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Resting state fMRI: A review on methods in resting state connectivity analysis and resting state networks

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Abstract

The inquisitiveness about what happens in the brain has been there since the beginning of humankind. Functional magnetic resonance imaging is a prominent tool which helps in the non-invasive examination, localisation as well as lateralisation of brain functions such as language, memory, etc. In recent years, there is an apparent shift in the focus of neuroscience research to studies dealing with a brain at 'resting state'. Here the spotlight is on the intrinsic activity within the brain, in the absence of any sensory or cognitive stimulus. The analyses of functional brain connectivity in the state of rest have revealed different resting state networks, which depict specific functions and varied spatial topology. However, different statistical methods have been introduced to study resting state functional magnetic resonance imaging connectivity, yet producing consistent results. In this article, we introduce the concept of resting state functional magnetic resonance imaging in detail, then discuss three most widely used methods for analysis, describe a few of the resting state networks featuring the brain regions, associated cognitive functions and clinical applications of resting state functional magnetic resonance imaging. This review aims to highlight the utility and importance of studying resting state functional magnetic resonance imaging connectivity, underlining its complementary nature to the task-based functional magnetic resonance imaging.

Keywords: Graph analysis, independent component analysis, resting state functional connectivity, seed-based analysis

Introduction

The resting state functional magnetic resonance imaging (rs-fMRI) technique has gained advantages over other functional magnetic resonance imaging (fMRI) techniques due to its ease in signal acquisition, requisite of least effort from the patients and proficiency in identifying the functional areas in different patient populations, for example the paediatric population, unconscious patients, patients with low intelligence quotient etc. The task-based fMRI, has evolved as an advanced magnetic resonance technique to analyse and evaluate the functional domains in the brain. During this techinique, the subjects are instructed to perform specific tasks, which are designed to target a single utility such as motor task, language, memory, vision, attention and sensory function.[1,2] Recent studies have observed that paediatric patients, patients with disorders of consciousness, i.e. coma, vegetative and minimally conscious state, are able to undergo rs-fMRI.[3] Rs-fMRI came into the clinical realm after the studies of Biswal and colleagues while investigating the transfer function in the motor cortex and the noise sources in the brain. It was found that resting state signals are consistent low frequency fluctuations in the range 0.01–0.08 Hz.[4,5] The human brain is in fact operational even during the resting or relaxing state. A very interesting aspect of rs-fMRI is that the signals that are discarded in task fMRI studies are taken into consideration as they are spontaneous fluctuations and are confined to distinct cortical network systems in the brain.[2] Even though blood oxygenation level-dependent (BOLD) contrast is the basic phenomenon behind the resting and task fMRI, studies have observed some notable differences between the two techniques.[2] Table 1 shows the comparison between rs-fMRI and task fMRI.

The brain consumes a surprisingly large amount of energy even in the resting state. The weight of an adult human brain is only 2% of the overall body weight, but energy consumed by the brain is approximately 20% of the total energy consumption.[6] Furthermore, studies confirm that the brain utilises 60–80% of the energy for communication between neurons and their supporting cells, which is the inherent activity, whereas for elicited activity the brain utilises only 0.5–1.0% of the total energy.[5] The major portion of energy consumption is utilised for the intrinsic activities of the brain, and is related to the existence of dark energy in the brain, similar to the dark energy in the cosmos.[6,7]

BOLD fMRI

The rs-fMRI relies on spontaneous low frequency fluctuations in the BOLD signal. In fact BOLD contrast forms the basis of fMRI formation, namely task-based and rs-fMRI. Ogawa et al. was the first to recognise the potential importance of the BOLD contrast that it is entirely dependent on the blood oxygen levels.[8] Due to the diamagnetic effect of oxyhaemoglobin and the paramagnetic effect of deoxyhaemoglobin, voxels having a low concentration of deoxyhaemoglobin give rise to an increased BOLD signal and those with a high concentration contribute to a decrease in the BOLD signal.[8–13] The deoxyhaemoglobin responsible for the BOLD effect is also influenced by physiological quantities such as cerebral blood flow, cerebral blood volume and cerebral metabolic rate of oxygen.[14]

Brain connectivity analysis techniques

Generally, connectivity is the study of the interaction between two different brain regions. The anatomical connectivity is the physical connections or interactions between two anatomical areas of the brain and can be obtained with the aid of structural imaging in collaboration with diffusion tensor tractography methods.[15] Functional connectivity (FC) attempts to establish the connection between two spatial regions of interest with the assistance of linear temporal correlation. The effective connectivity is a higher level of FC analysis because it estimates the underlying direct causal connections between functionally connected regions. Eventually effective connectivity is based on the mechanistic model of how the data get influenced.[16–18] FC is inferred on the basis of correlations among the parameters of neuronal activity, whereas effective connectivity refers to the influence which one neural system exerts over another. However, the article focuses on the FC analysis techniques such as seed-based analysis, independent component analysis (ICA) and graph theory analysis for studying rs-fMRI connectivity. For these techniques we have used software such as SPM, DPARSF, REST, MELODIC tool of FSL, CONN Connectivity toolbox, et. for preprocessing and post-processing analysis. Moreover, we have portrayed an overview of the different functional networks in the brain during the resting state.

Seed-based analysis

Seed-based analysis was the first method adopted by Biswal et al. to identify the resting state networks.[19] Essentially seed-based analysis is a model-based method in which we are able to select a seed or region of interest (ROI) and find the linear correlation of this seed region with all the other voxels in the entire brain, thereby yielding a seed-based FC map. The simplicity, interpretability and straightforwardness of this technique make it a good approach for rs-fMRI FC.[20,21] As this method is entirely dependent on the user defined ROIs, it is difficult to examine whole brain FC using this technique. Apart from the FC analysis, seed-based analysis may be used to quantify the amplitude of low frequency fluctuations (ALFF), fractional amplitude of low frequency fluctuations (fALFF), Kendall coefficient of concordance, regional homogeneity measures.[22] The ALFF represents the average power of the low frequency fluctuations in the range (0.01–0.08) and the fALFF indicates the ratio of low frequency power spectrum to the entire frequency range reliant on time of repetition of the analysis.[23,24] The Kendall coefficient of concordance examines the similarity of a number of time courses while regional homogeneity evaluates the similarity of the time series of the particular voxel with that of the nearby neighbours in a voxel-wise manner.[25] The chart shows the processing of seed-based FC analysis in Figure 1.[20,26,27] Figures 2–7 shown in the present review were obtained from data acquired from a 1.5 Tesla Siemens MRI Machine (Magnetom Avanto TIM, Erlangen, Germany). Figure 2 represents the seed-based FC analysis performed with the left Brodmann areas 44 and 45 as the seed region.

