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Editorial Article

A Brief History of Arguments in Resting state Functional Magnetic Resonance Imaging Research

Xiangyu Long

University of Calgary & the Alberta Children's Hospital Research Institute, Calgary, Alberta, Canada.

***Corresponding Author**: Xiangyu Long, University of Calgary & the Alberta Children's Hospital Research Institute, Canada. E-mail: xiangyu.long@ucalgary.ca

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All scientific research needs to go through years of arguments and debates to polish itself, including research of functional magnetic resonance imaging (fMRI) in human brain. fMRI is one of the state-of-the-art non-invasive techniques to investigate brain functions of human and animals. Since it is difficult and hardly practical to record vivo neural activity from human brain, fMRI provides an substitute measurement of neural activity which is based on the haemodynamic response in blood flow during the neural activity, also known as blood-oxygen-level dependent (BOLD) signal [1]. One of the usages for fMRI is to investigate neurophysiological mechanism of human mental or physical behavior, such as detecting the brain areas which related to motor performance by asking participants to mover their body parts inside the MRI scanner [2]. Another usage, which I have been working with for nearly a decade, is resting-state fMRI (rs-fMRI). This approach only need participant to stay in the scanner without doing anything particular. Therefore, the BOLD signal from rs-fMRI reflects intrinsic, fundamental neural activity of human brain [3]. In this editorial, I would like to go through several main arguments happened in the rs-fMRI research field.

One of the important and famous finding in rs-fMRI or resting brain is a set of brain regions which compose of a pattern named "the default mode network (DMN)" composed of the posterior cingulate cortex, the bilateral angular gyrus and the medial prefrontal cortex [4,5]. The reason it is named "network" because the BOLD signals from those regions also present temporal correlated to each other [6]. This finding implied human brain might have its "default" or "intrinsic" activity at rest. The DMN seems to be a perfect baseline when investigating human brain under varies of conditions, especially for mental disorders, such as Alzheimer's disease and depressive disorders [7,8]. However, the comprehensive understanding of the default mode network is still unclear and caused a serious of arguments. The baseline feature of the DMN was argued when applied to other psychological tasks [9]. The function and the anatomy of the DMN was further investigated and separated into subsystems [10,11,12]. Actually, arguments around the DMN helped to increase the understanding of more complex cognitive function, such as mind wandering [13], as well as the development of methodology, such as functional connectivity analysis and its application [14]. Up to date, researchers still excite when they found the DMN brain regions in their results, but the interpretations of those regions need to be more careful, especially when we still cannot see the full picture of the DMN.

Another argument happened in rs-fMRI is one of its pre-processing steps, named global signal regression (GSR). The GSR or the whole brain signal regression is the procedure to regress out the averaged signal of the whole brain from the fMRI data. This argument was rise from the finding of two anti-correlated brain networks (one of them is the DMN) by rs-fMRI [15]. Several researchers questioned that the anti-correlation might be induced by the GSR [16,10,17]. Even later the anti-correlated networks were still detected without the GSR [18,19], the inclusion of GSR in the pre-processing steps was still controversial. From the de-noising perspective, GSR could remove physiological noises to improve the data quality [20,21,22,23]. However, the GSP could also alter the group-level comparisons [24]. Nowadays, most of the researchers would include GSR to reduce the influences of noises, however, it is still necessary to process the rs-fMRI data with and without GSR to make sure their result is robust to GSR.

The last argument I would like to mention is still happening in the whole fMRI field rather than rs-fMRI. The reliability and statistical power is always big concern in scientific field. In fMRI, due to its feature of 3D images, the cluster-based statistical analysis was developed and could be implemented by several software, such as SPM (www.fil.ion.ucl.ac.uk/spm/), FSL (https://www.fmrib.ox.ac.uk/fsl) and AFNI (https://afni.nimh.nih.gov/), and those software are widely used in the fMRI community for many years. However, a group of researchers found that the cluster-based statistical analysis could introduce high level of false-positive rates [25]. This article warned fMRI community that a lot of previous fMRI studies might be inaccurate. There is no doubt that this article faced many questioning voices, such as the authors of the related software [26], and its authors made a correction to the article to extenuate the tone of their conclusion [27]. Nonetheless, this argument increased the awareness of implementing statistical analysis and brought other important issues such as data sharing among researchers.

Up to date, those arguments always inspires researchers to ameliorate the new findings, approaches and thoughts. There could be more arguments in future. One of my concern is the “Big data” fever in recent rs-fMRI studies. Bigger database could reveal new results that the small sample size could not, but from the clinical perspective, the conclusion of big data might overlook the small portions of distinctive cases. This might develop inaccurate treatments and evaluations for those cases. Personally, I am very glad about those arguments, even though they would bring extra workloads and cautions for my research. As long as the research in rs-fMRI and neuroscience intend to develop, those arguments are always important and necessary.

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