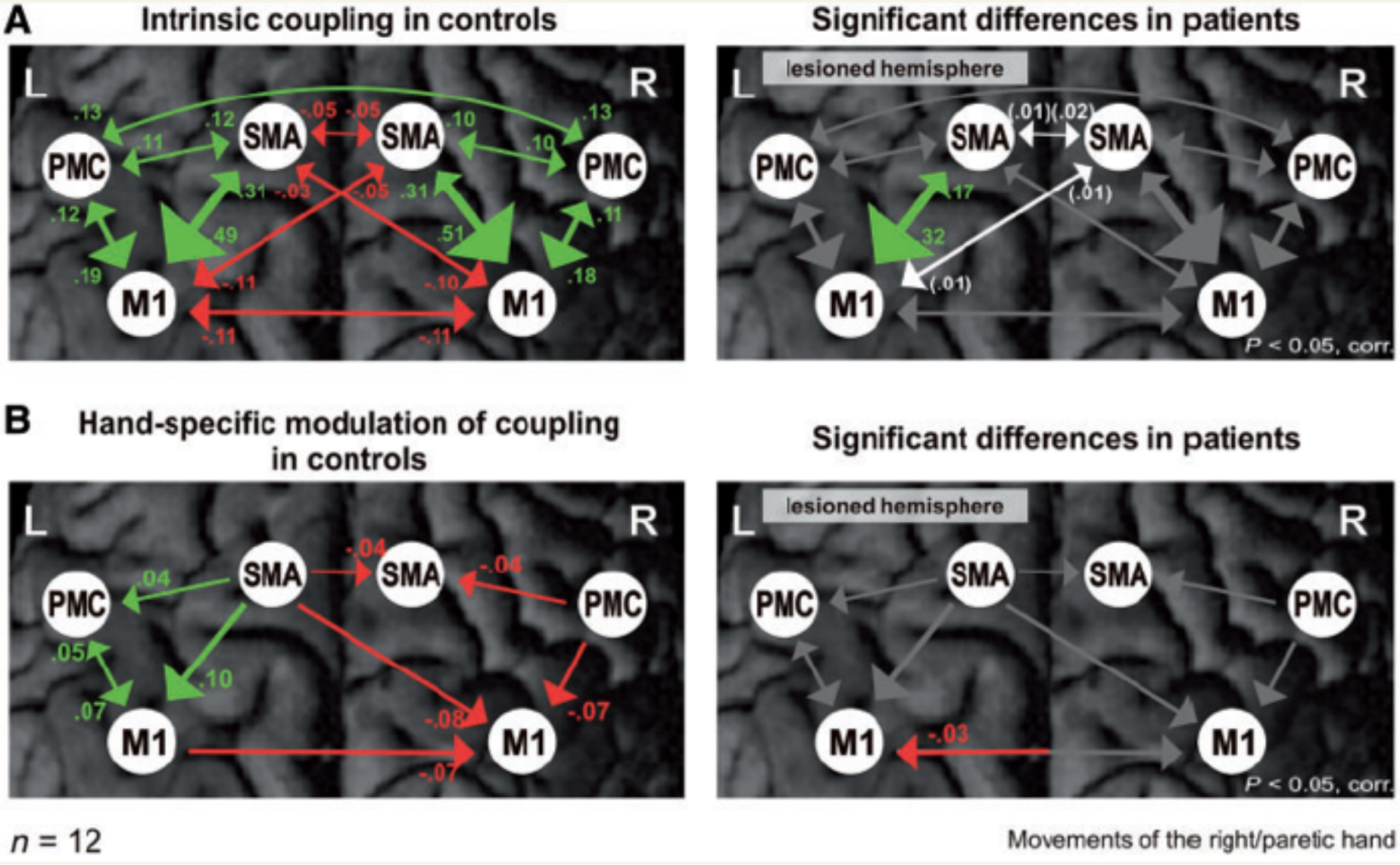


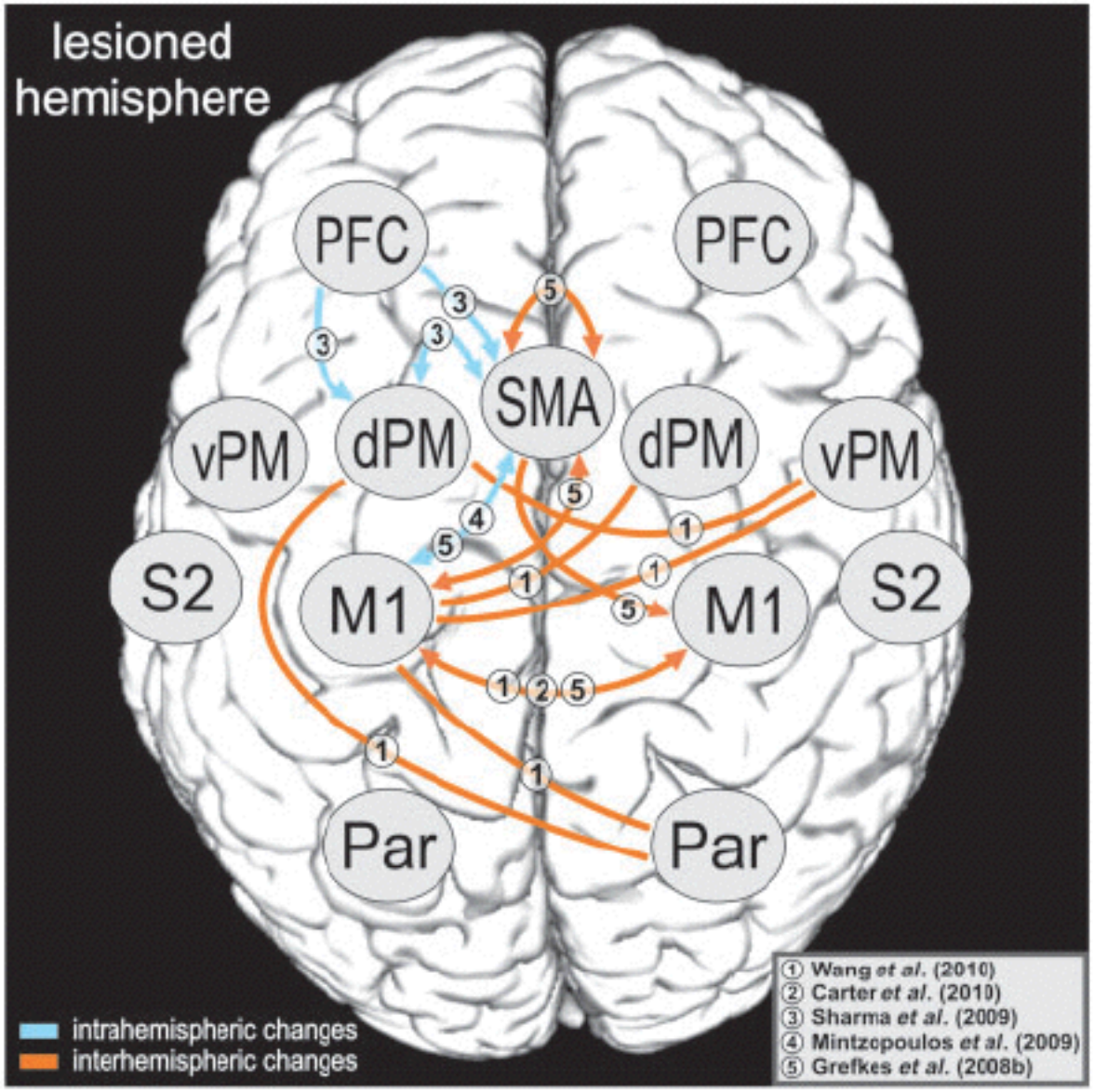
Figure 1 Neural activity during movement of the left or right hand in healthy subjects and in stroke patients with left-sided subcortical lesions ($P < 0.05$, corrected on the cluster level). Activation clusters were surface rendered onto a canonical brain. In stroke patients, movements of the impaired hand were associated with significant activations in ipsilateral (= contralesional) motor areas, which were absent in the healthy controls (**A**) or when moving the unaffected hand (**B**) (adapted from Grefkes *et al.*, 2008*b*, with permission).


A Modulations of coupling in healthy controls
L
R
PMC
SMA
SMA
PMC
M1
M1
0·04
−0·04
−0·04
0·05
0·1
0·07
−0·07
−0·08
−0·07
B Significant difference in patients
Lesioned hemisphere
L
R
PMC
SMA
SMA
PMC
M1
M1
−0·03 p<0·05, corr.
C Hand performance and effect of contralesional M1
r=0·74, p<0·01
Coupling strength of contralesional M1 with ipsilesional M1 (in 1/sec)
0·04
0·02
0
−0·02
−0·04
−0·06
−0·08
−0·10
0·6
0·8
1·0
1·2
1·4
1·6
Paretic hand performance (flexion frequency in 1/sec)
Negative coupling
Positive coupling
No significant difference with healthy controls