Independent component analysis

The human brain is composed of a vast network of neurons, which generate both high and low frequency fluctuations. Rs-fMRI relies on spontaneous low frequency fluctuations (<0.1 Hz) emerging from spatially separated, functionally linked, continuously communicating anatomical areas within a network. The rs-fMRI signal which we extract from a subject is in its composite form encompassing a signal of interest together with other artefacts. ICA facilitates the effective extraction of distinct rs-fMRI networks by employing mathematical algorithms to decompose the signal from whole brain voxels to spatially and temporally independent components. It describes the temporal and spatial characteristics of the underlying hidden components or networks.[20,28] Even though it is advantageous that prior knowledge is not required for the processing of the source signal, one should be able to identify the ICA network components from those of noise by prior knowledge or experience.

The rs-fMRI low frequency spontaneous fluctuations may be automatically recovered from the noise using ICA. ICA is a data-driven method that is based on a blind source separation algorithm.[29–31] Apart from the seed-based analysis, which finds the single interaction between the seed region and the entire voxel, ICA investigates multiple simultaneous voxel to voxel interactions of distinct networks in the brain. Therefore ICA is a powerful technique and can be utilised for performing group-level analysis as well as for the same group having different conditions such as different psychological, physiological and pharmacological conditions. Studies confirm that single ICA can be advocated in a group of subjects by temporally linking or concatenating the entire subject's dataset to a single large dataset. Figure 3 represents the resting state networks such as language, auditory and default mode network (a, b and c) obtained from ICA melodic.

To overcome the drawbacks of single subject ICA, group ICA using the dual regression approach was initiated.[31,32] In dual regression analysis, the regression technique is used for analysing the rs-fMRI data from a group of subjects. Dual regression is a unification of three stages. In the initial stage, ICA decomposes the concatenated multiple fMRI data, in order to identify distinct patterns of FC in each subject. In the next step, subject-specific spatial maps and associate time courses are identified for all the subjects. In the third stage, different component maps are generated for different subjects and are compiled into a single four-dimensional file to perform the non-parametric analysis, which is an intuitive methodology of statistical test done to extract statistical significance across groups or across subjects in a group.

There are several methods to analyse group ICA. As a discussion on the different methods of group analysis technique in detail is beyond the scope of this review, interested readers could refer to the previous articles by Calhoun et al.,[33] Guo and Pagnoni,[34] Esposito et al.[35] and Schmithorst and Holland.[36]

Graph theory

In neuroscience, graph theory is applied to establish mathematical models of complex network functions within the human brain. These networks have associations and connections between various regions and subregions in the brain and its combined dynamics constitute a larger single network. The graph theory approach predominantly deals with the study of nodes and edges, and here the relation between the nodes and edges can be established as $G = (V, E)$ where V is a gathering of nodes connected by edges E, which describes the interaction between nodes.[37]

The application of graph theory in brain FC analysis is capable of giving answers to different aspects of connectivity through different graph parameters. These are: (i) average path length; (ii) clustering coefficient; (iii) degree of node; (iv) centrality measures; and (v) the level of modularity. The clustering coefficient reflects the local connectedness of the graph and is the ratio between the number of connections between the direct neighbours of node i and the maximum number of possible connections between the neighbours of node i. Overall, it examines the local interconnection ability of the network. In another metrics, the degree is the simplest measurement which quantifies the total number of connections of the node. The node with a higher degree indicates that it plays an inevitable role in the flow of information in that particular network. Likewise, path length is another graph theoretical metrics that represents the level of global communication efficiency of a network. Thus the shortest path length signifies the smallest number of edges required to connect one node to the other nodes in the network. Subsequently the characteristic path length of node i shows the proximity of node i to all the other nodes in the network.[37–44]

While seed-based analysis focuses only on the strength of correlation between one ROI to other, graph theory measures the topological properties of the ROI within the whole brain or that network related to a particular function.[39] Integration and segregation are the ways of representation of brain networks because brain regions functions in such a manner. Functional integration observes the brain as an intercomponent network, which incorporates different networks in the brain to act cooperatively for a particular function whereas segregation imply the connections within the brain network. So graph theory is a promising technique in exploring the integrated and segregated networks in the brain. The graph metrics such as global efficiency and average path length indicate the integration of brain networks. For instance, global efficiency examines the proficiency of a brain network to propogate information on a global level and the average path length signifies the shortest number of edges connecting two nodes in a network. Consequently, local efficiency, clustering coefficient and centrality provide insight into the segregated activity of the networks. That local efficiency denotes the information flow in a local network, which is a subpart of the whole brain network. Accordingly, the clustering coefficient shows the degree to which nodes in a network tend to cluster together, and centrality signifies how important the node is in the whole brain network and examines whether the particular node has a cental role or leading role in propagating the information to other nodes in the network.[40–44] Figure 4 shows the overall connectivity obtained after graph analysis performed in controls using task fMRI and rs-fMRI using the Conn toolbox. In addition, Figure 5 shows the FC map obtained when the pars opercularis left and right was taken as the seed ROI for task and rs-fMRI.

A small world network is characterised by a high value of local and global efficiency and a small characteristic path length. A small world network may be termed a densely connected local clustered network having a slight characteristic path length that permits a prompt communication between the nodes in the network.[38,45] According to Supekar et al., a large scale network is characterised by slight short range connectivity and more supremacy from the part of long range FC.[40] The study observes that the clustering coefficient and characteristic path length are informative regarding the large-scale organisation of brain networks.

Protocols for rs-fMRI imaging in our hospital

The rs-fMRI protocol can be done in several ways. The subject can be instructed to follow any of these methods such as eyes closed, eyes opened and eyes opened while concentrating on a crosshair on the screen. During the eyes closed condition, the subjects are instructed not to fall asleep. The scanning session was performed with 1.5 T as well as 3 T magnetic resonance scanners using the following parameters for research applications as shown in Table 2. We have obtained institutional ethics committee approval for conducting the study.

Different resting state networks in the brain

The different networks in the brain are the salience network, auditory network, basal ganglia network, higher visual network, visuospatial network, default mode network, language network, executive network, precuneus network, primary visual network, sensory motor network, etc. Figures 6 and 7 show the respective networks in the brain obtained by using seed-based analysis.

