linkRbrain: Towards an integrated multiscale database for understanding the brain

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Brain : Complex System



NITRC: neuroimaging shared database

1000 functional connectomes resting state data consortium

current total = 1347 45% female, 54% male 33 sites

10

25

Databases used:

- Database of 198 healthy subjects from Cambridge university
- Database of 198 healthy subjects from Beijing university

extraction of 32 resting state networks (RSN)



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Identification of 32 RSN

What is that these 32 RSN?



 Yeo et al., The organization of the human cerebral cortex estimated by intrinsic functional connectivity. J Neurophysiol. 2011.



Laird et al. (2011) Behavioral interpretations of intrinsic connectivity networks. J Cogn Neurosci 2312: 4022–4037

- Meta-analisys of the literature
- Production of the 20 taskbased networks (TBN)



- Meta-analisys of the literature
- Production of the 20 TBN

Main TBN	Main functions
10;11;12	visual
7	visuo-somatomotor
8	somatomotor
17	auditory-somatomotor
16;17	auditory
10;16	auditory-visual
10;15	visual;right attention, WM
13;7	DMN; visuo-motor
15;7	visuo-motor; right attention and working memory
15	right attention and working memory
13	DMN
13,18	DMN; leftlanguage
13,7	DMN; visuo-somatomotor
13,2	DMN; olfaction, taste, reward;
18	left language
4,13,15;4,15	emotion, interoception; DMN



Comparing the RSN with TBN





The intertwined ring : the anatomofunctional architecture of the brain





The intertwined ring : the anatomo-functional architecture of the brain



Mesmoudi et al. (2013) Resting state networks corticotopy: **the dual intertwined rings architecture** PLOS ONE Jul 24;8(7)

The intertwined ring correspond to cerebral imaging results

C hASL v.s S. A SUBJECT S.W. (CONTROL) D) hASL v.s. left

deaf-blind subject.

<u>Neuroplasticity associated with tactile language communication in a deaf-blind subject.</u> **Obretenova** S, Halko MA, Plow EB, Pascual-Leone A, Merabet LB. Front Hum Neurosci. 2010;3:60.

Control

The intertwined ring correspond to cerebral imaging results



"Trends and properties of human cerebral cortex: Correlations with cortical myelin content" M F. Glasser et al. NeuroImage (2013)

The intertwined ring correspond to cerebral imaging results



"Trends and properties of human cerebral cortex: Correlations with cortical myelin content" M F. Glasser et al. NeuroImage (2013)

Second level : genetic hypothesis



What about the relationships between the cortex functional organization and the genetic expression ?

The cortical gene expression match the intertwined rings

Gene expression database from Allen institute :

- 2 complete brains
- 1000 genes expressed over 1000 cerebral regions

Corresponding analysis Discriminent corresponding analysis

The cortical gene expression match the intertwined rings



Cioli et al. 2014 . Differences in Human Cortical Gene Expression Match the Temporal Properties of Large-Scale Functional Networks. PloS ONE

	VSA ring	PTF ring	
Cortical topography			
Cognitive functions	Sensory-motor, uni and bi-modal	Memory, language and vital functions	
Temporal information processing	Real time interactions	Multi-temporal integratio	
Potassium channels	KCNA1, KCNC1	KCNG1	
	High temporal precision	Modulation of K currents	
Sodium channels	SCNA1, SCNB1	SCNA3, SCNB3	
	High temporal precision	Persistent currents, sustained activity	
Calcium channels	CACNA2D2	CACNA1H	
	Fast, stimulus driven release	Spontaneous release, Rhythms generation	
Synaptotagmins	SYT2	SYT5, SYT9, SYT10	
	Kiss and run, fast evoked release	Spontaneous, slower release	
Complexins	CPLX1	CPLX3	
	Stimulus driven control of release	Spontaneous release	
Synaptobrevins	VAMP1	VAMP2	
	High frequency evoked release	Maintains the pool of available vesicles	

Generalisation of the process

- Inhence the number of the network task based
 - From 20 to 300 TBN
- Inhence the number of genes
 - From 1000 to 21000 genes
- Addition of anatomical atlas
 - Talairach atlas

Reconstruction of the TBN from the literature

Neurosynth : meta-analysis of neuroscience literature

	Positive points	Negative points
NeuroSynth	 open acces automatic method ?? bottom up extraction of keywords comparison of experimental picks and the literature 	 the extracted keywords dont describe precisly the cognitive tasks we can't compare the experimental networks with the literature

CorText : dynamic reconstitution of knowledge



CorText : dynamic reconstitution of knowledge





5000 papers from Neurosynth

extraction des mots et n-gram d'intérêt « NLTK »

Results example: extraction of n-grams from 5000 papers

Valence verb Action observation Self face recognition Somatosensory stimulation Verbal episodic memory Visual working memory

...