“The brain can be regarded as a system of elements (e.g. neuronal populations in distinct cortical areas) that interact with each other in a temporally and spatially specific fashion. Functional neuroimaging can be used to investigate two fundamental dimensions of how the system ‘brain’ is organized (Friston, 2002).”

“the results of the functional connectivity studies in stroke thus far discussed imply that recovery of motor function depends on reorganization processes within both hemispheres leading to enhanced inter-hemispheric connectivity which might occur, however, at the cost of network efficiency underlying recovered function.”


A
Intrinsic coupling in controls
Significant differences in patients
lesioned hemisphere
L
R
SMA
SMA
PMC
PMC
M1
M1
.13
.12
.11
-.05
-.05
.10
.10
.13
.31
-.03
-.05
.31
.12
.49
.51
.11
.19
-.11
-.10
.18
-.11
-.11
(.01)(.02)
.17
(.01)
.32
(.01)
P < 0.05, corr.
B
Hand-specific modulation of coupling in controls
Significant differences in patients
lesioned hemisphere
L
R
SMA
SMA
PMC
PMC
M1
M1
-.04
.04
-.04
.05
.10
.07
-.08
-.07
-.07
-.03
P < 0.05, corr.
n = 12
Movements of the right/paretic hand


lesioned hemisphere
PFC
PFC
SMA
vPM
dPM
dPM
vPM
S2
M1
M1
S2
Par
Par
intrahemispheric changes
interhemispheric changes
① Wang et al. (2010)
② Carter et al. (2010)
③ Sharma et al. (2009)
④ Mintzopoulos et al. (2009)
⑤ Grefkes et al. (2008b)

Merci de votre attention !