

Editorial

Shedding Near-Infrared Light on Brain Networks

Andrei V. Medvedev*

Center for Functional and Molecular Imaging, Georgetown University Medical Center, USA

EDITORIAL

Near-infrared spectroscopy is a novel and promising technology for cost effective and noninvasive brain imaging in research and clinical practice. Utilizing the fact that near-infrared light is mostly absorbed by tissue hemoglobin, one can measure the intensity of light scattered and reflected by tissue (e.g., brain) to track local changes in hemoglobin concentrations within cortical layers (near-infrared spectroscopy, NIRS). Moreover, with multiple source-detector pairs, one can perform spatial reconstruction of an activation map for both oxygenated (HbO) and de-oxygenated forms of hemoglobin (in this case, the term 'Diffuse Optical Tomography' is used). Conceptually, NIRS detects hemodynamic modulations as an indirect measure of neuronal activity similar to the blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI) signal. Although spatial resolution of NIRS is lower than that of fMRI (about 1 cm), NIRS provides an imaging method with excellent temporal resolution (up to a few ms as found in electrophysiological methods such as EEG and MEG). Moreover, its low cost, portability and the ease of use make it ideally suitable for those subject and patient populations which are not easily amenable to the gold-standard imaging techniques of fMRI and positron emission tomography (PET). The modern NIRS instruments provide high density multi-channel recordings which allow for larger coverage of the head and it becomes possible to measure not only brain activation but also dynamic interactions between the brain areas. Those interactions can be assessed through temporal correlations of optical signals simultaneously recorded from multiple brain regions and thus a NIRS-based 'functional connectivity' similar to the functional connectivity measured by the fMRI BOLD signal [1] can be derived.

Recently, the brain imaging field has observed the exponential growth of studies concerning functional connectivity of the brain. Functional connectivity suggests new tools for the assessment of cognitive functions and for the study of functional architecture of the brain during task performance and the resting state. Since the pioneering study by [2] has provided the first evidence that resting state networks reflect interactions in cognitively relevant functional networks [2] and from the multitude of other fMRI studies, it becomes evident that functional architecture of the brain is relatively stable across different functional states from rest to various cognitive tasks.

With the advent of NIRS technology, it has been demonstrated

Corresponding author

Andrei V. Medvedev, Center for Functional and Molecular Imaging, Georgetown University Medical Center, Washington, DC, USA, Email: am236@georgetown.edu

Submitted: 13 August 2013

Accepted: 22 August 2013

Published: 24 August 2013

Copyright

© 2013 Medvedev

OPEN ACCESS

that NIRS can also detect spontaneous hemodynamic fluctuations in the brain [3-5]. However, due to relatively small head coverage in the early NIRS instruments and the lack of standardized methods of analysis, the studies of functional connectivity based on optical hemodynamic signals have been limited. Nevertheless, several groups have reported the use of NIRS to measure functionally relevant correlations within spontaneous fluctuations of hemodynamic signals to assess regional functional connectivity [6-10].

One of the interesting questions about functional connectivity is its distribution across hemispheres and whether it has any hemispheric asymmetry. Hemispheric asymmetry is a well-established phenomenon and can be easily demonstrated in the context of specific behavioral (sensory, cognitive and motor) tasks. Hemispheric asymmetry has a clear hemodynamic correlate usually measured by BOLD fMRI, which is greater *activation* of the dominant hemisphere during relevant tasks. The best example is the dominance and greater activation of the left hemisphere during language related tasks in the absolute majority of right-handed people. Hemispheric asymmetry regarding functional *connectivity* has not been studied in a consistent way and the data are sparse for both active and resting states. There are only a few imaging studies addressing the laterality of connectivity. In one of the first studies [11], laterality was measured from intrinsic on-going brain activity during passive fixation (this is one of the 'eyes open' variants of the resting state). The authors found both leftward and rightward regional laterality across different brain systems and the degree of asymmetry was dependent on multiple factors including gender. Overall, the brain asymmetry appeared to be more pronounced in males than in females [11]. In particular, this study demonstrated that the inferior frontal gyrus had rightward laterality among some other brain regions [11]. The greater resting state connectivity in the cognitive division of the right-hemispheric anterior cingulate cortex in right-handed participants during resting state was also demonstrated by Yan et al. [12].

