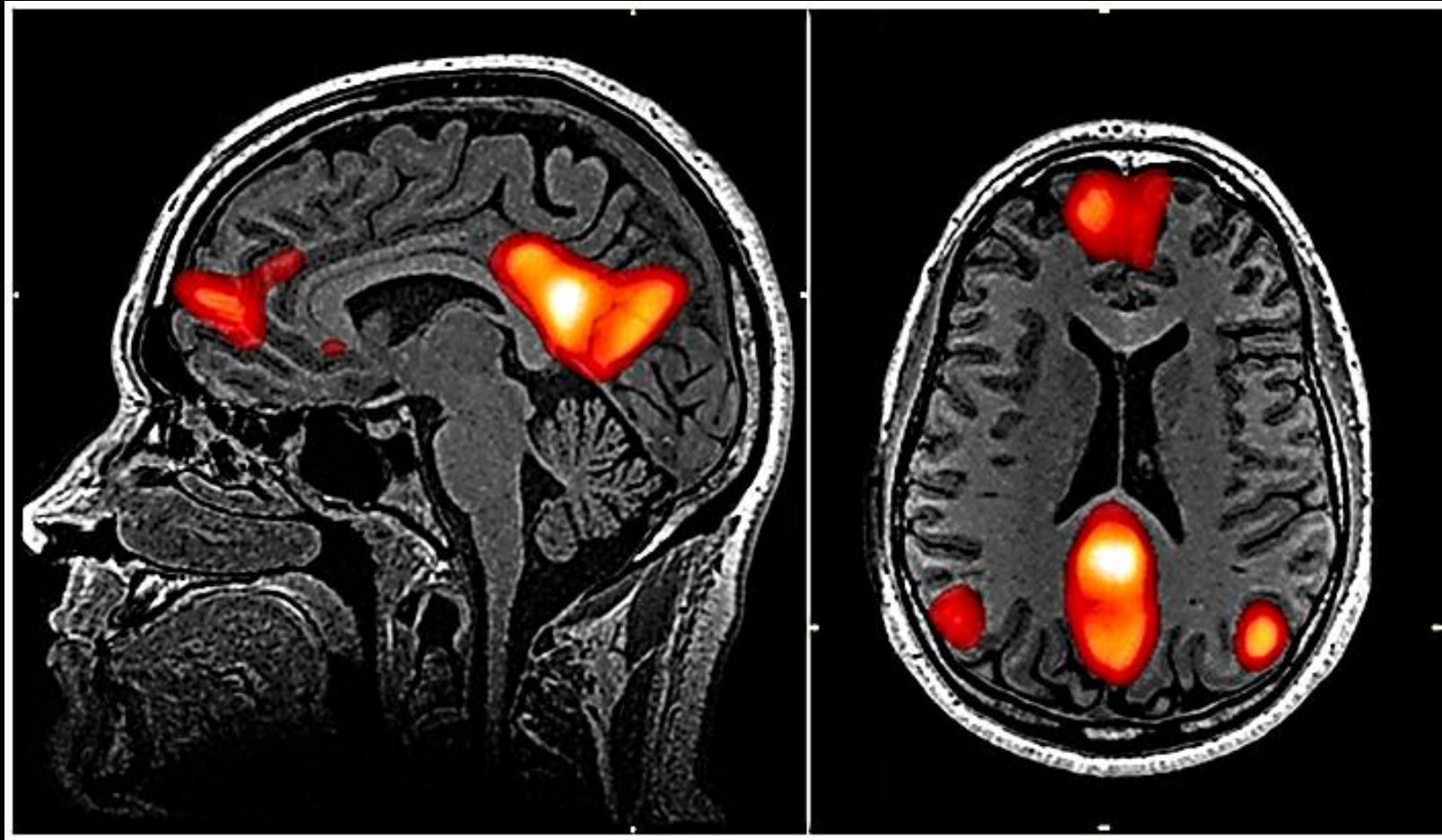


# ΛΕΙΤΟΥΡΓΙΚΗ ΜΑΓΝΗΤΙΚΗ ΤΟΜΟΓΡΑΦΙΑ ΣΕ ΚΑΤΑΣΤΑΣΗ ΑΔΡΑΝΕΙΑΣ (rs-fMRI)



Λιούτα Ευαγγελία, MSc, Dr Sc υποψ.

Νευροχειρουργική Κλινική, ΕΚΠΑ, Νοσοκομείο Ευαγγελισμός

# Εισαγωγή

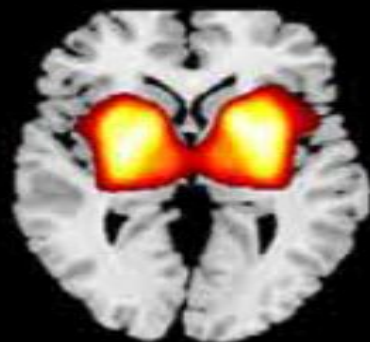
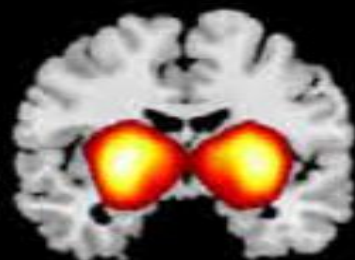
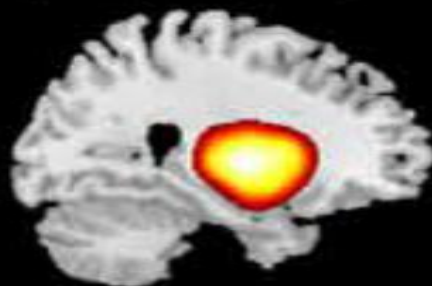
- Λειτουργική Μαγνητική Απεικόνιση σε αδράνεια (RS-fMRI)
- Biswal et al. (1995)
- Χαμηλής συχνότητας ( $<0.1$  Hz) «αυθορμητη-αυτοματη» εγκεφαλική δραστηριότητα.
- Συγχρονισμένη πυροδότηση νευρικών κυττάρων

Allen et al. (2011)

ΠΑΡΑΔΕΙΓΜΑΤΑ

BASAL GANGLIA NETWORK

IC 21  
(-28, -7, -1)

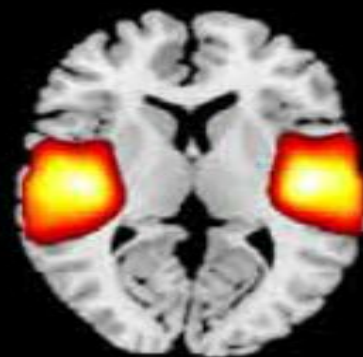
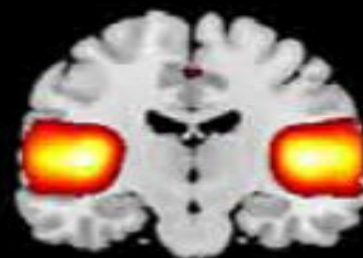
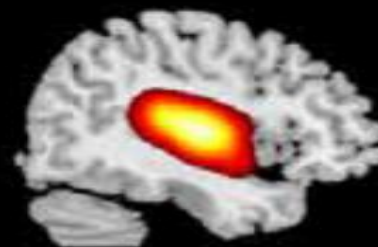


L

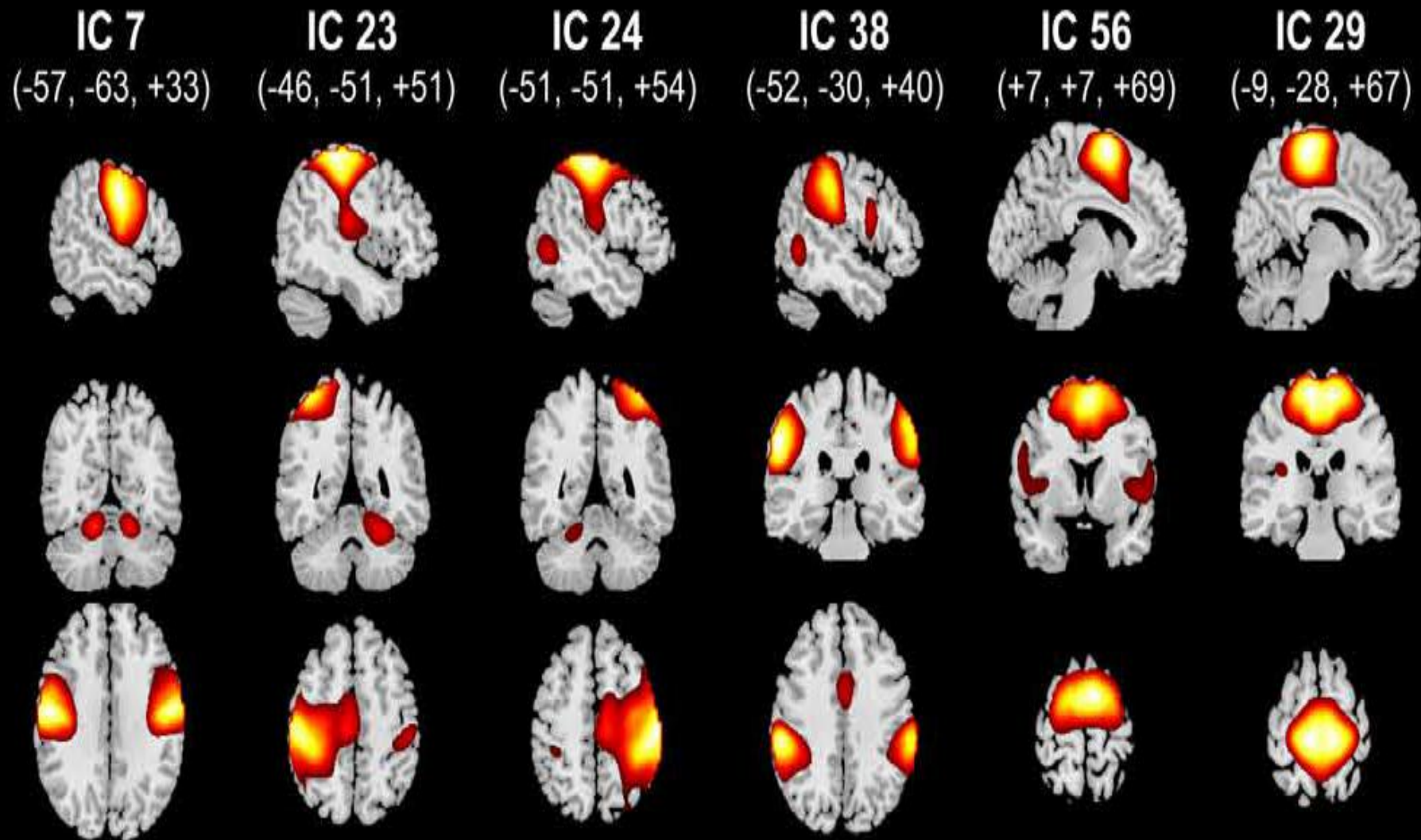
R

AUDITORY NETWORK

IC 17  
(-46, -16, +6)