Salience network

The salience network constitutes the dorsal anterior cingulate cortex, bilateral insula and presupplementary motor area. The dysfunction of the network will disrupt the functioning of other networks, because it has a key role in regulating the dynamic changes in other networks. Moreover, the network is indispensable during the rapid change of behaviour. That is, what to do next or not to do is decided by the appropriate functioning of the network. For these reasons the salient network's proper functioning is inevitable for the commencement of control of cognition processes.[46–48]

Auditory network

The regions involved for the auditory network are the right and left primary auditory cortex, Heschl's gyrus, planum polare and temporale, lateral superior temporal gyrus and posterior insular cortex.[49,50] The auditory cortices were functionally well defined as reliable to the anterolateral Heschl's gyrus, left and right, respectively.[50]

Basal ganglia network

The network involves the basal ganglia, substantia nigra, subthalamic nucleus, striatum, global pallidum externa and interna. Functional changes in the basal ganglia are mostly understood in Parkinsonism because previous studies observed that it lies at the heart of Parkinson's disease. It is a deep brain structure located at the brain's basement. It is involved in many functions such as control of motor areas, emotion, cognition, etc.[51–54] Accordingly, they play a key role in the learning of difficult and complex behaviours, and due to its strong coordination during movement they are are involved in goal-directed behaviours which require movement.

Visual network

Beckmann et al. have observed synchronous activations in the bilateral and medial calcarine sulcus, extrastriate regions, namely the lingual gyrus, inferior area of precuneus and lateral geniculate nucleus of the thalamus, which collectively form the visual network, among which the lateral geniculate nucleus of the thalamus functionally connects the visual input to the primary visual cortex.[55] The areas such as the peristriate area, lateral occipital gyrus and superior occipital gyrus were recognised as primary visual areas by Damoiseaux et al. through investigations on the consistent rs-fMRI networks.[56] The study clarifies that there are medial and lateral visual cortical areas. The report by Beckmann et al.[55] informs that visual areas situated in the extrastriate regions of the lingual gyrus, inferior division of precuneus and lateral geniculate nucleus of the thalamus constitute the medial visual areas. The occipitotemporal junction, spreading out from the occipital pole and the superior parietal region constitutes the lateral visual areas.[55–57]

Visuospatial network

Synchronous activations at the posterior parietal cortex of the occipitoparietal junction, midline of the precuneus, posterior cingulate cortex and the frontal pole are collectively known as the visuospatial network. Many studies have observed that lesions in the lateral posterior parietal regions can affect spatial attention. So these findings suggest that the posterior parietal cortex is engaged in orienting to salient visuospatial cues.[55,58–60]

Default mode network

The default mode network involves the posterior cingulate cortex, medial prefrontal cortex and lateral parietal cortex. The default mode network executes increased activity only when the individual is in the resting condition. It is also known as the task-negative network because it becomes de-active when the individual does some task and of course is studied in a broader way by many of the investigators. This network is otherwise known as the mentalising network due to its participation in social cognition such as introspection, mind wandering, emotional processing, thinking others mental state, etc.[60–62]

Language network

The language network not only involves Broca's and Wernicke's areas, but it also extends to the prefrontal, temporal parietal and subcortical regions. The network is involved in functions such as speech, comprehension, reading, interpreting, mimicking, etc. In addition, Broca's area is the location of mirror neurons where the neuron's firing rate increases when the individual performs goal-irected activities and while observing similar movements of others. The mirror neurons help to understand and imitate motor activities.[63–66]

Executive network and executive control network

The excecutive network is the network which gets activated during fMRI tasks involving executive functions. It constitutes the dorsolateral prefrontal cortex and posterior parietal cortex.[67–69] The medial frontal gyrus, superior frontal gyrus and the anterior cingulate cortex, paracingulate gyri, ventrolateral prefrontal cortex, subcortical regions of the thalamus constitute the executive control network. This network is active during a task which needs cognitive control and working memory.[70] Like the attention network, the executive network is also active during the task condition and exhibits anticorrelated network during the resting condition. The executive control network is concerned to be functioning during target-directed activities and during control of intellectual activities.[71]

Precuneus network

Precuneus, the associated area within the default mode network, is characterised as hot spots with high metabolic rates compared to other networks during the resting state. Several studies have admitted the importance of precuneus in the default mode network as it assists in various behavioural functions. The involvement of precuneus in the manipulation of mental images and internally guided attention derived from visuospatial imagery studies implicate their unique capacity in mental representation of the internal self. Many studies confirm the vital role of precuneus in tasks such as autobiographical memory retrieval, emotional stimulus processing and reward outcome monitoring.[72–74] All the reports on the regard of precuneus states that it has a central role within the default mode network, at the same time its unique contributions can be observed in a variety of behavioural processing states.[75–77]

The sensorimotor network

This network was in fact the first rs-fMRI network studied by Biswal et al., by using seed-based analysis.[4] It is the network which shows a high correlation between the left and right regions when the FC was studied. Many studies have shown that there exists a high level of functional correlation between the left and right hemispheric motor cortex.[4,19,78] In the somatosensory motor cortex, the Brodmann areas 1, 2 and 3, located on the posterior bank of the central sulcus, represent the different motor areas of the body such as the legs, hands and face. The unique signals from the face are totally different from the signals from the hands or legs due to the fact that each signal from different motor areas form different separable clusters so that it may be clearly understood.

The rs-fMRI connectivity is a novel technique that offers an excellent opportunity to explore cognitive studies as it was found trustworthy in clinical pathologies such as Alzheimers, schizophrenia, autism spectrum disorders, depression and mood disorders, Parkinson's disease, traumatic brain injury, learning disability disorders, etc.[79–83] As different techniques help in generating different aspects of connectivity in the brain, completely different steps are involved in the processing of each technique and the final quantification parameters also change with respect to the preferred technique.

