Neuroscience Letters 567 (2014) 68–73

Contents lists available at ScienceDirect

Neuroscience Letters

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

Integration of visual and motor functional streams in the human brain

Jorge Sepulcre [a,b,*]

[a] Division of Nuclear Medicine and Molecular Imaging, Department of Radiology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA
[b] Athinioula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

HIGHLIGHTS

- Streams of visual and motor cortices integrate in key multimodal brain areas.
- *Parietal operculum-4* area serves as the major relay station for the motor stream.
- Direct evidences of visual and motor streams converging in mirror neuron areas.
- Perception, action and cognition connect in the multimodal integration network.

ARTICLE INFO

Article history:
Received 30 November 2013
Received in revised form 27 January 2014
Accepted 21 March 2014

Keywords:
Visual streams
Motor streams
Visuo-motor integration
Brain network
Graph theory
Mirror neuron system

ABSTRACT

A long-standing difficulty in brain research has been to disentangle how information flows across circuits composed by multiple local and distant cerebral areas. At the large-scale level, several brain imaging methods have contributed to the understanding of those circuits by capturing the covariance or coupling patterns of blood oxygen level-dependent (BOLD) activity between distributed brain regions. The hypothesis is that underlying information processes are closely associated to synchronized brain activity, and therefore to the functional connectivity structure of the human brain. In this study, we have used a recently developed method called stepwise functional connectivity analysis. Our results show that motor and visual connectivity merge in a multimodal integration network that links together perception, action and cognition in the human functional connectome.

1. Introduction

The ability to adapt to the environment through visual perception and motor responses is essential for many animals in nature, including humans. Perception and motor programs combine in our brains to produce coherent temporo-spatial representations that mediate the interaction with the external world. However, it is still under debate how from high local-modular organized areas, such as early sensory and motor cortex, the brain assembles its functional streams into multimodal and further association regions of elaboration [1,2].

In the past, neuroanatomical studies – especially in macaque monkeys – brought solid evidence about the brain transitions from primary-to-association cortex. For instance, prefrontal areas such as BA10, BA46 and orbitofrontal cortex were proposed as final cortical destination where visual and somatomotor pathways converge [3]. Nevertheless, it has been the work of the mirror neuron system (MNS) that greatly expanded the visuo-motor integration research. The MNS is defined as the brain regions that actively engage both when individuals observe and perform the same action [4,7]. The connectivity between the ventral premotor area (vPM) at the inferior frontal gyrus and the inferior parietal lobule – often called the parieto-frontal mirror circuit – [7,8] has been proposed as the prominent system of mirror properties. Originally, the MNS was discovered during neural recordings in macaque monkey, particularly in ventral premotor area F5 and ventral inferior parietal lobule area PFG [7]. Later, brain neuroimaging studies have shown potential MNS regions in humans [7,9–18] but its significance and homology with monkey studies are still controversial [19]. For instance, the location of regions with mirror properties seems to be wider and more distributed in humans than in monkeys. Other regions such as the dorsal premotor, supplementary motor area (SMA), anterior insula (aI),

* Correspondence to: Harvard University, 52 Oxford Street, Northwest Building, 280.02, Cambridge, MA 02138, USA. Tel.: +1 857 869 2078.
E-mail address: sepulcre@nmr.mgh.harvard.edu