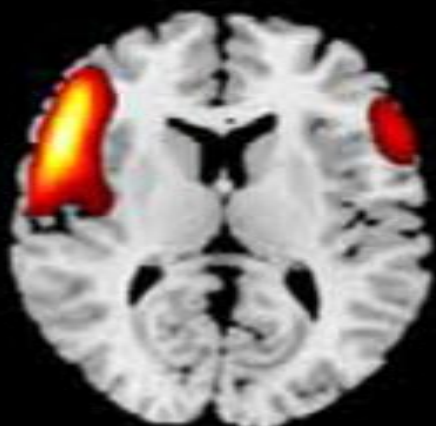
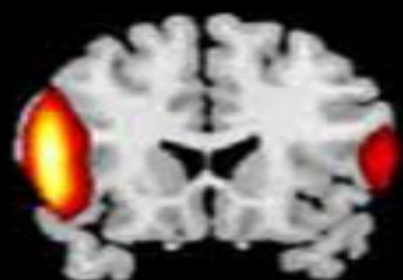
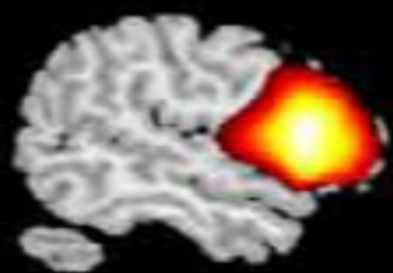
SENSORIMOTOR NETWORKS





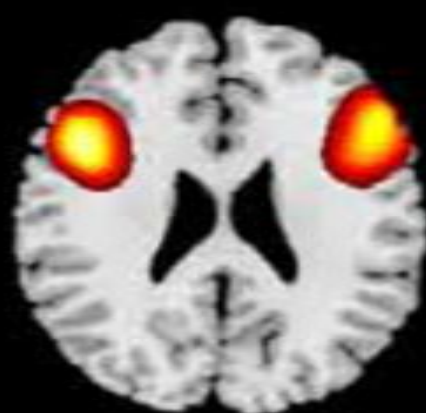
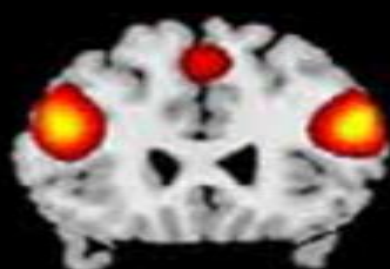
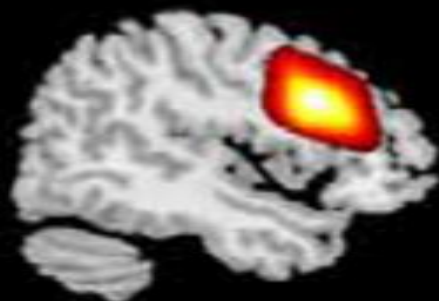
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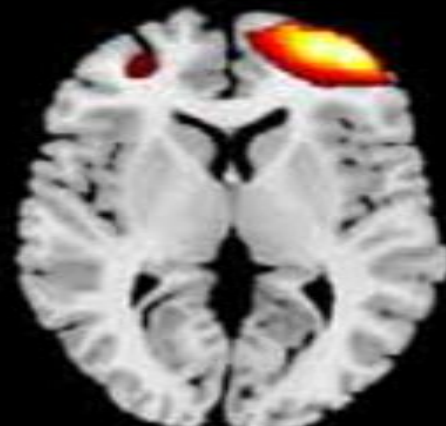
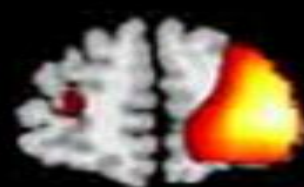
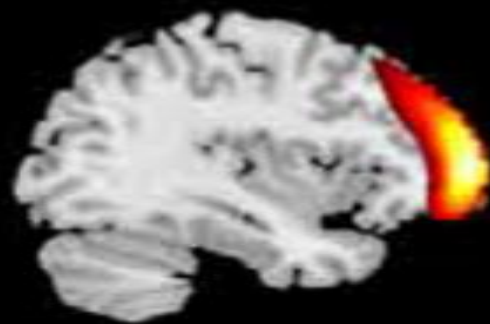
**IC 47**

(-49, +27, +24)



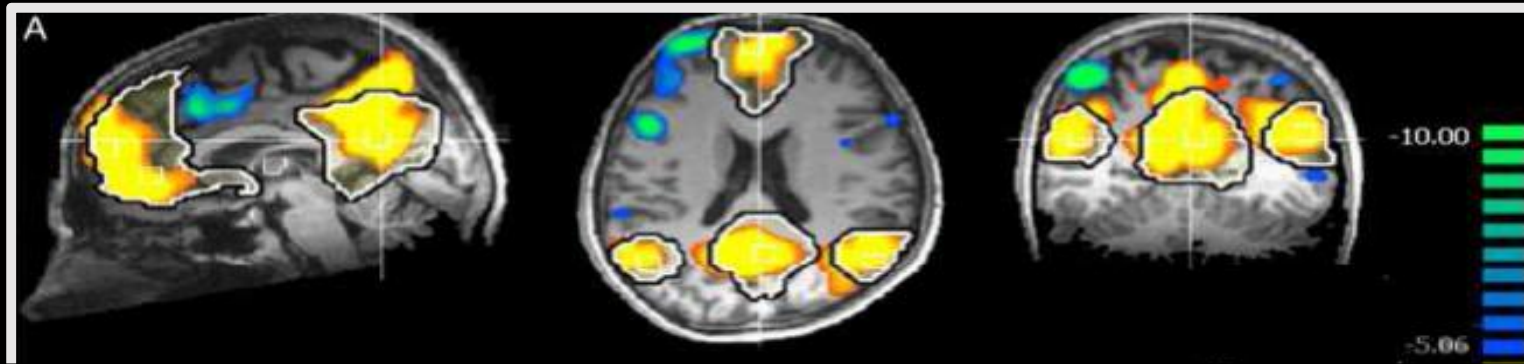
**IC 49**

(+39, +57, +4)



Εφαρμογές?

# Διαταραχές συνειδητοτητας – Φυτική κατάσταση/ Unresponsive wakefulness syndrome (UWS)



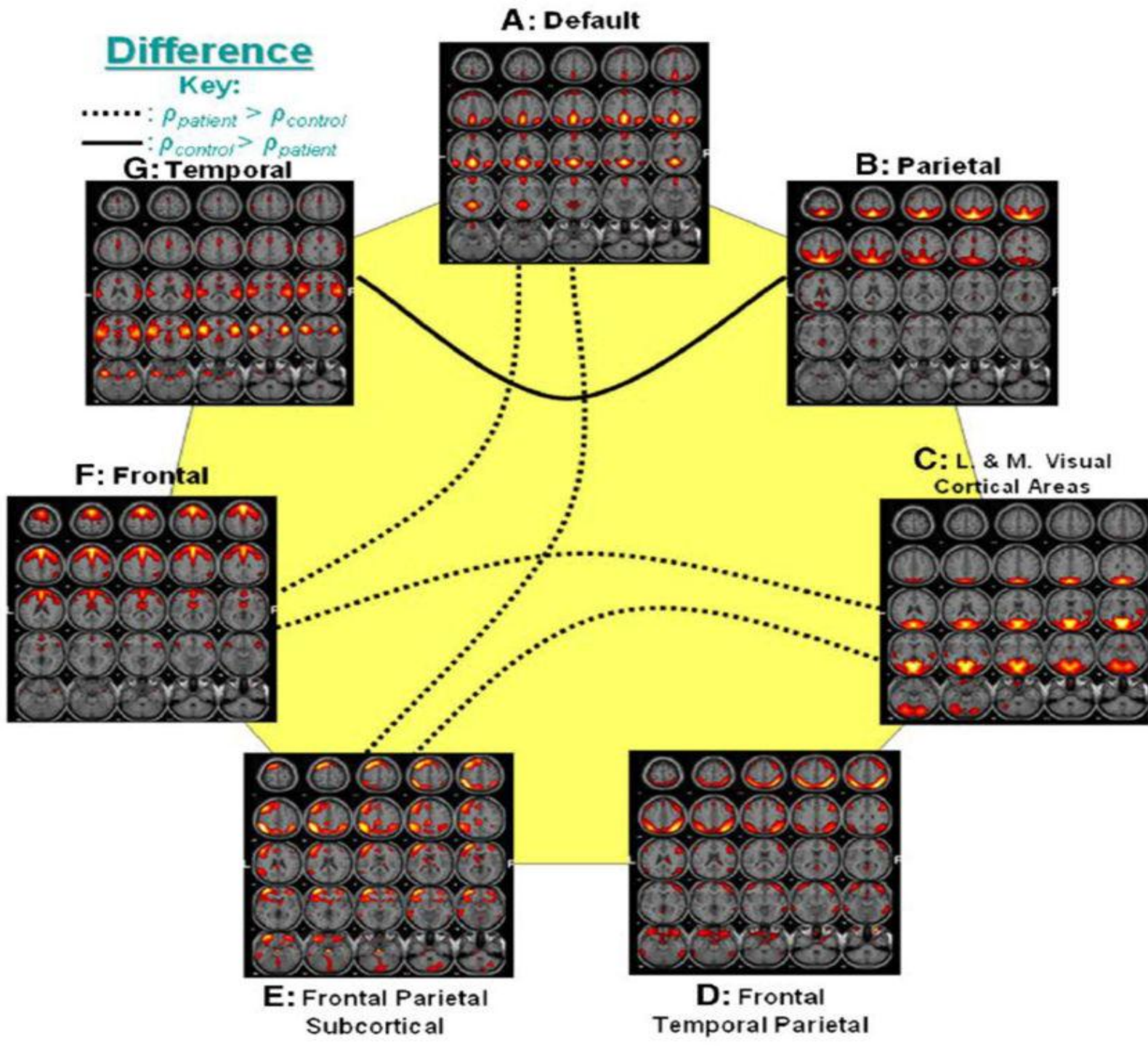
# Νευροψυχιατρική

Yu et al., 2012

“Brain connectivity networks in *schizophrenia* underlying resting state functional magnetic resonance imaging”

## Disconnection Hypothesis

**Figure 2.** Group differences of FNC (from Jafri et al. [63]). Out of 21 possible correlation combinations between 7 components, only 5 combinations passed the two sample t-test ( $p < 0.01$ ). The solid line represents the significant connectivity where controls have higher mean correlation than patients, while dotted line represents connectivity where patients have higher mean correlation. Presence of dotted lines rejects the hypothesis that controls should have more correlation between two components than patients.