Clinical applications of resting fMRI

Numerous studies have evaluated the potential of rs-fMRI for clinical applications. However, it is not certain whether neuroradiologists have started using the technique for clinical decision-making. In most of the centres it is being used as a research tool to understand the prospective application of this technique. ICA of rs-fMRI has emerged as a promising technique to assess the functional language networks, thereby finding application in various neurological diseases.[84,85] It has been reported that rs-fMRI can localise the sensorimotor cortex and provide anatomical specificity of hand, foot and mouth subregions.[86] Rs-fMRI connectivity analysis in brain tumour patients assists in the identification as well as the visualisation of critical networks, thereby aiding in the preservation of functions.[86–88] The whole brain rs-fMRI connectivity abnormality in patients with mesial temporal lobe epilepsy with right hippocampal sclerosis during the interictal period found that they exhibited decreased rs-fMRI connectivity within the right hemisphere and increased rs-fMRI connectivity in the left hemisphere.[89–92] Studies suggest that Alzheimers affects not only the default mode network connectivity, but it also affects the large scale networks with equal strength.[93] Network to connectivity analysis in behavioural variant frontotemporal dementia elucidated decreased connectivity between regions, different from those regions found related to Alzheimers disease.[93–95]

Few studies have analysed the rs-fMRI connectivity focusing on graph analysis and its other metrics such as ALFF and fALFF in patients with schizophrenia. It was found that schizophrenia patients exhibit significantly less global connectivity compared with healthy controls, while bipolar patients had intermediate global connectivity markedly different from schizophrenia patients and healthy controls.[24,80] Studies have found that the overall organisation of the brain network is disturbed in the early stage of Parkinsonism. It revealed decreased global efficiency, disrupted modularity and hub distribution in its early stage.[96] Another study focused on Parkinsonism with tremor found a correlation between altered FC and the clinical performance of patients.[97] In addition, rs-fMRI had found its application in predicting the mental states after yoga and meditation. It was demonstrated that experienced meditators had weaker connectivity between default mode network areas that deal with self-referenced processing, while showing increased connectivity between the dorsomedial prefrontal cortex and right inferior parietal lobule of the default mode network.[98,99] Even though rs-fMRI still remains as a research tool, the scientific literature arising from the same is increasing day by day. If this technique can be relied on to get consistent results, we presume that rs-fMRI can be used as a promising clinical tool and it may replace the conventional fMRI techniques in the near future.

Conclusion

Task fMRI and rs-fMRI are twin techniques rooted on BOLD signal change and are effective predominantly because of their non-invasiveness. As haemodynamic response is the marker of a hidden state of neural population, rs-fMRI can bring up the more clinical significance with minimal effort from patients. Even though each of these techniques may not complement one another, there are still some options of similarities. This initiates and entails researchers exploring more applications from brain connectivity analysis, identifying abnormality in the low frequency fluctuations of the BOLD signal due to pathological changes that may help in diagnosis and prognosis of the disease, thereby offering a promising option in the treatment, presurgical as well as post-surgical monitoring of the functional network architecture of the brain.

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Conflict of interest

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Figures and Tables

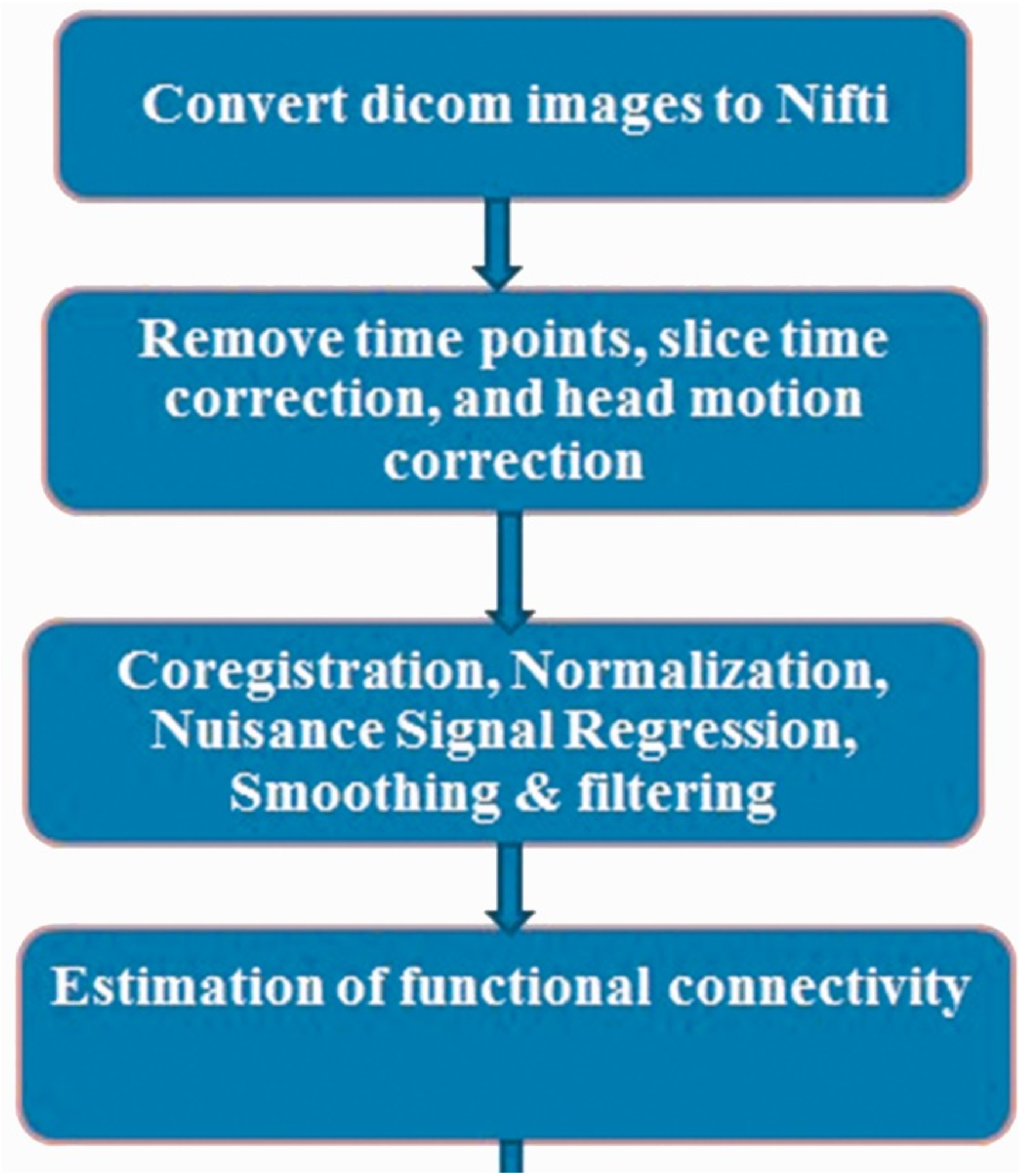
Table 1.

Presents a brief comparison between task based fMRI and Resting state fMRI.