Example of literature exploration Sakamoto et al., 2005. neuroimage

Text mining

Table of coordinates

Abstract

Posttraumatic stress disorder (PTSD) has been widely studied, but its neural mechanism is still unclear. The purpose of this study is to identify dysfunctional areas in PTSD throughout the whole brain to help to elucidate the neural mechanisms of PTSD. Sixteen patients with PTSD and sixteen healthy controls participated in this study. Traumatic images under perceptual threshold including scenes of earthquakes, traffic accidents, ambulances, emergency rooms, and crimes were presented to the participants, and brain activation was measured using functional MRI. Functional brain images of both groups were evaluated with random effect analysis for the whole brain. In the control group, activation in the ventral frontoparietal areas correlated significantly with presentation of the masked traumatic stimuli. In the PTSD group, activation was not observed in these areas, but significant activation correlated with the masked traumatic stimuli in the parahippocampal region including the left parahippocampal gyrus and tail of the left hippocampus. These results suggest that in PTSD patients activation in the ventral frontoparietal network associated with visual attention processing is attenuated, while the left hippocampal area associated with episodic and autobiographical memory is abnormally easily activated. This pattern of activation corresponds well to the clinical characteristics of PTSD, in which even slight traumatic stimuli tend to induce intrusive recollection or flashbacks, despite a general decrease in attention and ability to concentrate.

intrusive recollection

Table 2.

Talairach coordinates in the control group and PTSD group

Region	Brodmann area	Talairach coordinates		KE (voxels)	z score	
		x	у	z		
Control group						
Right inferior parietal lobule	40	44	-56	48	41	3.57
Right precentral gyrus	4	28	-16	52	31	3.55
Left inferior parietal lobule	40	-28	-76	42	122	3.36
Left precentral gyrus	4	-28	-18	54	38	3.33
Left middle frontal gyrus	8	-34	20	44	25	3.30
Left middle frontal gyrus	9	-16	14	26	26	3.19
PTSD group						
Left parahippocampal gyrus/tail of left hippocampus	19/30	-14	-42	-4	25	3.79
					Table	options

Reconstruction of 300 TBN from 5000 papers

Generalisation of the process

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Topographical distances

Let A and B two nodes (set of points) :

$$A = \{(M_i, \mu_i) \mid i \in [\![1, m]\!]\}$$

 $B = \{(N_j, v_j) \mid j \in [[1, n]]\}, \qquad \mu_i \text{ and } v_j \text{ are the weights of } M_i \text{ and } N_j \text{ respectively}$

The correlation between the two nodes :

$$cor(A, B) = \sum_{d(M_i, N_j) \le r} \mu_i \cdot \nu_j \frac{d(M_i, N_j)}{r},$$

r is the reference radius = 10mm

The overlap :

$$s(A, B) = \frac{cor(A, B)}{\sqrt{cor(A, A) \cdot cor(B, B)}}$$

3D visualization of the cognitive and somatosensory functions topography



Mapping of the networks corresponding to the cognitive functions "syllables production", "pure tone" and "lips movement" in blue, red, and green respectively.

Global view of cognitive networks



Mapping of the networks corresponding to the cognitive functions "speech" and "sentences" in purple and magenta respectively.

Multi-level integration of gene and cognitive knowledges



Mapping of the regions where the genes coding for oxytocin receptor (OXTR) and dopamine receptor D5 (DRD5) (in blue and red, respectively) are the most expressed.

Multi-level integration of cerebral regions and cognitive networks or gene expressions



Identification of new networks by topographical similarities (overlap) with the 300 cognitive tasks.



LinkRbrain: multi-sources et multi-level paltform to understand the brain

www.linkrbrain.org

50000 genetic probes 5000 papers in neuroscience Talairach atlas linkRbrain } online tool for neuroscience Unified multiscale integrator of the brain Global view ofrelations between cognitive tasks From neuroanatomical regions to cognition From genetics to cognitive tasks

LinkRbrain: multi-scale data integrator of the brain. Mesmoudi et al. 2015 Journal of neuroScience methods 31