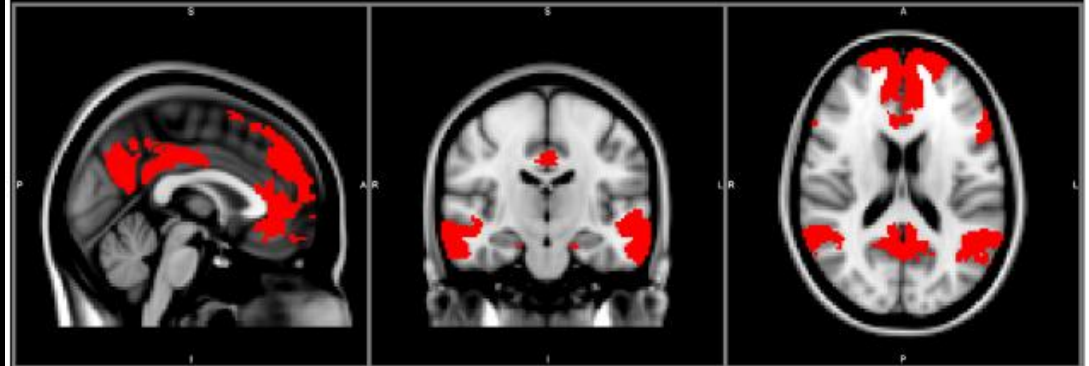


# Άνοια Alzheimer

- Ιππόκαμπος- DMN
- Οπίσθιος βρεγματικός φλοιός- DMN

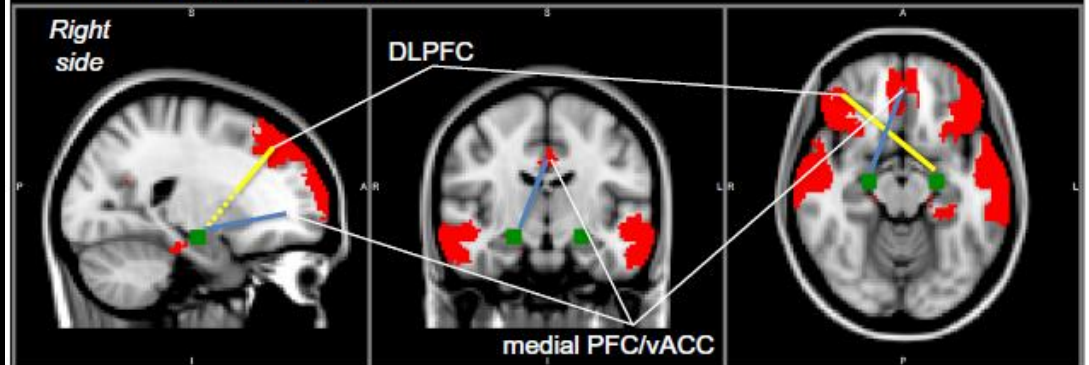
• Fig. 1 Functional connectivity in resting-state in Alzheimer's disease (AD). Regions of connectivity loss or increase in AD, a case of hippocampus (Wang et al. 2006) and b PCC (Zhang et al. 2009) in DMN. The yellow is showed increase and blue is decrease. Green of square is showed seed region. Mask of DMN is referred to yeo and colleagues (Yeo et al. 2011)

Default mode network

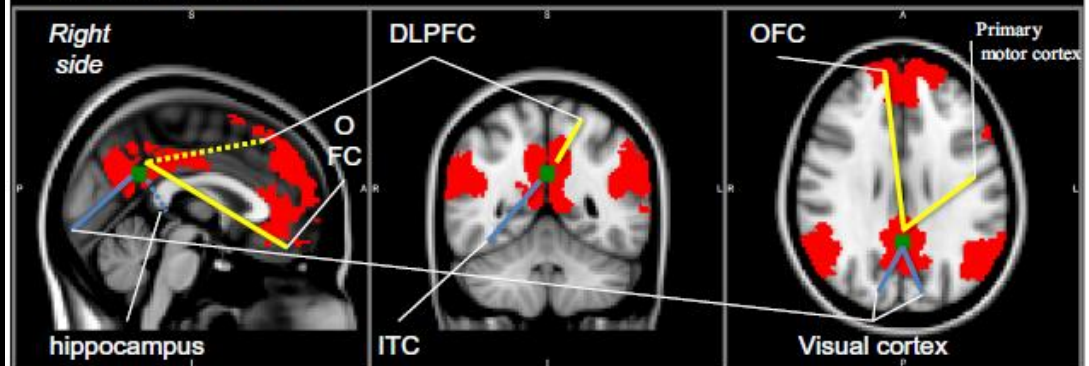


Alzheimer's disease vs. Healthy Controls

a. Seed region: hippocampus



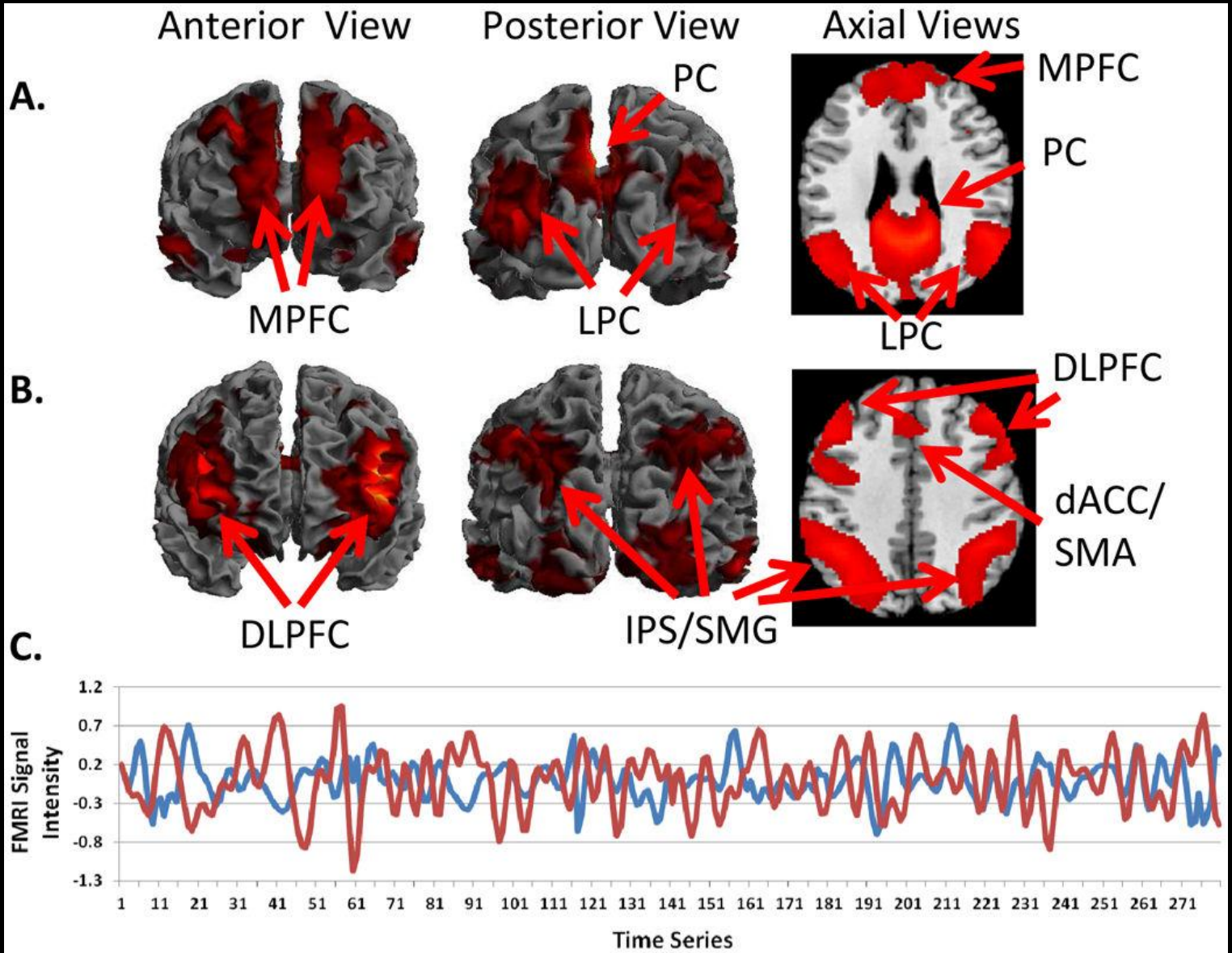
b. Seed region: PCC



Increase Decrease Seed region

# ΔΕΠ

- Αντιστροφή συσχέτιση μεταξύ DMN & γνωστικό δίκτυο σε υλεις
- Μειωση της αντιστροφης συσχέτισης σε παιδια με ΔΕΠ





# ΑΕΕ

- 26 Ασθενείς - ισχαιμικό επεισόδιο
- 26 Υγιείς-control
- Εκτίμηση συμπεριφοράς (VF) & rs-fMRI

a) 4 μέρες

b) 4.5 μήνες

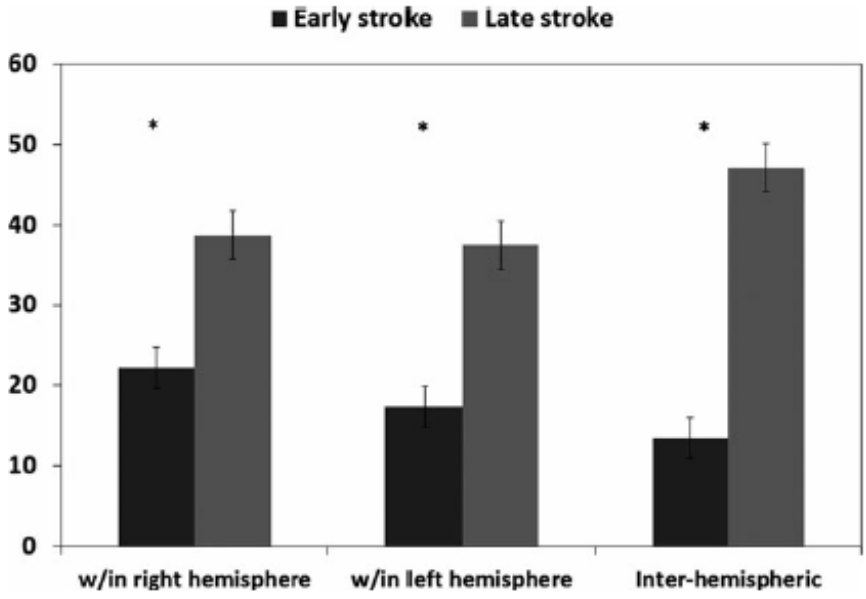


Figure 3. Within hemisphere and interhemispheric total connectivity scores in the subnetwork significantly different between early and late stroke.  $P < 0.0002$ .

