Improved localization of neural sources and dynamical causal modelling of latency-corrected event related brain potentials and applications to face recognition and priming

Rajan Kashyap
Hong Kong Baptist University

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THESIS TITLE: Improved Localization of Neural Sources and Dynamical Causal Modelling of Latency-corrected Event Related Brain Potentials and Applications to Face Recognition and Priming

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Improved Localization of Neural Sources and Dynamical Causal Modelling of Latency-corrected Event Related Brain Potentials and Applications to Face Recognition and Priming

KASHYAP Rajan

A thesis submitted in partial fulfillment of the requirements for degree of
Doctor of Philosophy

Principal Supervisor: Dr. ZHOU Changsong

Hong Kong Baptist University

December 2015
DECLARATION

I hereby declare that this thesis represents my own work which has been done after registration for the degree of PhD at Hong Kong Baptist University, and has not been previously included in a thesis or dissertation submitted to this or any other institution for a degree, diploma or other qualifications.

Signature:

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Date: December, 2015
Abstract

Event related potentials (ERPs) are obtained from noninvasive electroencephalograms (EEG) which measure neuronal activity of brain on the scalp. However, conventional ERPs derived by averaging of single EEG trials have strong latency variability and are smeared, resulting in blurred scalp topography, especially in late components of ERP. The smearing problem had been addressed by reconstructing ERPs after latency correction with a new EEG analysis method Residue Iteration Decomposition (RIDE), which was demonstrated in a face priming paradigm to improve distinctness in scalp topography (Ouyang et al., 2011). This thesis aims to (1) extend the benefits of RIDE to neural source space by localizing the neural generators of ERPs, thereby developing an integrated RIDE framework for improvement in source localization and causal modeling of effective source networks, and (2) apply the framework to the face priming paradigm for famous faces, to explore the dynamics of face processing and priming.

We localized sources through brain electrical source analysis for both conventional ERP and RIDE derived ERPs (RERPs). RERPs allowed localization of an additional motor execution source (Premotor Cortex, PMC), apart from 5 other common sources, of which 2 (Occipital Lobe, OL; Fusiform Gyrus, FG) were obtained from early activity (< 250 ms) and 3 (Mediotemporal lobe, MTL; Prefrontal Cortex, PFC; Anterior Temporal Lobe, ATL) from late activities (> 250 ms) of RERPs respectively. Priming effects, i.e., the difference between primed famous (PF) and unprimed famous (UF) face conditions in source waveforms (SWFs), were extended and enhanced in RERPs, especially for late sources. The priming effects revealed (1) the role of sources in each hemisphere that play in perception, memory and execution, (2) parallel processing of information in sources, (3) early processing in the right hemisphere, and (4) predominance of the right hemisphere in face recognition.

Results confirmed SWFs of RERPs as better choice for the dynamic causal model (DCM). Two candidate DCM models, forward (F) and forward-backward (FB) were outlined on each hemisphere with SWFs from PF and UF conditions of RERP data. Priming has tendency to facilitate the FB model in the left hemisphere. On the other hand, independent of model preference, priming strengthened a bidirectional connection between FG and PFC in both hemispheres; this indicates a strong role of FG in structural representation and of PFCs in controlling decisions about face familiarity. Priming modulates the pathway FG → MTL → PFC
differently in the two hemispheres, strengthening the involvement of MTL in the left hemisphere and weakening in the right hemisphere. This indicates proficiency of the left and right MTL in processing different aspects of facial information. Further, a backward connection ATL→PFC in the left hemisphere was found to be functionally relevant for both conditions in speeding up response time in individual subjects, reinforcing the role of PFC in executive functioning and ATL in naming of famous faces.