Resting state functional connectivity of the default mode network in both right- and left-handed groups of subjects was studied by Saenger et al. [13]. They found various degrees of asymmetry (either leftward or rightward) in different brain regions. In particular, they found a rightward greater connectivity in the middle frontal and middle/superior temporal gyri in

the right-handed subjects. Importantly, despite the observed rightward asymmetries of functional connectivity, this study did not find similar hemispheric differences in gray matter volume (measured by voxel-based morphometry). This finding again emphasizes the fact that *functional* connectivity is not identical to *structural* connectivity and therefore the former provides additional information on the functional architecture of the brain which cannot be inferred from anatomical measurements.

In a recent study, Tomasi and Volkow have developed a new method of 'functional connectivity density mapping' and applied it in the study of laterality for both short-range (implicated in functional specialization) and long-range (implicated in functional integration) connectivity [14]. Rightward laterality of short-range connectivity was found in the areas around the lateral sulcus. The results for long-range connectivity were mixed with the rightward laterality in lateral sulcus and leftward lateralized in inferior prefrontal cortex and angular gyrus. The authors have also found moderate effects of gender on connectivity in that the males had greater rightward lateralization of brain connectivity in superior temporal and inferior frontal cortex.

Functional asymmetry has also been studied by electrophysiological methods. Although these methods have lower spatial resolution compared to fMRI, source reconstruction techniques can still delineate functional networks on the sublobar scale (i.e., within specific anatomical lobes). One of the early studies based on surface EEG coherence found higher right versus left hemispheric coherence [15]. This result was confirmed later by [16] who used current source correlations derived from the resting state EEG with source imaging LORETA software. They found higher intrahemispheric source correlations in the right compared to the left hemisphere [16].

Thus, both brain imaging and electrophysiological studies provide evidence that functional connectivity is higher in the right hemisphere. These results can be discussed in the context of anatomical differences between hemispheres. As discussed by [16], the architecture of the left hemisphere favors more local processing whereas the right hemisphere is better wired for the integration of information across distant regions [16]. Overall, the anatomical and functional data provide the basis for the existing view initially suggested by [17], that the left hemisphere is more involved in analytical and sequential processing while the right hemisphere is more involved in the integration and synthesis of multimodal information [17].

In our recent study, we analyzed functional connectivity and its hemispheric asymmetry using NIRS and measuring coherence of optical signals at low frequencies (0.01-0.1 Hz) in the prefrontal cortex in healthy subjects at rest [18]. Connectivity matrices showed specific patterns of connectivity which was higher within each anatomical region (inferior frontal gyrus, IFG and middle frontal gyrus, MFG) and between hemispheres (e.g., left IFG <-> right IFG) than between IFG and MFG in the same hemisphere. Laterality indexes were calculated as t-values for the 'left > right' comparisons of intrinsic connectivity. Significantly higher connectivity in the right hemisphere was demonstrated in all subjects regardless of handedness. Moreover, Granger Causality between hemispheres revealed a greater flow of information from the right to the left hemisphere than in the opposite way. These

results suggest that the left hemisphere is more 'controlled' by the right hemisphere in the resting state. This finding raises some intriguing questions.

First, it should be noted that during the resting state subjects fall asleep quite often experiencing brief episodes of nap (this was confirmed in the current study by the analysis of concurrently recorded EEG where sleep spindles were occasionally noticed thus indicating NREM sleep stages 1-2). Does this mean that during sleep-like states the right hemisphere plays a more active role? If so, the proactive role of the right hemisphere may point to its involvement in information processing usually associated with sleep such as re-evaluation, post-processing, classifying and storing of previously acquired information. These processes are thought to eventually lead to the consolidation of new information into long-term memories.

As discussed above, the anatomical and functional architecture of the right hemisphere may favor such 'consolidating' and 'house-keeping' roles because the right-hemispheric connectivity is broader compared to the left hemisphere and spans across different modalities thus facilitating the formation of associative memories. The relative roles of both hemispheres in the resting state and sleep-related processes are yet unknown but the recent findings on hemispheric asymmetry of functional connectivity encourage further studies of the role of both hemispheres in different functional states of the brain.