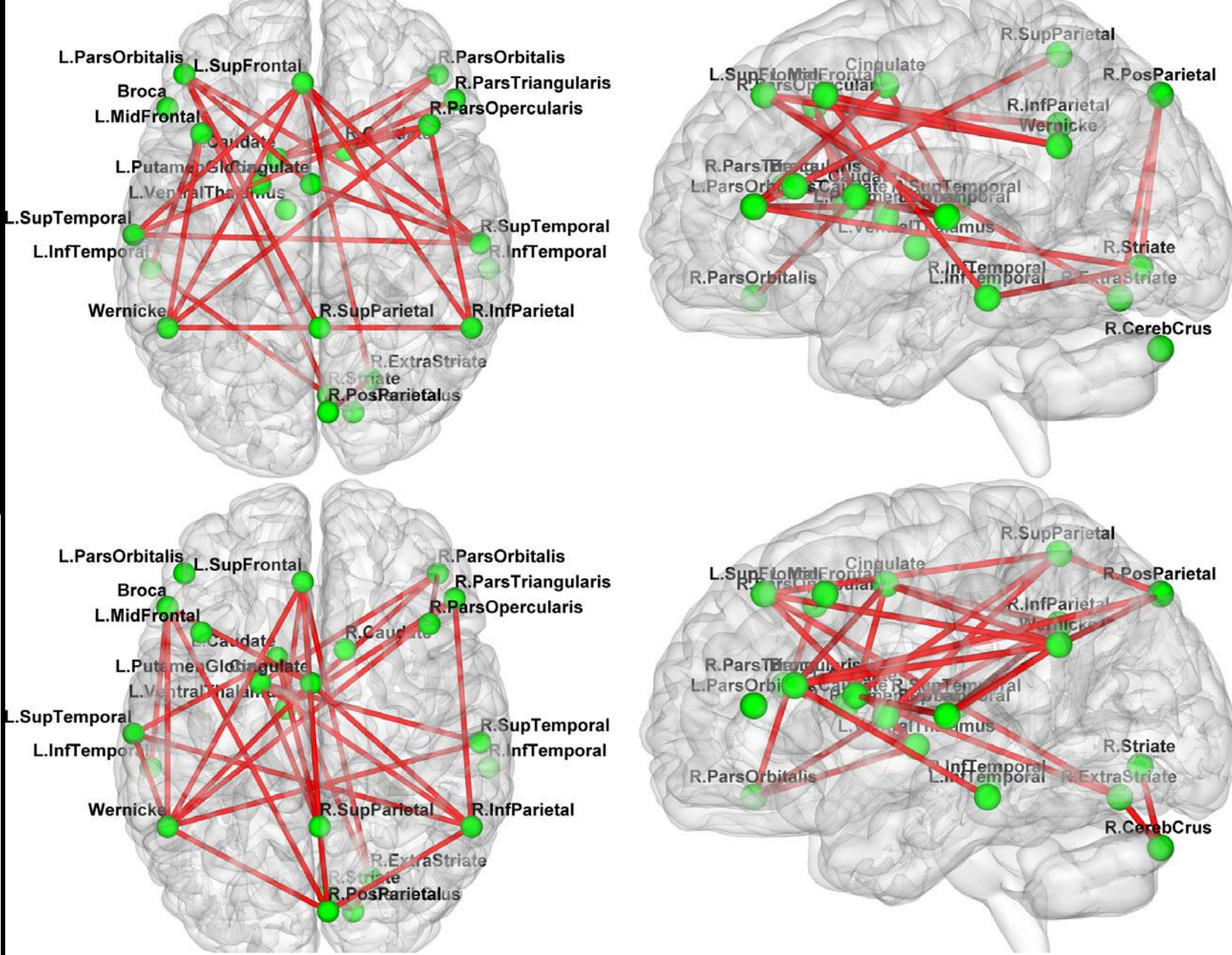


Figure 2. FC maps in the axial (left) and sagittal (right) sections. **Top panel (A)** shows subnetwork of connections more impaired in early stroke compared to HC. **Bottom panel (B)** shows subnetwork of connections that strengthened in late stroke when compared to early stroke patients. Node/Node labels that are further away appear indistinct. Left hemisphere is on left in axial view. FC, functional connectivity.

# Νευροχειρουργική

- Νεοπλασίες

1. Συσχετιζόμενες με γλοιώματα αλλαγές σε γειτνιάζουσες περιοχές /μεγαλης κλιμακας δίκτυα

2. Χαρτογράφηση «eloquent» περιοχων

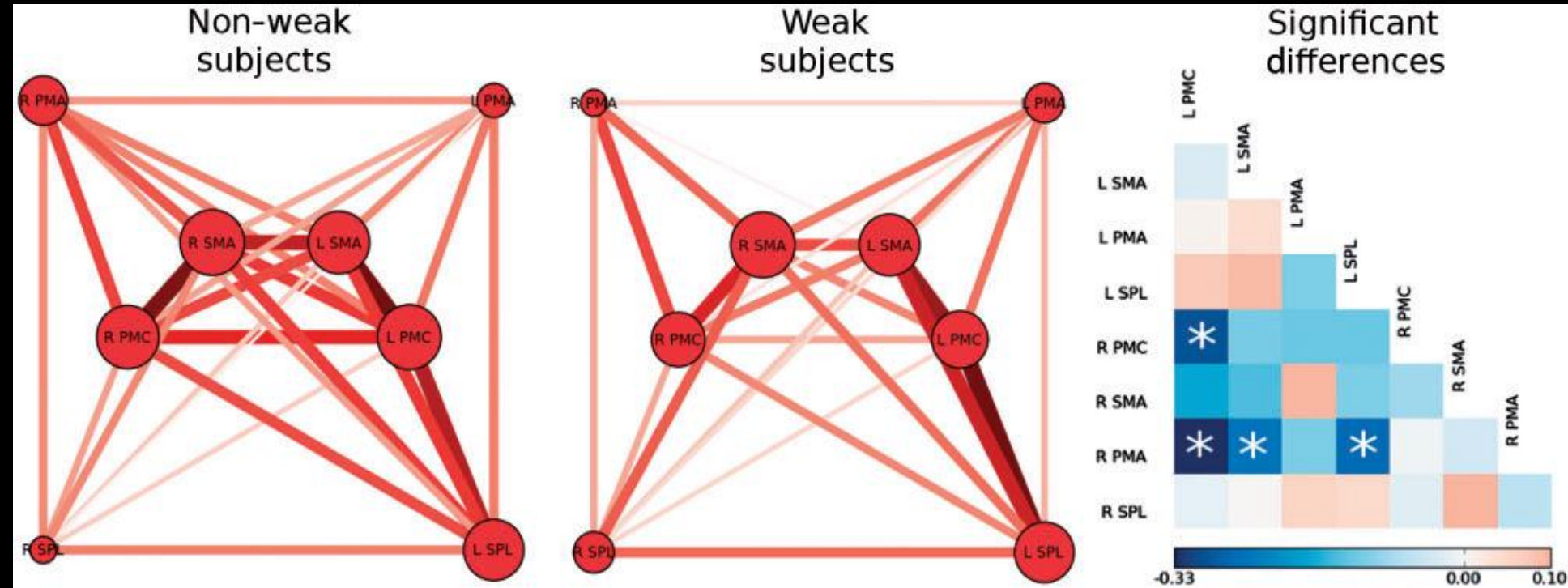


# Αλλαγές σε γειτνιάζουσες περιοχές /μεγάλης κλίμακας δίκτυα

- Μείωση λειτουργικής συνδεσιμότητας

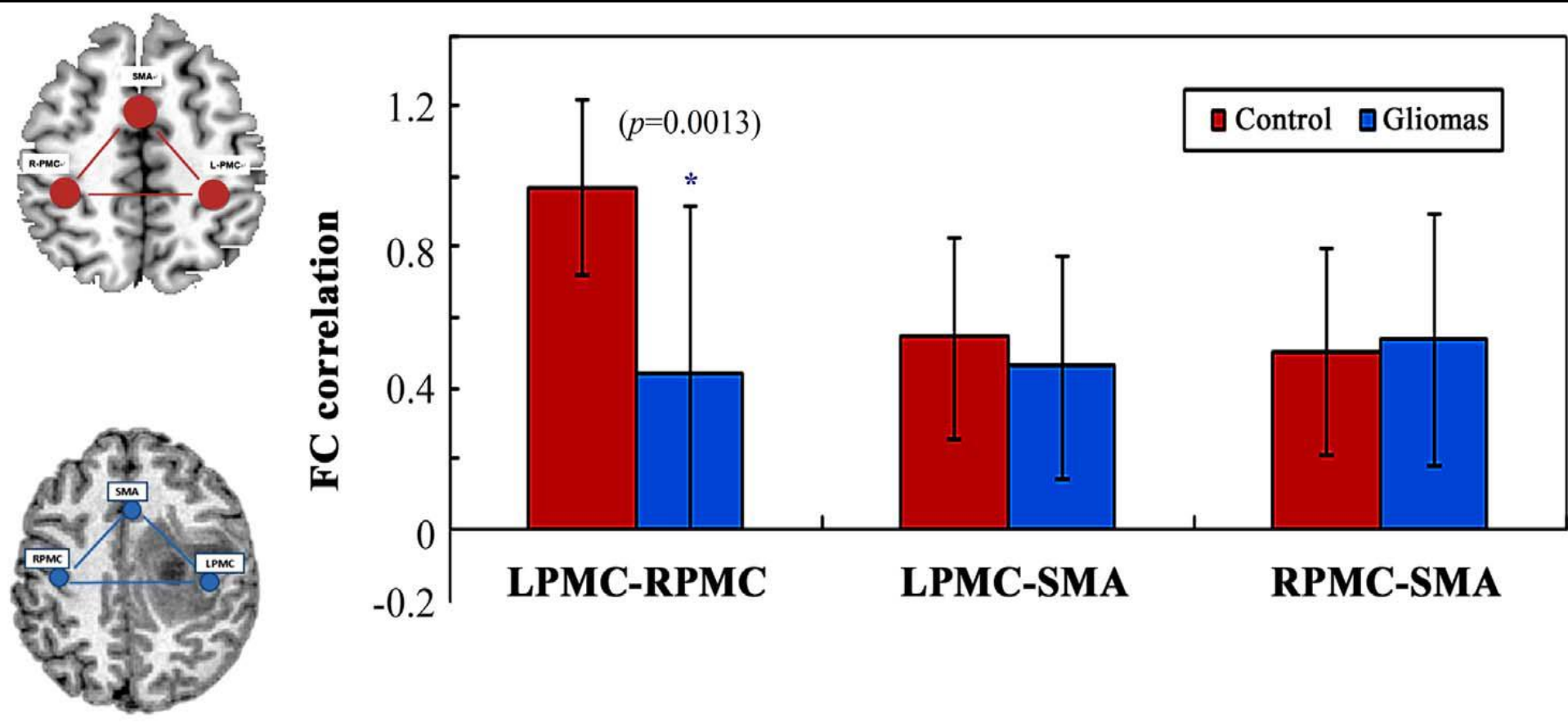
- Λειτουργία κίνησης

- Otten et al.,2012



**Figure 2** Weak subjects have significantly weaker mean connectivity than control subjects. Left: The overall structure of the motor network in patients with brain tumours is similar to that of controls. Connectivity is most pronounced between the SMAs, PMCs and the dominant SPL. Middle: Subjects with motor weakness largely preserve intrahemispheric connectivity, but interhemispheric connections are significantly weaker. Right: The largest differences in connectivity between weak and non-weak subjects were between the left PMC and right PMA, the left and right PMCs, the right PMA and left SMA, and the right PMA and left SPL. Scale bar, Pearson correlation. \*P<0.05.