SI no.	Task-based fMRI	Rs-fMRI
I	Analyses of the spontaneous modulations in the BOLD signal in the presence of a particular activity (e.g. finger-tapping, eye-blinking, naming, memorizing, etc.)	Analyses of the spontaneous BOLD signal in the absence of any explicit task or an input
II	Task-related increase in neuronal metabolism are less than 5%	60–80% of brain's energy is consumed during resting state
III	During task-based activity the focus is only on a very small fraction of the brain's overall activity	In terms of overall brain function, the resting state brain activity is far more significant than task-related activity
IV	The signal during a task-related activity is very small compared to the noise, i.e. 80% of the BOLD modulation is discarded as noise	The signals which are discarded as noise in task fMRI is taken as signals in rs-fMRI as they are the low frequency spontaneous fluctuations in the BOLD signal
V	Due to discarding of signal as noise, task fMRI has a low SNR	Have improved SNR since it takes the overall spontaneous low frequency fluctuations
VI	For the interpretation of results, a large number of trials are required in task fMRI	No need of more trials like task fMRI
VII	If one wants to analyse the motor function and language function, a separate task may be required to analyse each function in task-based fMRI	In rs-fMRI, the acquired may be used to analyse one or more functions
IX	Patient cooperation is essential to do task fMRI	Paediatric patients, patients with low IQ and even patients in the vegetative and coma state are able to do rs-fMRI
X	Repeated sessions of task-based activity to assess the disease prognosis, treatment effect etc. will result in familiarity with the task which will affect the output adversely	In rs-fMRI even we are taking different sessions, due to the absence of task, we are able to avoid the task-related confusions and uncertainties faced by task fMRI

fMRI: functional magnetic resonance imaging; rs-fMRI: resting state functional magnetic resonance imaging; BOLD: blood oxygenation level-dependent; SNR: signal to noise ratio.

Figure 1.



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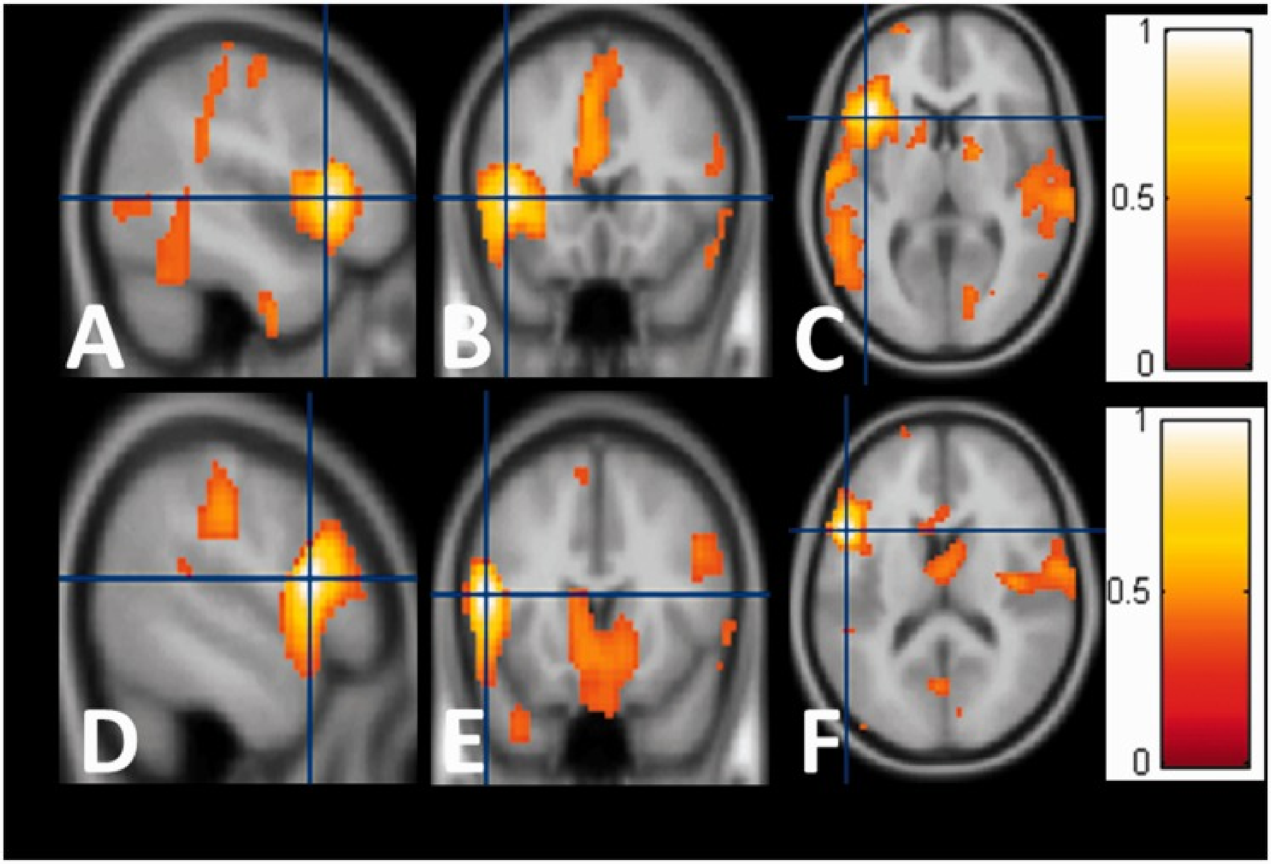
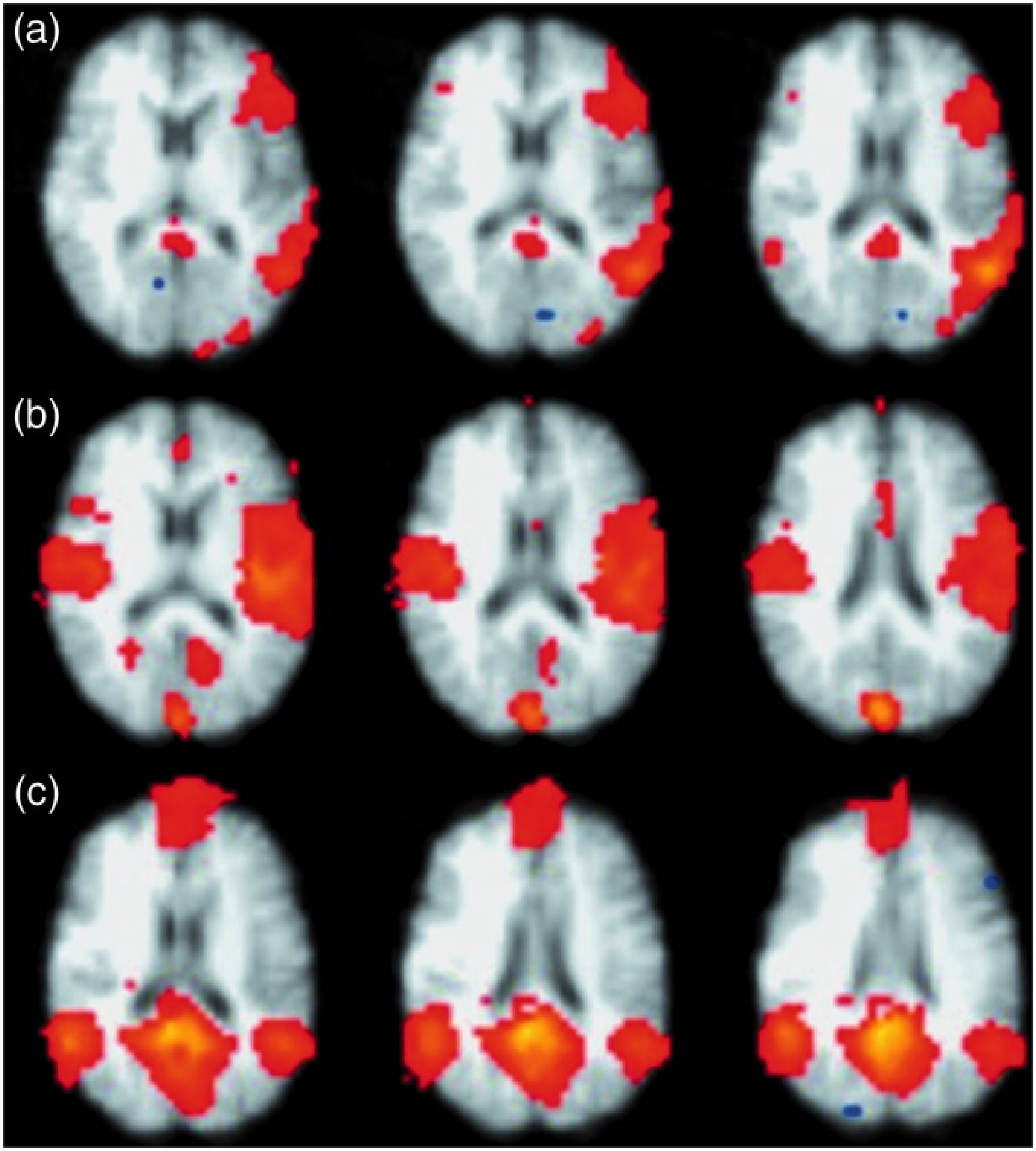
The flow chart represents the fundamental steps involved in resting state connectivity analysis using seed-based technique.