Thus, an integrated framework of source localization and DCM with RERPs allows a novel, comprehensive understanding of time resolved dynamics in face recognition and priming, thereby piloting prospects of its application to other experimental paradigms.
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<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ANOVA</td>
<td>Analysis of Variance</td>
</tr>
<tr>
<td>ATL</td>
<td>Anterior Temporal Lobe</td>
</tr>
<tr>
<td>BMA</td>
<td>Bayesian model average</td>
</tr>
<tr>
<td>BMS</td>
<td>Bayesian model selection</td>
</tr>
<tr>
<td>C</td>
<td>C component cluster</td>
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<tr>
<td>DCM</td>
<td>Dynamic causal model</td>
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<tr>
<td>DTI</td>
<td>Diffusion tensor imaging</td>
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<tr>
<td>EEG</td>
<td>Electroencephalography</td>
</tr>
<tr>
<td>ERP</td>
<td>Event-related potential</td>
</tr>
<tr>
<td>F</td>
<td>Forward model</td>
</tr>
<tr>
<td>FB</td>
<td>Forward-Backward model</td>
</tr>
<tr>
<td>FFA</td>
<td>Fusiform face area</td>
</tr>
<tr>
<td>FG</td>
<td>Fusiform gyrus</td>
</tr>
<tr>
<td>fMRI</td>
<td>Functional Magnetic resonance imaging</td>
</tr>
<tr>
<td>FRU</td>
<td>Face recognition unit</td>
</tr>
<tr>
<td>IAC</td>
<td>Interactive activation and competition</td>
</tr>
<tr>
<td>LFP</td>
<td>Local field potential</td>
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<tr>
<td>MTL</td>
<td>Mediotemporal Lobe</td>
</tr>
<tr>
<td>MEG</td>
<td>Magnetoencephalography</td>
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<tr>
<td>NRU</td>
<td>Name recognition unit</td>
</tr>
<tr>
<td>OL</td>
<td>Occipital Lobe</td>
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<tr>
<td>OFA</td>
<td>Occipital Face area</td>
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<tr>
<td>PCA</td>
<td>Principal Component Analysis</td>
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<tr>
<td>PET</td>
<td>Positron emission tomography</td>
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<td>PF</td>
<td>Primed familiar face</td>
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<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>PFC</td>
<td>Prefrontal Cortex</td>
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<td>PMC</td>
<td>Premotor Cortex</td>
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<td>PIN</td>
<td>Person identity node</td>
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<tr>
<td>R</td>
<td>R component cluster</td>
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<tr>
<td>RV</td>
<td>Residual variance</td>
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<tr>
<td>RIDE</td>
<td>Residue iteration decomposition</td>
</tr>
<tr>
<td>RT</td>
<td>Response Time, Reaction Time</td>
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<tr>
<td>RERP</td>
<td>RIDE derived ERP</td>
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<td>S</td>
<td>S component cluster</td>
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<tr>
<td>SIU</td>
<td>Semantic information unit</td>
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<tr>
<td>SPM</td>
<td>Statistical parameter mapping</td>
</tr>
<tr>
<td>STS</td>
<td>Superior Temporal Sulcus</td>
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<tr>
<td>SWF</td>
<td>Source waveform</td>
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<tr>
<td>UF</td>
<td>Unprimed familiar face</td>
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Chapter 1

Introduction

1.1. Background

Human brain has been the most complex of all organ systems. Researchers worldwide have been trying to unwind the complexity of its working mechanism using numerous techniques like fMRI, PET, DTI, MEG, EEG/ERP, LFP etc.

Our group at the Centre for Nonlinear studies, Hong Kong Baptist University is primarily concerned with improved analysis of Electroencephalography (EEG) data in collaboration with cognitive neuroscientists. EEG is a safe and non-invasive technique to record the time series of the electrical potential from the brain scalp. Epochs (segments of time from a continuous recorded data) of single trial EEG data are preprocessed and conventionally averaged to create event related potentials (ERPs). Different components of ERP act as valid indicators of sensory, cognitive and motor processing. High temporal resolution in ERPs provide a direct measure of the underlying neuronal activities (Michel, & Murray, 2012; Pereda, Quiroga, & Bhattacharya, 2005). Different neuronal structures inside the brain get selectively integrated to construct the dynamic networks that perform various cognitive tasks (Jensen, Kaiser, & Lachaux, 2007; Le Van Quyen et al., 2001; Ward, 2003). One such tasks for which the human brain has expertise, is the recognition of human faces, especially famous/familiar ones in comparison to unfamiliar ones.

Human faces are a rich source of information regarding their semantics that include information about their familiarity, gender, age, social status etc. Researchers worldwide have come to the consensus that identification of faces could guide social behavior of a person (Bate
Identifying faces may apparently sound not so important, but six million patients worldwide are suffering from face processing disorders (http://www.prosopagnosiaresearch.org/). Patients suffering from Prosopagnosia are unable to identify faces; and people suffering from Capgras delusion—though are able to identify familiar faces, but lack a sense of familiarity and believe that impostors or aliens have replaced the familiar faces. There is a high negative impact on the quality of life of patients suffering from such face recognition disorders (Yardley, McDermott, Pisarski, Duchaine, & Nakayama, 2008). Impairments of the face responsive areas in the brain are the major cause of such face recognition disorders (Breen, Caine, & Coltheart, 2000). Hence, identification of face responsive areas becomes an important part of research for clinical applications.