# Niu et al. 2014



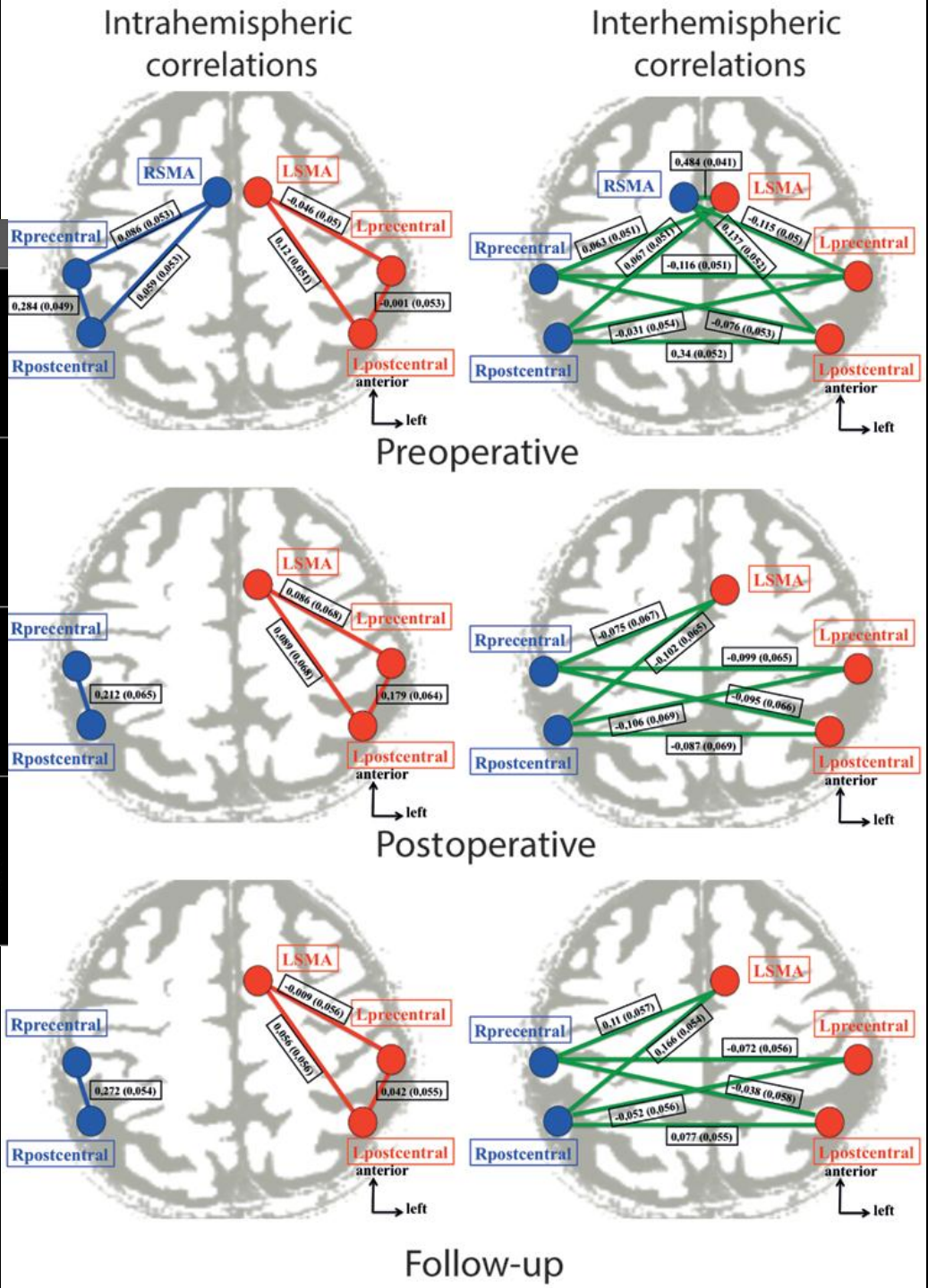
- Γλοιώματα II & III
- Πρωτοταγής κινητικός φλοιός
- 15 Ασθενείς άθικτοι νευρολογικά
- 15 υγείς-control

Figure 2. Group differences in the functional connectivity of the motor network between patients with brain gliomas and healthy controls. Error bars represent standard error of the mean. A blue asterisk indicates significant differences between groups ( $z = 23.215$ ,  $P = 0.001$ , Mann-Whitney U test). LPMC, left primary motor cortex; RPMC, right primary motor cortex; SMA, supplementary motor area. doi:10.1371/journal.pone.0096850.g002

# Vassal et al., 2017

- SMA διάχυτα χαμηλόβαθμα γλοιώματα
- SMA σύνδρομο
- Μεγαλης κλιμακας αναδιοργανωση του αισθητικο-κινητικου δικτυου
- Διημισφαιρικη συνδεσιμοτητα ελλατωμενη σε αμεση μεταω περιοδο και αυξημενη παλι κατά την αναρρωση
- Συνδεσιμοτητα μεταξυ βεβλαμενης κινητικης περιοχης και ετεροπλευρης SMA αυξηθηκε σε συγκριση με προεγχειρητικα
- Ενδο-ημισφαιρικη συνδεσιμοτητα ελλατωμενη σε αμεση μεταω περιοδο και αυξημενη παλι κατά την αναρρωση

	Preoperative FLAIR	Postoperative diffusion-weighted imaging	Follow-up FLAIR
Patient N°1			
Patient N°2			
Patient N°3			
Patient N°4			



**FIG. 3.** Evolution of correlation maps within the resting state sensorimotor network. Correlation coefficients between the sensorimotor network nodes, at both intrahemispheric (*left column*) and interhemispheric (*right column*) levels, in the preoperative period (*top*), in the immediate postoperative period (*center*), and at 3 months' follow-up (*bottom*). In both hemispheres, network nodes include the precentral region, the postcentral region, and the SMA; the SMA was resected on the lesional side and is therefore absent postoperatively. Each correlation is presented with its associated standard deviation. Note that in these data the right hemisphere is always the lesional hemisphere, the left hemisphere being the healthy hemisphere.



# Αλλαγές σε γειτνιάζουσες περιοχές /μεγάλης κλίμακας δίκτυα

- Μείωση λειτουργικής συνδεσιμότητας

- Λειτουργία λόγου

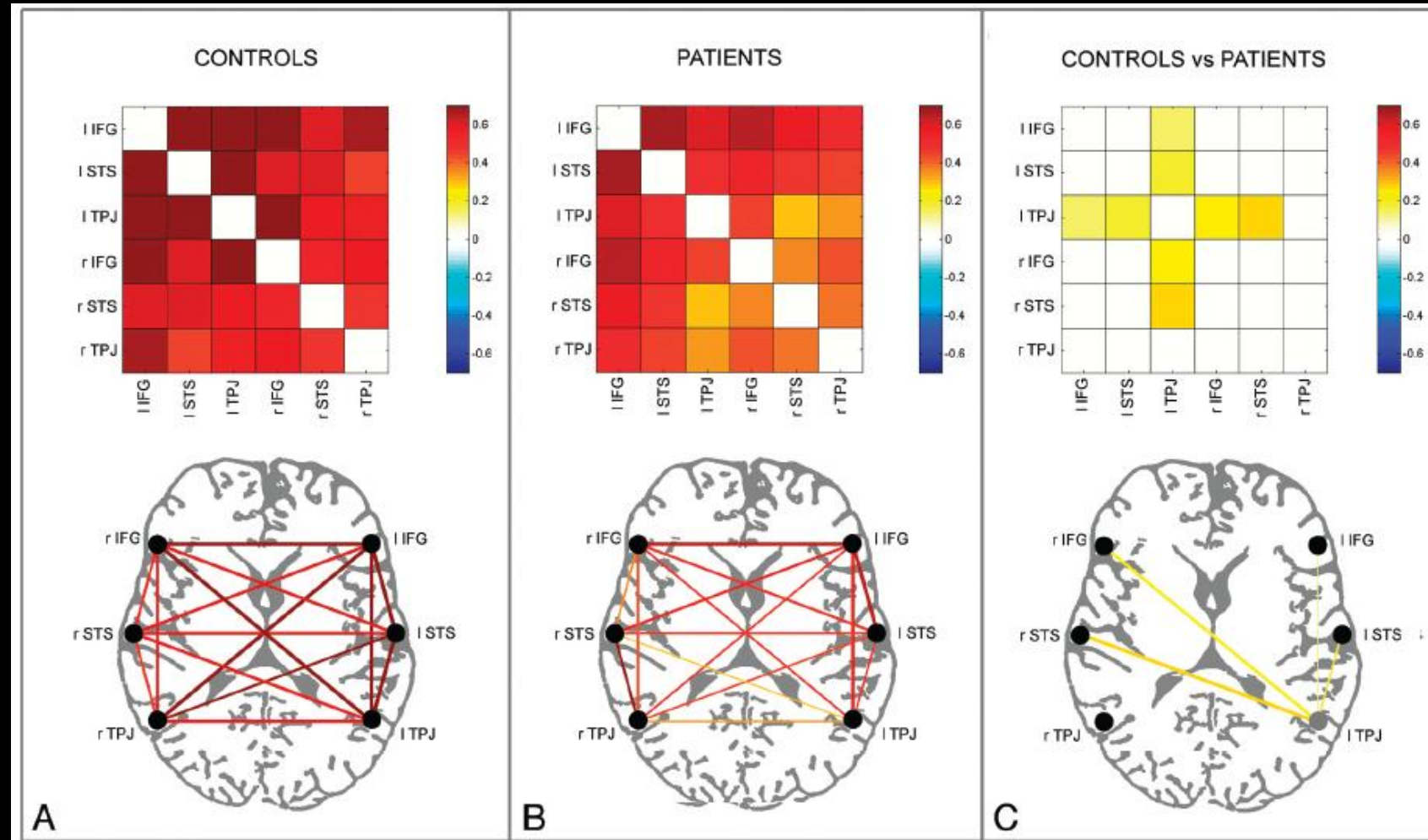
- Briganti et al., 2012

- Γλοιώματα ΑΡ ημισφ.

Καθολική λειτουργική συνδεσιμότητα Ασθενείς < Υγείς

(Κυρίως ενδο-ημισφαιρικά και μεταξύ TPJ των 2 ημισφαιρίων)

Στους ασθενείς το αριστερό TPJ παρουσίασε τη μεγαλύτερη ελάττωση λειτουργικής συνδεσιμότητας από ολόκληρο το δίκτυο





# Χαρτογράφηση «eloquent» περιοχών-Λειτουργία Κίνησης

Liu et al., 2009

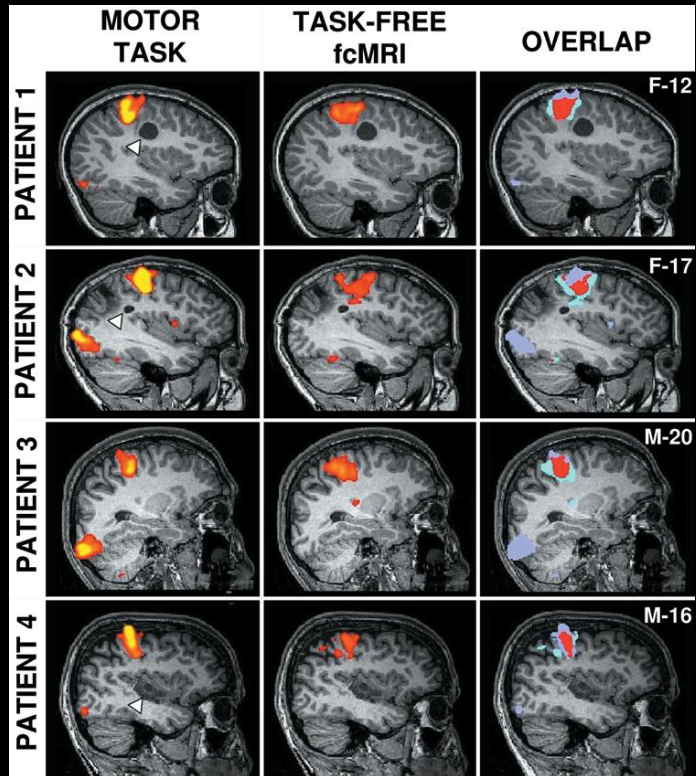


Fig. 1. Task and fcMR imaging-based mapping localizing similar regions. Hand motor regions defined by actual motor task movements (*left column*) and task-free fcMR imaging (*center column*) are plotted on sagittal sections for each patient (overlaid on their structural image). Colors represent Z values, with the threshold set to  $Z = 0.4-0.5$ . The overlap of the two techniques is shown in red (*right column*). Each row displays a different patient, with the sex (M or F) and age (in years) indicated in the rightmost panel. Brain lesions are indicated by the *white triangles* for the patients in Cases 1, 2, and 4; the patient in Case 3 has no visible lesion.