Figure 2.



The seed based functional connectivity analysis done with left Brodmann areas 44 (a, b, c) and 45 (d, e, f) as the seed region depicted on sagittal, coronal and axial images.

Figure 3.



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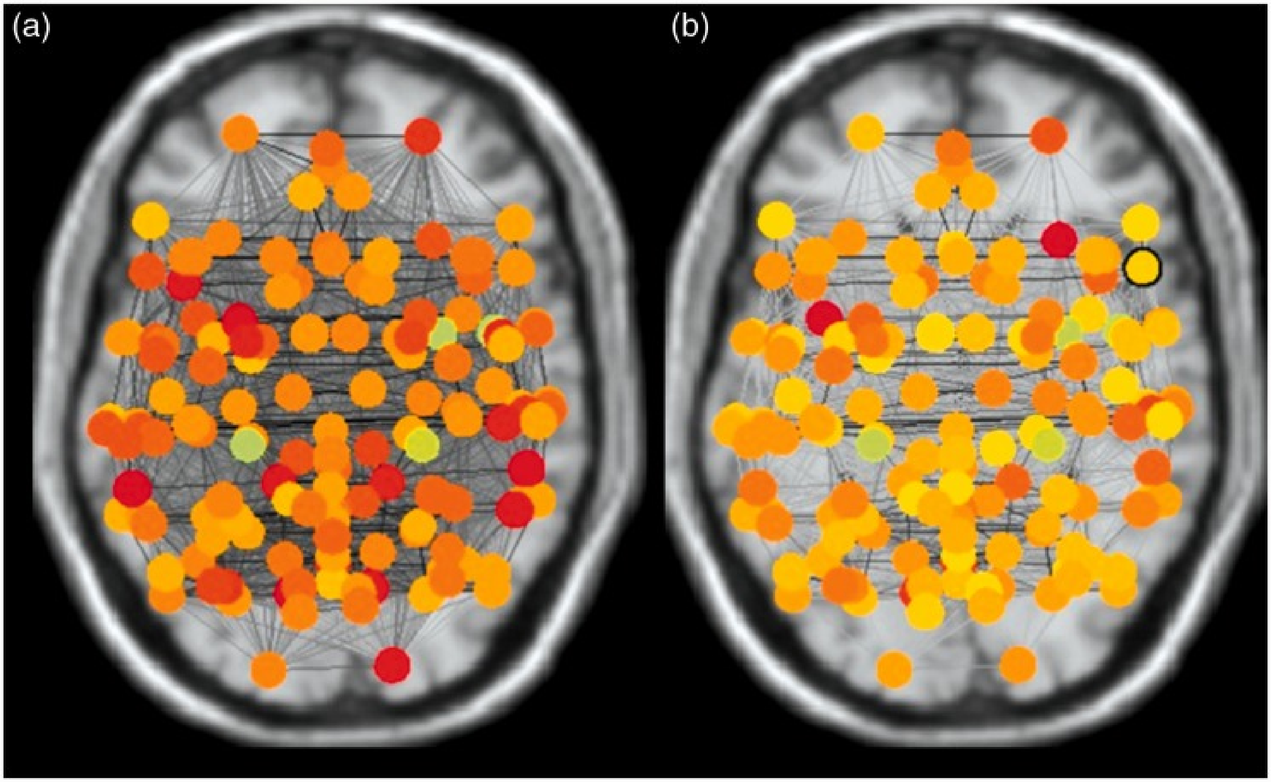
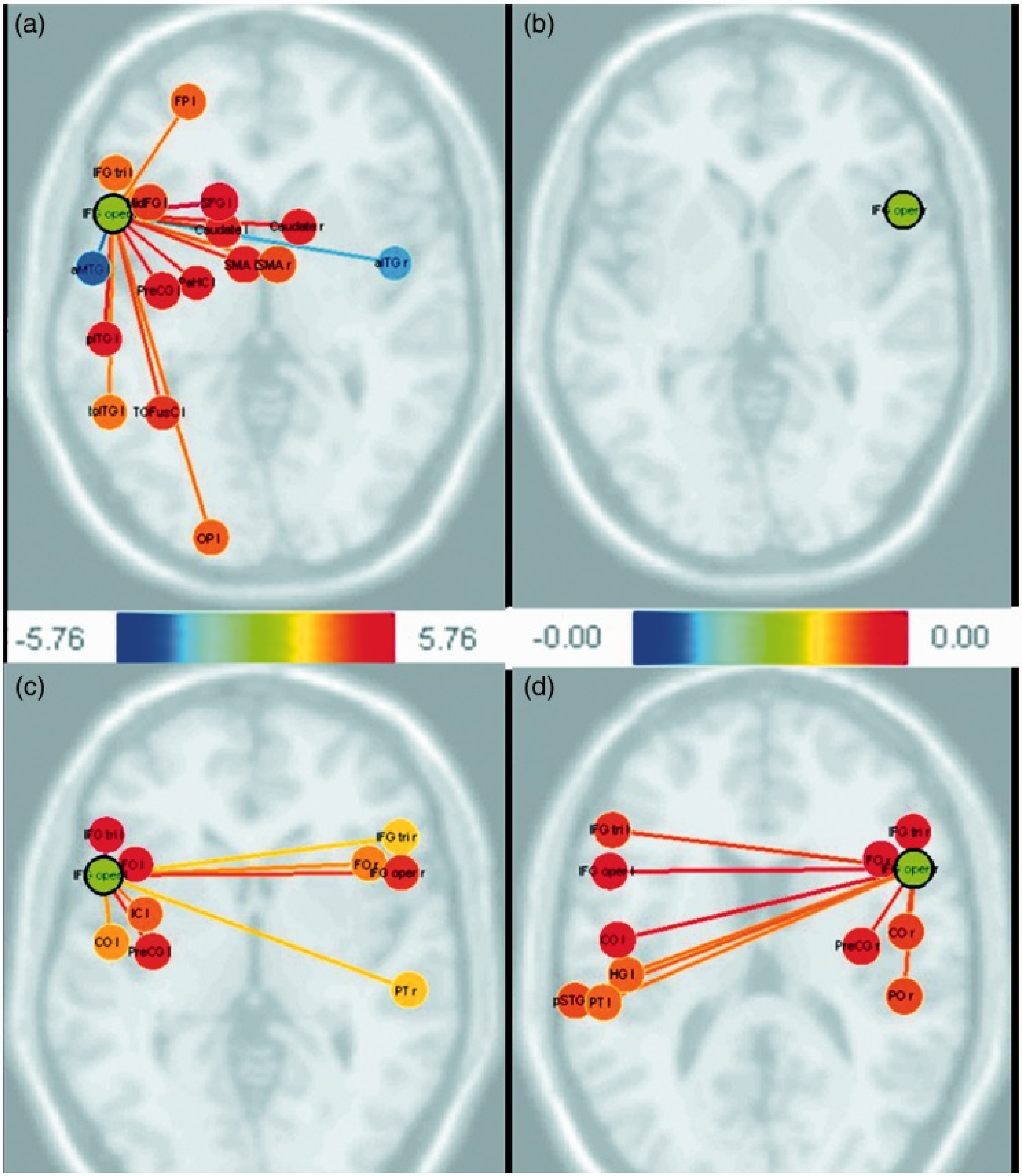
The language network (a), auditory network (b) and default mode network (c) obtained from resting state functional magnetic resonance imaging connectivity analysis using independent component analysis melodic.

Figure 4.