http://dx.doi.org/10.1016/j.neulet.2014.03.050
0304-3940/

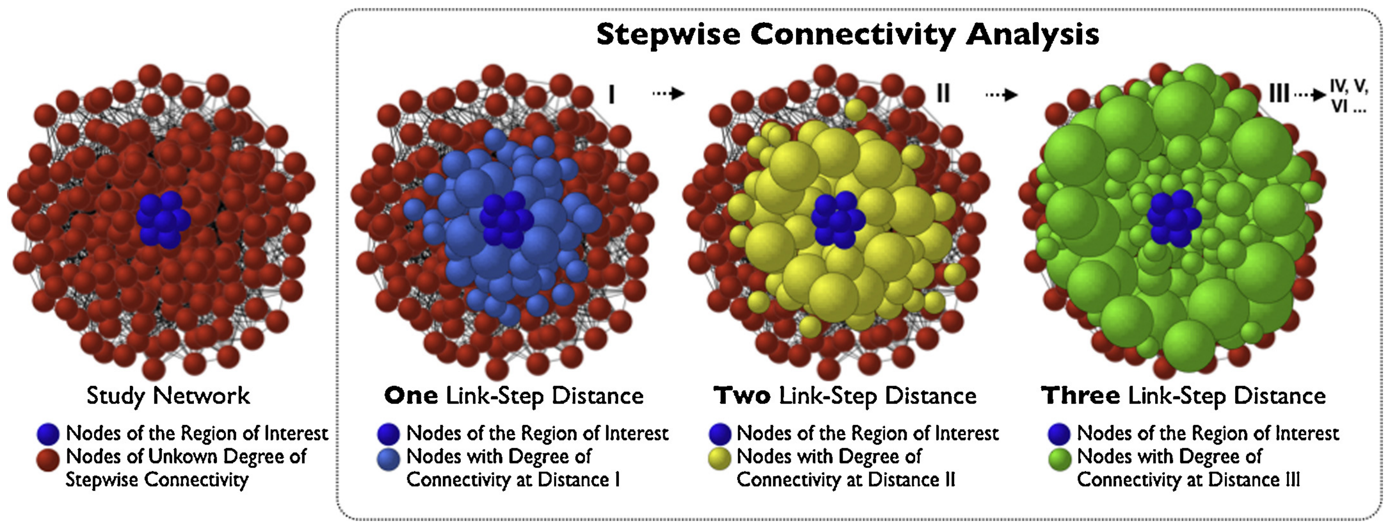

Fig. 1. (A) Illustrates the SFC method. Size of nodes represents the degree of connectivity at different link-step distances in a hypothetical network for a ROI (dark blue nodes). Node size is re-scaled in each condition for better visualization. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

medial temporal lobe, superior parietal lobule (SPL) and even primary motor areas have been described as part of the human MNS [12,15,16,20–25]. Moreover, several authors have criticized a possible over-interpretation of the MNS theory regarding its potential role in action understanding and encoding of actions [19]. The evidence that these functions are taking place in the MNS areas are sparse and divisive [19]. Other questions about brain processing of visuo-motor information remain open [26]. For instance, what is the functional brain connectivity structure that supports visuo-motor integration in humans? How does information flow from sensory to high-order cognitive areas? Where are the precise areas of convergences of the visual and motor pathways in the brain?

In this study, we investigate the visual and motor functional streams across the entire human brain by using a novel neuroimaging method called stepwise functional connectivity (SFC) [2,27]. Our findings facilitate a comprehensive description of the large-scale connectivity integration of the visual and motor systems.

2. Materials and methods

2.1. Participants

All analyses were based on a dataset of 100 healthy young adults (mean age = 21.3 yr, 37% male) examined before in Sepulcre et al. [27]. Therefore, the present investigation has developed from a previous study that focused only on sensory modalities of the human brain [27], extending its analysis to the motor system. Subjects were recruited as part of a neuroimaging collaborative effort across multiple laboratories at Harvard University, the Massachusetts General Hospital and the greater Boston area [28,29].

2.2. MRI acquisition and stepwise functional connectivity analysis

Scanning was acquired on a 3 T TimTrio system (Siemens, Erlangen, Germany) using the vendor 12-channel phased-array head coil. Imaging preprocessing steps were optimized for fcMRI analysis [30–32] extending an approach developed by Biswal et al. [33] (see Supplementary data for acquisition parameters and fcMRI preprocessing information).

SFC is a graph theory method [27] base on the signal couplings of spontaneous low-frequency BOLD fluctuations between brain regions – see Fig. 1 for a graphical display – also referred as intrinsic activity [33,34]. The SFC method complements the conventional intrinsic activity approach by detecting not only direct functional couplings of a brain region but also its indirect – but meaningful – associations in successive steps of connectivity. A mask of 4652 voxels covering the whole brain (cortex, subcortex, brain stem and cerebellum) was used to extract the time courses (124 time points). The FDR thresholded matrices were binarized to obtain undirected and un-weighted graphs for each individual that will serve as input data for the SFC analysis. Finally, The SFC analysis computes the degree or count of *all* paths that: (1) connect a given voxel in the brain to a primary cortex area of interest in (2) an *exact* length of connectivity distance. Connectivity distance refers here to the number of edges (link-steps) that have to be in between the voxel under analysis and the seed voxel (*e.g.* a voxel in the V1 visual cortex). In other words, SFC analysis finds the network pathways associated to a region of interest (ROI) without any other *a priori* selection constrain. Accordantly to our previous investigations, it is well-known that SFC maps reach a final stable state that collapsed into regions now considered to be the cortical hubs of the human brain [27]. The cortical hubs are the regions with the greatest number of functional connections to other areas of the brain and seem to be at the top of the brain hierarchical structure [35,36]. Only the most representative transitions of the SFC maps were displayed in the main figures (see SF 1 and 3 for further SFC distances). As a final step before cortical projection, individual SFC volumes from the SFC analysis of each subject were *z*-score transformed using the mean and standard deviation of the entire study sample. In order to achieve consistent maps, we only considered *z*-score values equivalent to a *p*-value lower than 0.005.

Of note, the SFC is a method that detects functional connectivity patterns, but specially in the high degree range of connections and it may underestimate alternative connectivity routes that do not necessarily have numerous pathways compared to some cortical regions, such as in subcortical structures. Therefore more work is needed to fully understand the complete motor and visual functional streams, particularly the thalamus and basal ganglia participation.

In this study, we used specific regions of the motor and visual cortices as regions of interest (ROIs) for the SFC analysis. A