Kokkonen et al., 2009

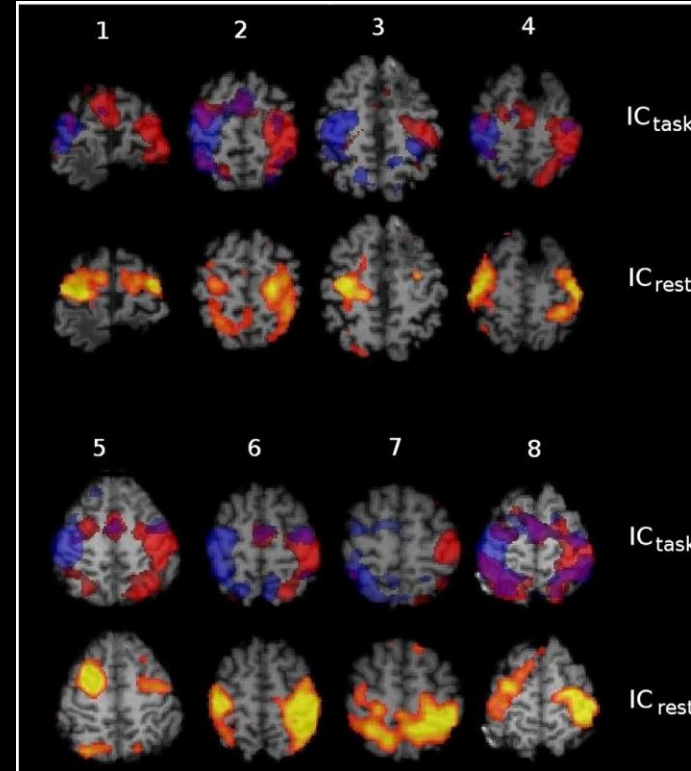


Fig. 1. Detected sensorimotor areas of the eight cases (2.3bzb5.0) presented in the same order as in Table 1. The upper rows represent ICA during the motor task ( $IC_{task}$ ) (red, right-hand task; blue, left-hand task) and the lower rows represent ICA during the resting state ( $IC_{rest}$ ). The ICs are superimposed on each patient's individual anatomical MR image.

- Rosazza et al., 2014
- Seed based εντοπισμος > ICA εντοπισμος
- Μερική συσχέτιση με fMRI .rsfMRI =μεγαλύτερες σε χώρο ενεργοποιήσεις

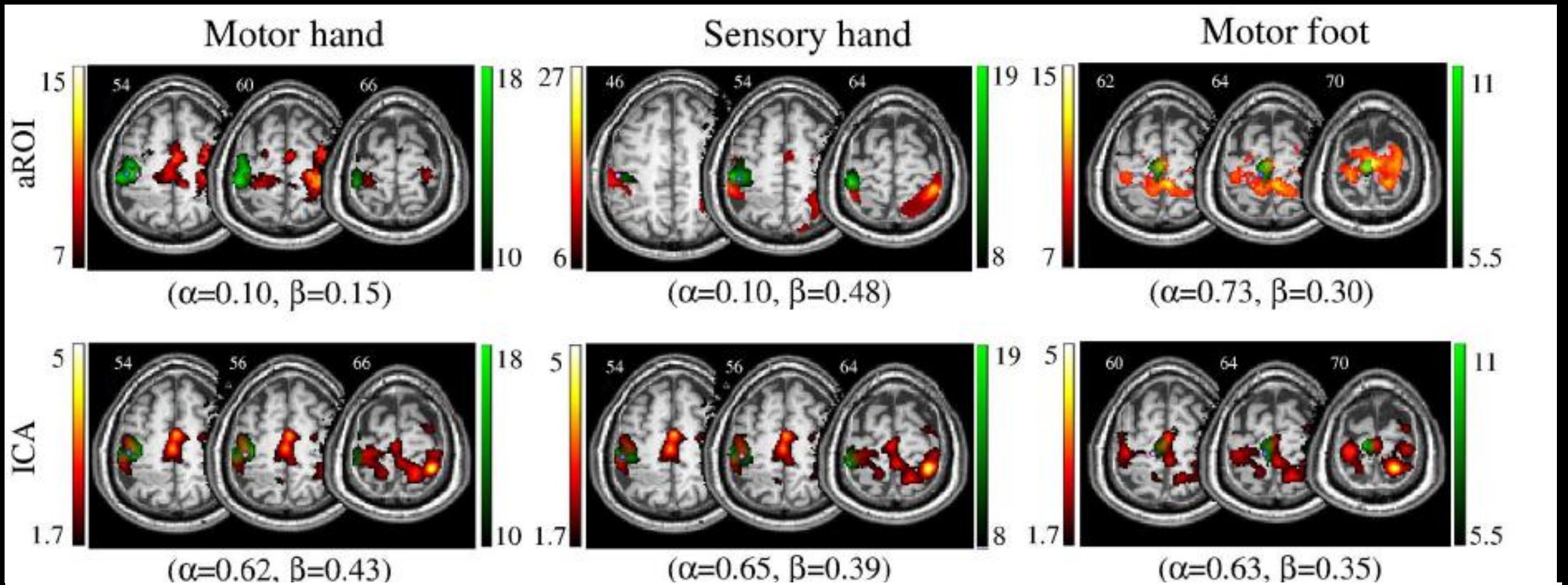
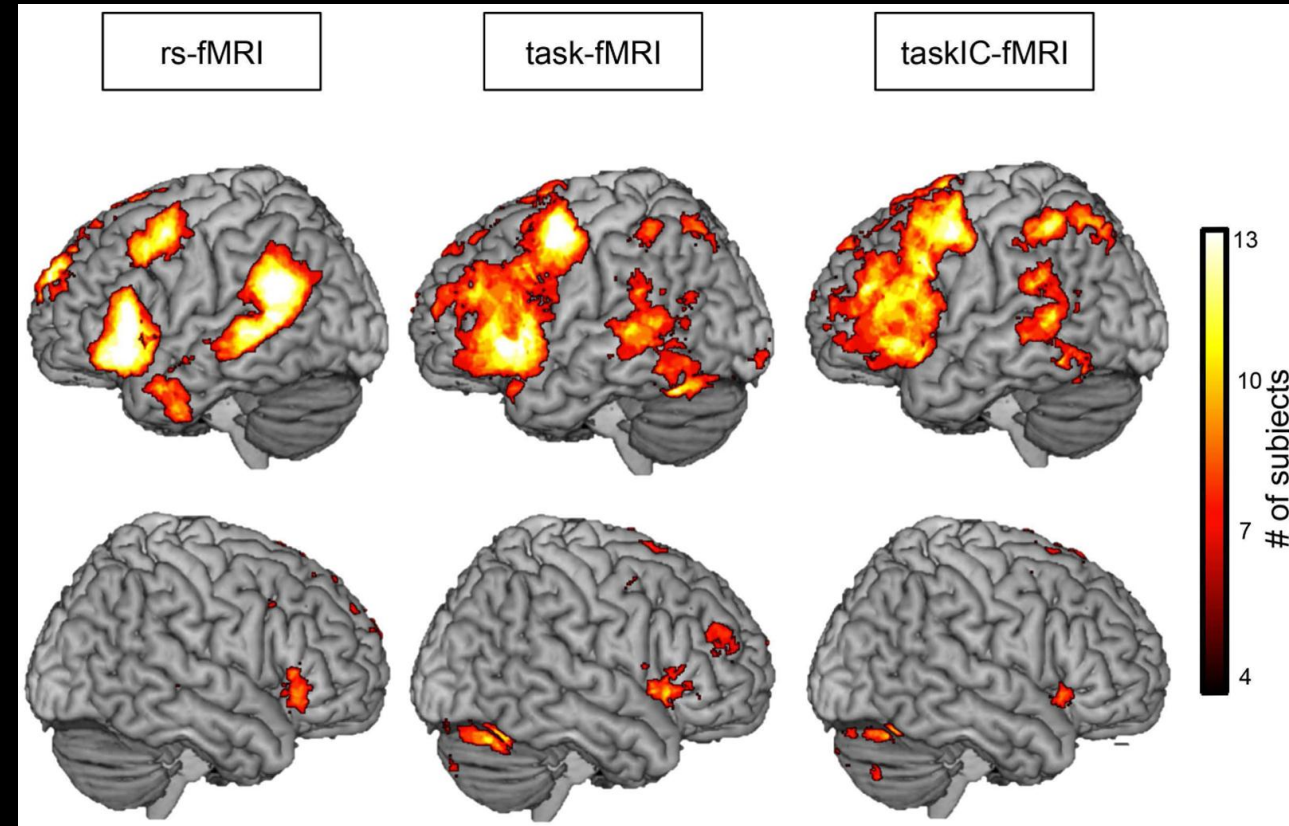


Figure 1. Concordance between task-based (tb-fMRI, in green) and resting-state (rs-fMRI, in red) fMRI maps computed with aROI (top row) and ICA (bottom row). Overlap sensitivity (a) and specificity (b) of rs-fMRI with respect to tb-fMRI, obtained with operator-dependent thresholds, are reported. Light blue circle represents the Centre of Mass (CoM) of tb-fMRI, and pink circle represents the CoM of rs-fMRI. Images are shown in neurological convention (left is left) and MNI coordinates are reported on top of each slice. a) For Case 5 concordance was optimal in terms of overlap values and CoM distance. b) For Case 9 the aROI and ICA maps were extremely similar to each other, in particular for the hand area. However, the aROI was more useful than ICA to localize the foot area as it included the paracentral lobule.  
doi:10.1371/journal.pone.0098860.g001

# Χαρτογράφηση «eloquent» περιοχών

- Εγκυρότητα σε χαρτογράφηση λογού
- Branco et al., 2016
- Καλη αλληλοκαλυψη μεταξυ rs-fmri & fMRI
- Rs-fMRI ευαισθησια & ειδικοτητα = fMRI ευαισθησια & ειδικοτητα



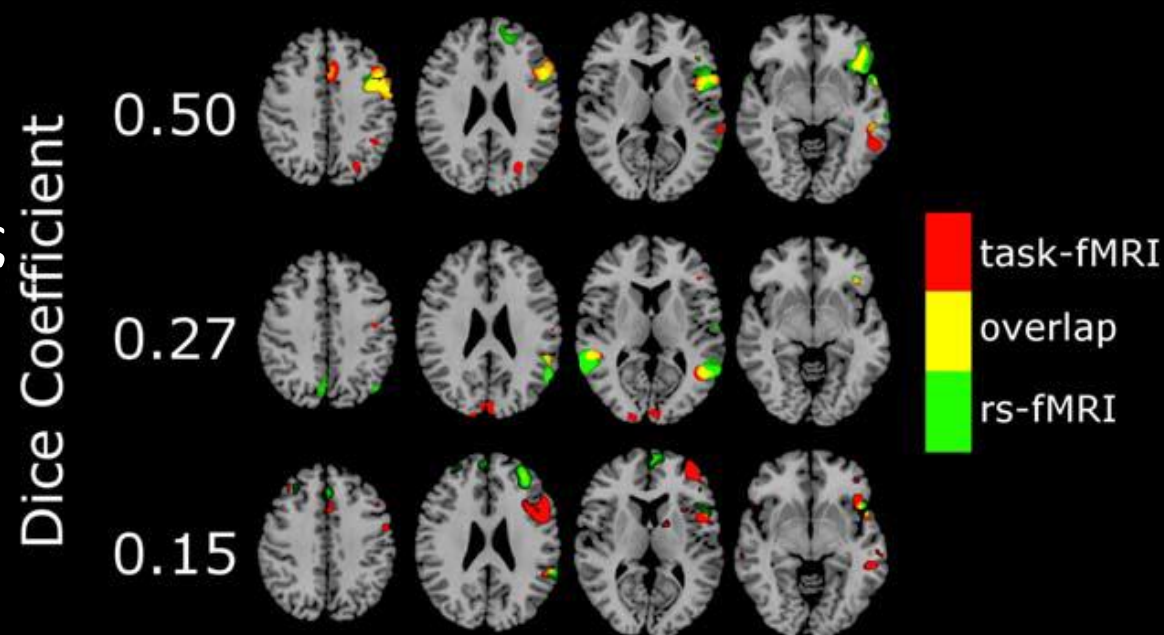
**FIGURE4** | Probabilistic overlap map across subjects for rs-fMRI, task-fMRI and task IC-fMRI. Colors represent the number of subjects with significant activations at each voxel. Images were thresholded between 4 and 13 subjects for better visualization.