The whole brain connectivity with significant correlation obtained by applying a false discovery rate correction threshold of 0.05 is depicted on an axial slice with region of interest (ROI) to ROI analysis done in controls using task functional magnetic resonance imaging (fMRI) and resting state fMRI.

Figure 5.



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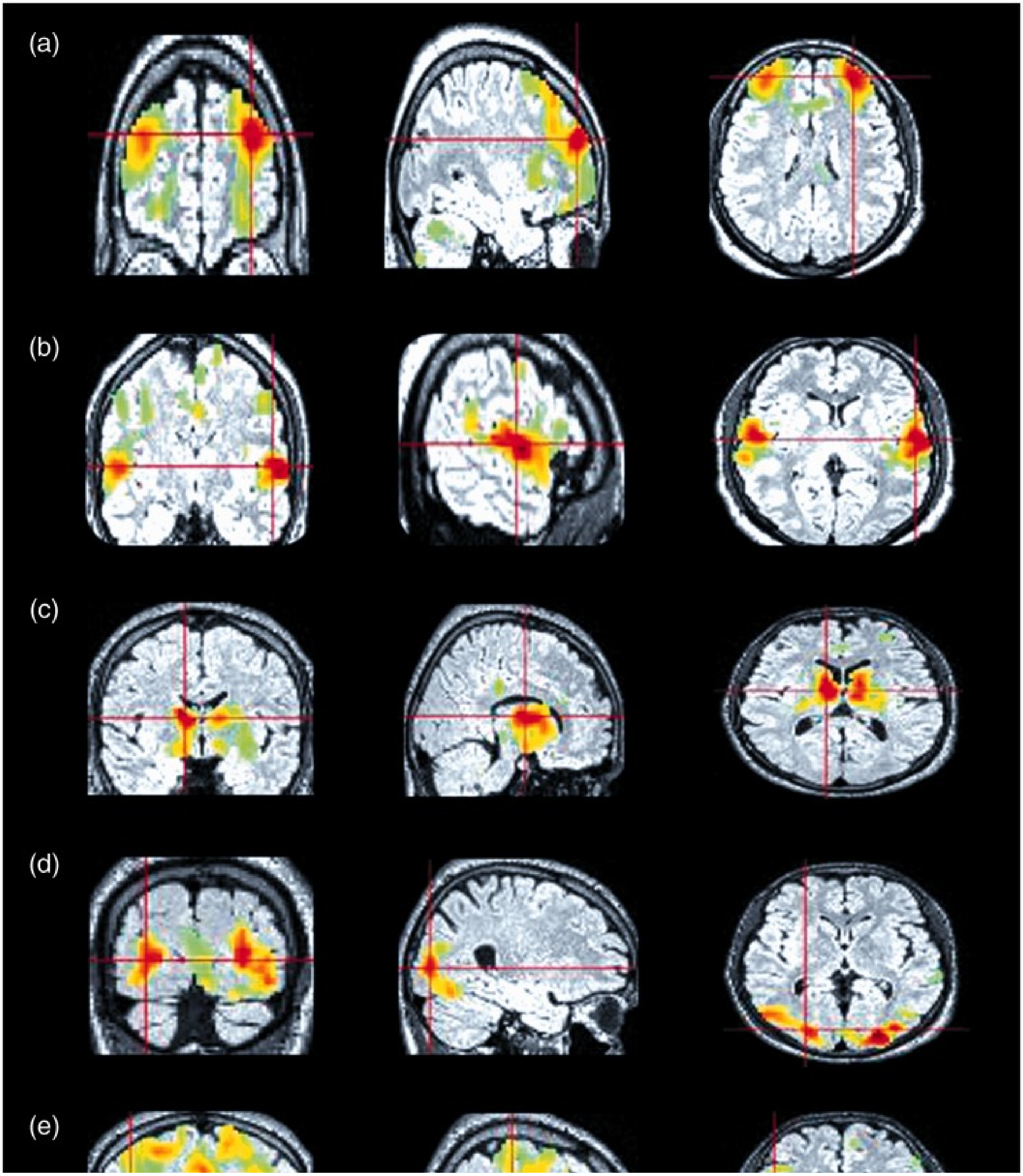
The connectivity map with significant connections obtained for false discovery rate corrected two-sided *P* value threshold less than 0.05 applied, when the pars opercularis left and right was taken as the seed region of interest for task and resting state functional magnetic resonance imaging.