ACKNOWLEDGMENT

The project was supported by awards R21RR025786 from the National Center for Research Resources and R21GM103526 from the National Institute of General Medical Sciences. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

REFERENCES

1. Friston KJ, Frith CD, Liddle PF, Frackowiak RS. Functional connectivity: the principal-component analysis of large (PET) data sets. *J Cereb Blood Flow Metab.* 1993; 13: 5-14.
2. De Luca M, Beckmann CF, De Stefano N, Matthews PM, Smith SM. fMRI resting state networks define distinct modes of long-distance interactions in the human brain. *Neuroimage.* 2006; 29: 1359-67.
3. Hoshi Y, Kosaka S, Xie Y, Kohri S, Tamura M. Relationship between fluctuations in the cerebral hemoglobin oxygenation state and neuronal activity under resting conditions in man. *Neurosci Lett.* 1998; 245: 147-50.
4. Obrig H, Neufang M, Wenzel R, Kohl M, Steinbrink J, Einhupl K, et al. Spontaneous low frequency oscillations of cerebral hemodynamics and metabolism in human adults. *Neuroimage.* 2000; 12: 623-39.
5. Toronov V, Franceschini MA, Filiaci M, Fantini S, Wolf M, Michalos A, et al. Near-infrared study of fluctuations in cerebral hemodynamics during rest and motor stimulation: temporal analysis and spatial mapping. *Med Phys.* 2000; 27: 801-15.
6. Rykhlevskaia E, Fabiani M, Gratton G. Lagged covariance structure models for studying functional connectivity in the brain. *Neuroimage.* 2006; 30: 1203-18.
7. White BR, Snyder AZ, Cohen AL, Petersen SE, Raichle ME, Schlaggar BL, et al. Resting-state functional connectivity in the human brain

- revealed with diffuse optical tomography. *Neuroimage*. 2009; 47: 148-56.
8. Lu CM, Zhang YJ, Biswal BB, Zang YF, Peng DL, Zhu CZ. Use of fNIRS to assess resting state functional connectivity. *J Neurosci Methods*. 2010; 186: 242-9.
 9. Zhang YJ, Lu CM, Biswal BB, Zang YF, Peng DL, Zhu CZ. Detecting resting-state functional connectivity in the language system using functional near-infrared spectroscopy. *J Biomed Opt*. 2010; 15: 047003.
 10. Hu XS, Hong KS, Ge SS. Reduction of trial-to-trial variability in functional near-infrared spectroscopy signals by accounting for resting-state functional connectivity. *J Biomed Opt*. 2013; 18: 17003.
 11. Liu H, Stufflebeam SM, Sepulcre J, Hedden T, Buckner RL. Evidence from intrinsic activity that asymmetry of the human brain is controlled by multiple factors. *Proc Natl Acad Sci U S A*. 2009; 106: 20499-503.
 12. Yan H, Zuo XN, Wang D, Wang J, Zhu C, Milham MP, et al. Hemispheric asymmetry in cognitive division of anterior cingulate cortex: a resting-state functional connectivity study. *Neuroimage*. 2009; 47: 1579-89.
 13. Saenger VM, Barrios FA, Martínez-Gudiño ML, Alcauter S. Hemispheric asymmetries of functional connectivity and grey matter volume in the default mode network. *Neuropsychologia*. 2012; 50: 1308-15.
 14. Tomasi D, Volkow ND. Laterality patterns of brain functional connectivity: gender effects. *Cereb Cortex*. 2012; 22: 1455-62.
 15. Tucker DM, Roth DL, Bair TB. Functional connections among cortical regions: topography of EEG coherence. *Electroencephalogr Clin Neurophysiol*. 1986; 63: 242-50.
 16. Thatcher RW, Biver CJ, North D. Spatial-temporal current source correlations and cortical connectivity. *Clin EEG Neurosci*. 2007; 38: 35-48.
 17. Kinsbourne M. Mechanisms of hemisphere interaction in man. In: Kinsbourne, M., Smith, L., (Eds.). *Hemispheric Disconnection and Cerebral Function*, Thomas, Springfield, IL, 1974; pp. 71-96.
 18. Medvedev AV. Does the resting state connectivity have hemispheric asymmetry? A near-infrared spectroscopy study. *Neuroimage*. 2013. doi: 10.1016/j.neuroimage.2013.05.092

Cite this article

Medvedev AV (2013) Shedding Near-Infrared Light on Brain Networks. *J Radiol Radiat Ther* 1: 1002.