# Χαρτογράφηση «eloquent» περιοχών

Sair et al., 2016

- Μετρια συμφωνία σε επίπεδο ομάδας μεταξύ rs-fMRI & fMRI.
- Όμως διακυμανση σε ατομικο επίπεδο.



Sample subjects at varying Dice coefficients. Each row denotes a different subject with fMRI overlays onto standard brain template for comparison. Task-fMRI and rs-fMRI were thresholded at the peak Dice coefficient value for each of these subjects. Task-fMRI is shown in red, the rs-fMRI in green, and the overlapping areas in yellow. For the subject in the top-most row, there is an excellent concordance of task-fMRI and rs-fMRI. For the subject in the bottom-most row, there is a low concordance of task-fMRI and rs-fMRI, reflected in the low Dice coefficient. The subject in the middle row demonstrates an intermediate level of task-fMRI and rs-fMRI concordance. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]





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Original Article

## Motor and language deficits correlate with resting state functional magnetic resonance imaging networks in patients with brain tumors

Evangelia Liouta<sup>b, c, \*</sup>, Vasileios K Katsaros<sup>a, b, c</sup>, George Stranjalis<sup>b</sup>, Edyta Leks<sup>d</sup>, Uwe Klose<sup>c</sup>, Sotirios Bisdas<sup>c, e, f</sup>

<sup>a</sup> Department of Radiology, General Anti-Cancer and Oncological Hospital of Athens "St. Savvas", Athens, Greece

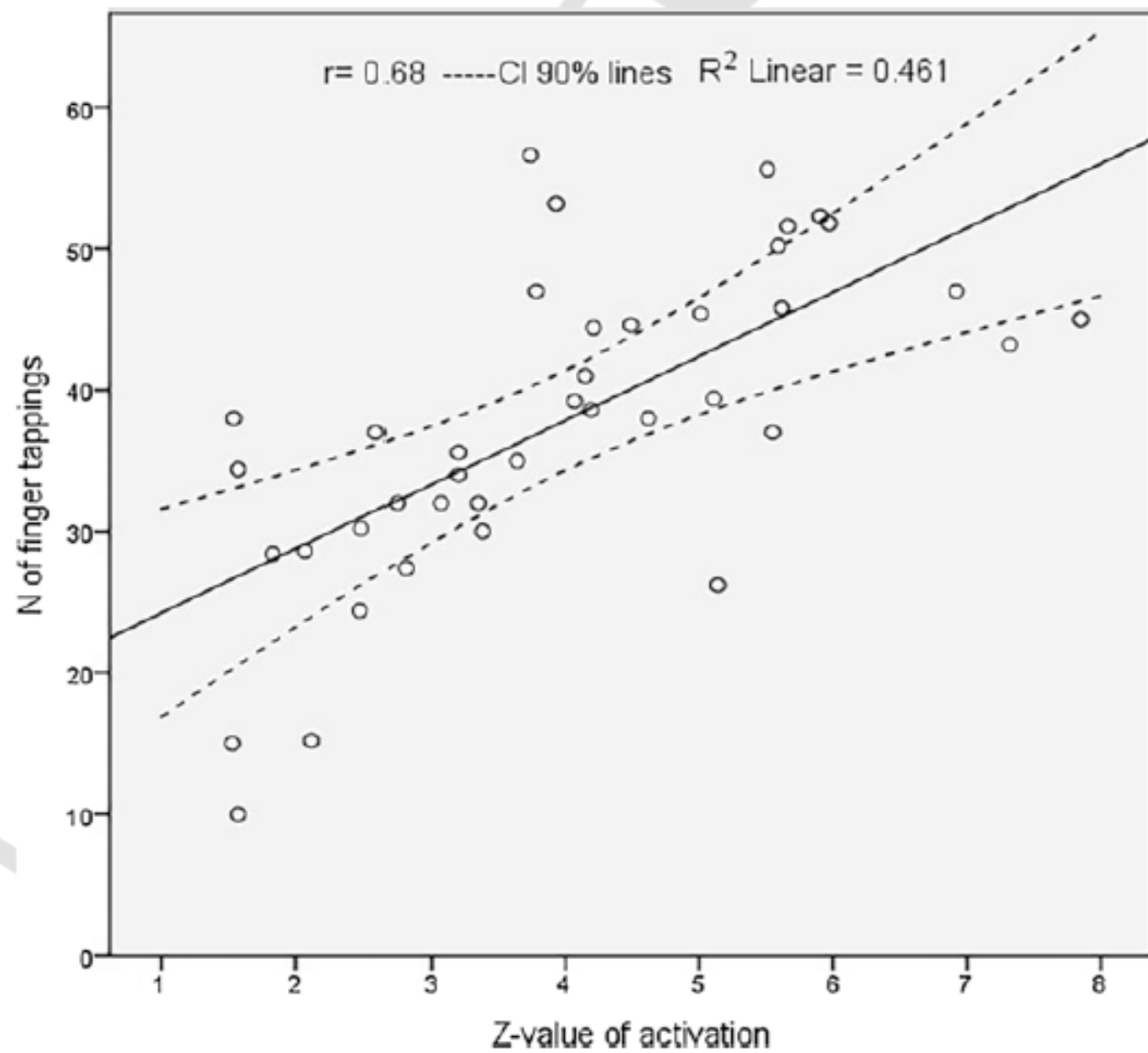
<sup>b</sup> Department of Neurosurgery, University of Athens, "Evangelismos" Hospital, Athens, Greece

<sup>c</sup> Department of Neuroradiology, University Hospital of Tübingen, Tübingen, Germany

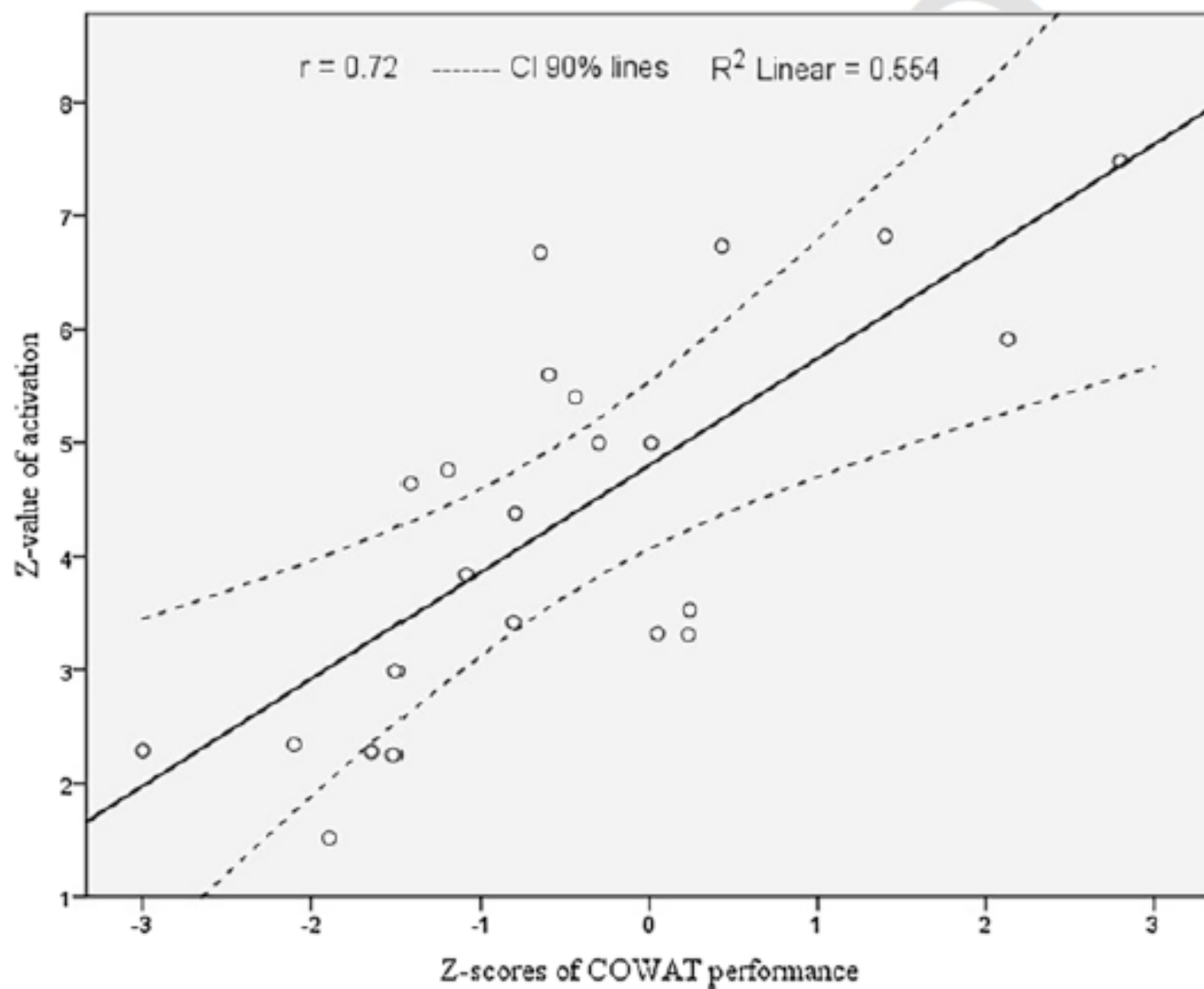
<sup>d</sup> Department of Biomedical Magnetic Resonance, University Hospital of Tübingen, Tübingen, Germany

<sup>e</sup> Department of Neuroradiology, National Hospital for Neurology and Neurosurgery, University College London Hospitals, London, UK

<sup>f</sup> Institute of Neurology, University College London, London, UK



g. 3. Ipsilesional precentral gyrus' activation as a function of contralesional finger tapping performance in patients with lesions near motor cortex.



**Fig. 5.** Left inferior gyrus' activation (BA 44) as a function of verbal phonemic fluency in patients with lesions near Broca's area without aphasia. z-Scores of COWAT test are standardized data. Minus values represent standard deviations below the average normal performance (0-value); positive values represent standard deviations above average normal performance. BA: Brodmann area; COWAT: controlled oral word Association Test.