Figure 6.



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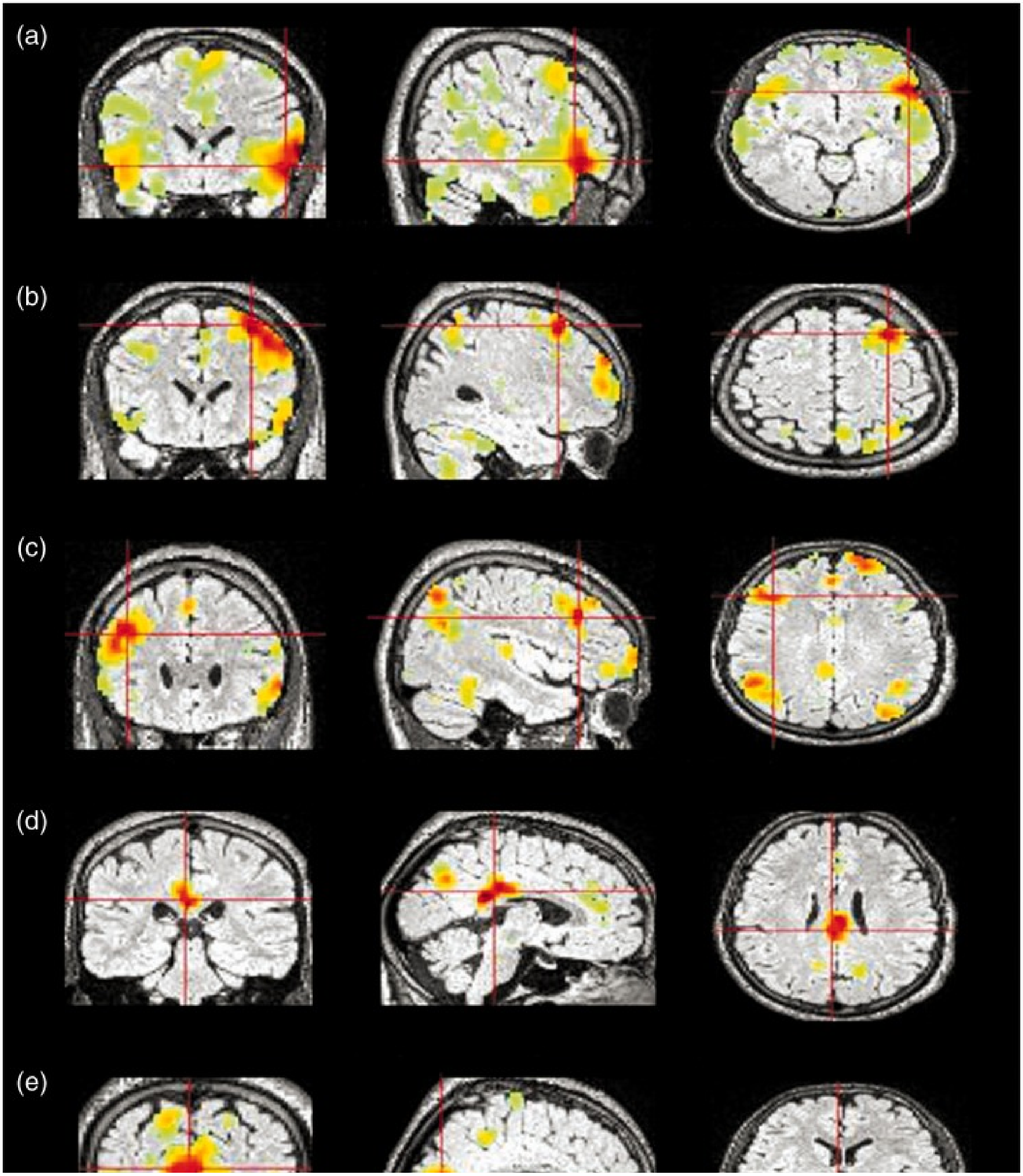
The coronal, sagittal and axial images of the (a) salience network, (b) auditory network, (c) basal ganglia network, (d) higher visual network, (e) visuospatial network and (f) default mode network.

Figure 7.



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The coronal, sagittal and axial images of the (a) language network, (b) left executive control network, (c) right executive control network, (d) precuneus network, (e) primary visual network and (f) sensory motor network.

Table 2.

Presents the imaging protocols in 1.5T and 3T used in our laboratory for research applications.

Rs-fMRI imaging protocol	1.5 T Siemens Magnetom Avanto	3T GE Discovery MR750w
Sequence	Gradient echo echo planar imaging sequence	Gradient echo echo planar imaging sequence
TR	2000	3000
TE	20	30
Flip angle	90	80
Slice thickness	5	3
Imaging matrix	320 × 320	64 × 64
Isotropic voxel size	3.75 × 3.75	3.31 × 3.31
Number of slices	25	36
Acquisition order	Interleaved bottom up	Interleaved bottom up

Rs-fMRI: resting state functional magnetic resonance imaging.