Areas in the brain responsible for face recognition were initially divided into core and extended systems by Haxby, Hoffman, & Gobbini, (2000). Their model was then updated by Haxby, et al., (2011), with more areas being incorporated into the system. Fairhall, & Ishai, (2007) explored the interaction between face responsive regions through effective connectivity, which was further modified by Ishai, (2008). White matter connectivity between some of these face responsive regions was analyzed by Gschwind, Pourtois, Schwartz, Van De Ville, & Vuilleumier, (2011); Pyles, Verstynen, Schneider, & Tarr, (2013). Similarly, a functional network of the face responsive regions in detail was outlined by Zhen, Fang, & Liu, (2013) using fMRI (functional Magnetic Resonance Imaging), which is based on the indirect signal of the slow fluctuations of blood-oxygen based contrast. All the above studies and majority of other face recognition studies that define the face recognition network are fMRI based, having high spatial resolution but low temporal resolution.
The face identification process happens in the time range of a few hundreds of milliseconds. The fMRI based studies therefore, could not account for complete understanding of the face network. For instance, the repetition priming refers to a faster processing of repeated versus initial presentation of a stimulus. When famous faces are primed, they are found to be identified faster (faster reaction time) than their unprimed counterpart (Herzmann & Sommer, 2010). Since, the difference in reaction time (RT) between primed and unprimed are in the time range of milliseconds (200-300 ms), therefore temporally resolved face networks could better correlate the behavioral performance of priming. For these reasons, discriminatory way of analysis would be strongly preferred for outlining the face recognition network which should have both spatial and temporal resolutions.

1.2. Motivation

Currently, the predominant approach for face recognition network is to use fMRI to spatially locate the areas, use DTI (diffusion tensor imaging) and Fractional Anisotropy (FA) to confirm the white matter connectivity, and then creates an effective network from these areas through dynamic causal modeling (DCM) on fitting the model dynamics to fMRI data. Effective connectivity can reflect how structural connections between areas might enact their influence across different experimental conditions. However, low temporal resolution of fMRI restricts our understanding to link the behavioral performance to the effective network connectivity. A complimentary solution using brain signals with high temporal resolution is therefore desirable when human face recognition network has to be constructed.

In this aspect, connectivity analysis could be done based on coherence or synchronization from temporally resolved MEG or EEG/ERP at the surface level in the frequency domain of the signals (Doesburg & Ward, 2009). However, such connectivity analysis
in terms of coherence and phase synchrony across two electrodes is problematic and ambiguous because of (1) volume conduction: the electromagnetic signals from the neuronal sources in the brain spread across many sensors on the scalp, and (2) the reference electrode which has an influence on signals obtained across different electrodes (Guevara, et al., 2005; Hu, Stead, Dai, & Worrell, 2010; Schiff, 2005). This ambiguity of coherence and phase analysis of the potential between scalp electrodes could be best resolved by assessing the connectivity from the time series extracted from EEG inverse solution, commonly known as “source localization” (Michel & Murray, 2012). Moreover, source sensitivity of EEG/ERP is higher than MEG, as EEG/ERP can detect all sources (superficial and radial) equally, whereas MEG is insensitive to radial sources and can only detect superficial sources (Ahlfors, Han, Belliveau, & Hämäläinen, 2010; Malmivuo, 2012).

EEG, with its high source sensitivity, is considered to be an ultimate brain imaging tool when temporal dynamics of a large scale brain network is involved (Michel & Murray, 2012). However, when single trial EEGs are conventionally averaged to obtain ERPs, due to latency variability of these signals across many trials, their shape gets broadened and amplitude gets diminished, especially in the late components (after 250 ms of stimulus onset). These smeared late components therefore pose a difficult problem in source localization. A new EEG data analysis technique “Residue Iteration Decomposition (RIDE)” was developed at our Centre by Ouyang, Herzmann, Zhou, & Sommer, (2011) to ward off the smearing problem by reconstructing the ERP components to its respective most probable latencies. The RIDE reconstructed ERPs (RERPs) were found to increase the amplitude of the late components of ERP and to improve the topography at the surface level than the conventional ERPs (Ouyang, Sommer, & Zhou, 2015a, 2015b).
Thus, it seems promising to apply this new technique to better localize the sources/areas responsible for face recognition from RERPs than from conventional ERPs obtained from a face priming experiment conducted by Herzmann, & Sommer, (2010). Priming effects at the source space could then be analyzed and compared for both ERP and RERP derived sources. Since, connectivity across sources should not be analyzed in the sensor space because of volume conduction, but should be analyzed in source space (Michel, & Murray, 2012), this comparison of ERP and RERP derived source activity could build a foundation for constructing the face network from the sources whose activity might intensely retain the priming effects. We hypothesized that RERP sources could possibly enhance and extend the priming effects in the source space, especially for the sources obtained from the late components. Reasoning behind this hypothesis lies in the work of David, Harrison, & Friston, (2005), who suggested that the late components influence feedback connectivity in an effective network, that reflects the reentry of dynamics to hierarchically lower processing areas. In this aspect, effective face network can be outlined from sources that could intensely retain the priming effects in the source space and can therefore correlate the behavioral effects of priming (reaction time) with network level properties.