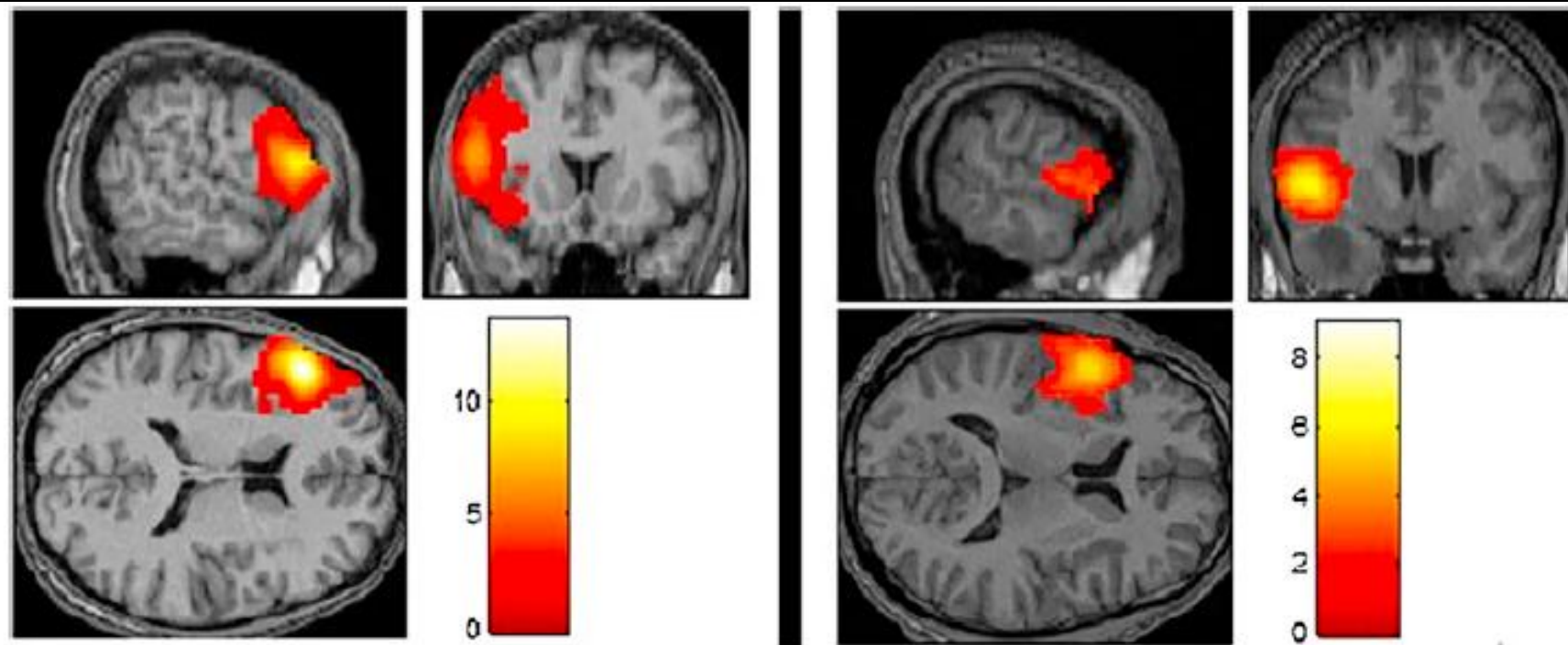


Fig. 6. RS-fMRI language networks. Left part: sagittal, coronal and axial views of frontal-language network in a patient with a left frontal low-grade glioma presented with a good performance on the verbal fluency test. Ipsilesional network  $z$ -value activation on BA 44 is 6.82. Right part: sagittal, coronal and axial views of frontal-language network in a patient with a left temporal low-grade glioma presented with low performance on verbal fluency test. Ipsilesional network  $z$ -value activation on BA 44 is 3.84. Functional images are super-imposed into anatomical images for both patients. Images are not radiological (left side is left hemisphere/right side is right hemisphere). BA: Brodmann area.

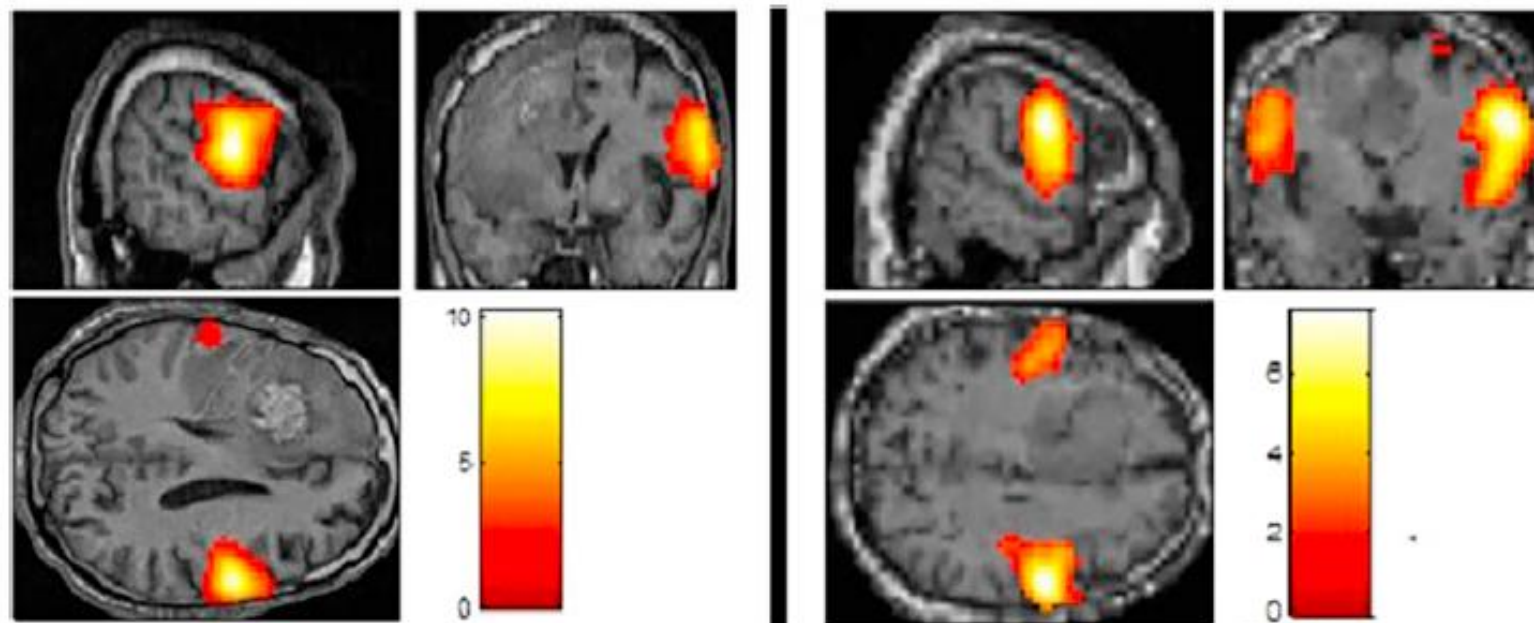
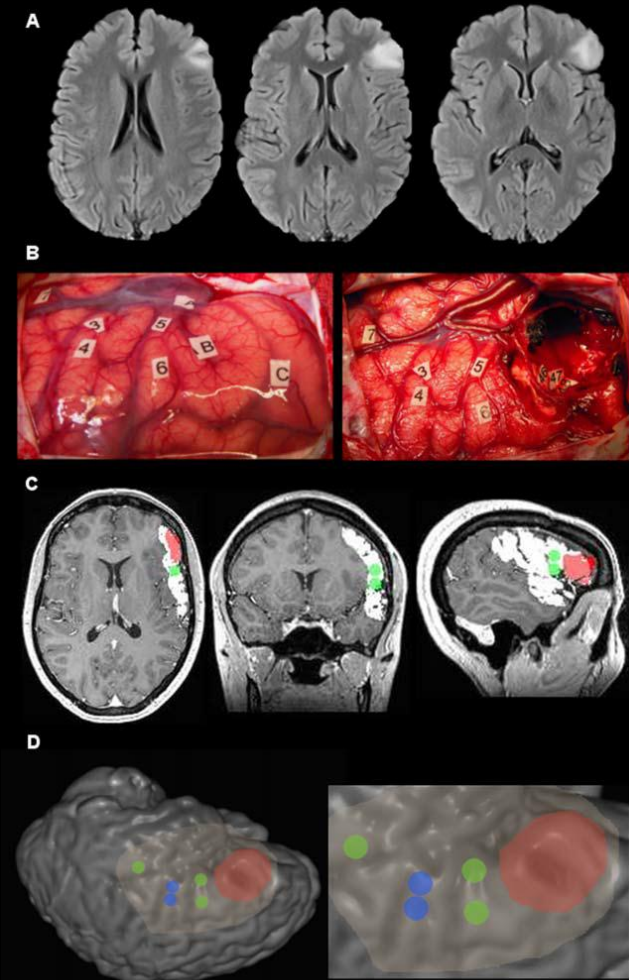


Fig. 4. RS-fMRI motor networks. Left part: sagittal, coronal and axial views of motor network in a patient with a left frontal high-grade glioma presented with right paresis. The ipsilesional network activation is significantly lower ( $z$ -value = 1.66) than the contralesional one ( $z$ -value = 10.2). Right part: sagittal, coronal and axial views of motor network in a patient with a left frontal meningioma presented with no paresis but low performance on finger tapping task. The ipsilesional network activation is lower ( $z$ -value = 2.6) than the contralesional one ( $z$ -value = 4.4). Functional images are superimposed onto anatomical images for both patients. Images are not radiological (left side is left hemisphere/right side is right hemisphere).

# Rs-fMRI & διεγχειρητική χαρτογραφηση

- Cochereau et al., 2016
- $96 \pm 11\%$  περιοχών αισθησης-κινησης που βρεθηκαν με ερεθισμο εντοπιστηκαν μεσα σε 10χιλ της rs-fMRI ενεργοποιησης
- $84 \pm 24\%$  % περιοχών αισθησης-κινησης που βρεθηκαν με ερεθισμο εντοπιστηκαν μεσα σε 5χιλ της rs-fMRI ενεργοποιησης
- $92 \pm 21\%$  περιοχών λογου που βρεθηκαν με ερεθισμο εντοπιστηκαν μεσα σε 5χιλ της rs-fMRI ενεργοποιησης
- $70 \pm 41\%$  περιοχών λογου που βρεθηκαν με ερεθισμο εντοπιστηκαν μεσα σε 5χιλ της rs-fMRI ενεργοποιησης



Illustrative case of stimulation points and resected cortex registration on patient's anatomical imaging. (A) FLAIR axial slices of a patient's left fronto-opercular glioma. (B) Intraoperative photograph of the cortical surface before (left) and after (right) resection. Number tags represent cortical eloquent sites elicited by DCS whereas letter tags represent tumor boundaries defined with intraoperative ultrasound imaging. (C) Multiplanar reconstruction of preoperative 3DT1 MP-RAGE imaging. White delineation5exposed cortical surface. Red delineation5resected cortex. Green dots5language stimulation points represented with a 5 mm radius sphere. (NB: motor stimulation points are not visible here). (D) Surface rendering (operative view) of the patient's brain. Stimulation points are represented with 5 mm radius spheres (blue for motor and green for language). Highlighted cortex5exposed cortical surface. Red cortex5resected cortex. [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]



# Συμπεράσματα

- Πολύτιμο απεικονιστικό εργαλείο στην καλύτερη κατανόηση διαταραχών εγκεφάλου
- Λειτουργική σχέση των δικτύων και όχι απλά ανατομική
- Καταλληλο για ασθενεις που παρουσιαζουν ελλειμματικη συνεργασια στη κλασικη fMRI –παρετικοι, αφασικοι, παιδια, ηλικιωμενοι κτλ
- Συμπληρωματικό εργαλείο για προ εγχειρητική χαρτογράφηση λειτουργιών