At this backdrop, an integrated RIDE framework of research can be constructed, wherein; the users can unite RIDE with source localization and analysis software “Brain Electrical Source Analysis (BESA) 6.0” and with effective network creation and analysis software “Statistical Parametric Mapping” employing DCM (http://www.fil.ion.ucl.ac.uk/spm/) In future, this framework could be extended for the analysis of other ERP experimental paradigms.
1.3. Objectives

The research work in this thesis aimed to extend the existing RIDE framework (http://cns.hkbu.edu.hk/RIDE.htm) to an integrated RIDE framework, so as to (1) localize the sources of both RIDE derived ERPs (RERPs) and conventional ERPs obtained from a face priming experiment on famous faces conducted by Herzmann, & Sommer, (2010), (2) analyze and compare the priming effects in the source waveforms of both ERP and RERP derived sources, and (3) then outline an effective face recognition network in humans from the sources which retain the priming effects intensely in the source space, so that hemispheric contribution to reaction time of priming could be correlated to the connectivity parameters.

1.4. Scope and Organization of the Thesis

In Chapter 2, the motivation and background for developing the integrated RIDE framework are reviewed. In Chapter 3, basics of key methodological elements that form the integrated RIDE framework, namely, (i) scalp potentials: RIDE derived ERPs (RERPs), (ii) source localization through brain electrical source analysis (BESA), and (iii) dynamic causal modelling (DCM) are discussed. Chapter 4 covers the experimental details of Herzmann & Sommer, (2010) for obtaining the face priming ERPs, and provides an overview of the comparative improvement by RIDE on these ERPs at scalp level from the study of Ouyang et al., (2011). In Chapter 5, ERPs and RERPs in source space are evaluated and results are discussed. Analyses of the dynamics of sources network involved in face recognition and priming from RERPs through DCM are documented in chapter 6. In Chapter 7, conclusion, future prospects, and limitations of this work are noted.
Chapter 2

Face Recognition and Priming: Motivation and Background

In this chapter, we will introduce importance of the face recognition. We will provide an overview of anatomical construction of brain and interconnecting white fibers. We will also explain some of the available models for face recognition and priming, so also will provide an outline of existing information on derived network architecture of face recognition areas. Our explanations will include some questions and limitations of earlier works, and would lay down the scope for further research to overcome such limitations. To provide a platform view on established face recognition areas including lateralized perspective in processing facial information, few of the analogous works being done elsewhere, will be reported for ready reference.

2.1. Importance of face recognition

According to the claims of World Health Organization (WHO) in 2007, about 1 billion people (one in six of the world’s population) suffer from various neurological disorders, of which, each year 6.8 million people die as a result of neurological disorders (http://www.who.int/mediacentre/news/releases/2007/pr04/en/). Neurological disorders can impair our daily functions like audition, visual recognition, memory formation and retrieval, sensory touch, smell etc. These disorders affect people over all age groups. Disorders of these kinds affect the quality of life of the people suffering from them. Impairment in face recognition is one such problem which is hard to diagnose and slowly degrades the social life and behavior of the people suffering from it.

Identifying faces may sound not so important, but six million patients worldwide are suffering from face processing disorders (http://www.prosopagnosiaresearch.org/). As mentioned
earlier in introduction, major disorder includes patients suffering from Prosopagnosia who are unable to identify the faces familiar to them. People suffering from Capgras delusion, though able to identify familiar faces, lack a sense of familiarity and believe that impostors or aliens have replaced the familiar face. Some form of prosopagnosia is found in children with Autism and Asperger’s syndrome, and in adults with stroke, traumatic brain injury or certain neurodegenerative diseases. This broadens the spectrum of face recognition disorders and importance of its mitigation.

The face recognition disorders can happen due to impairments in the face recognition areas in the brain, or the white matter connectivity across these areas, or both. In this aspect, a brief introduction to the anatomical overview of the brain is important.

2.2. Anatomy of brain involved in face recognition

The brain can be broadly divided into Cerebral Cortex and the subcortical structures. The cerebral cortex is divided into Occipital, Temporal, Parietal and Frontal Lobe as shown in Figure 2-1 (A). Functional demarcations of the lobes and intercommunication between them are very important for information transfer across the brain.

The two fundamental principles of the functional organization of sub-cortical and cortical structures in the brain are integration and specialization. Specialization relates to the expertise of completing a task (e.g. face recognition) that the areas achieve by connecting or integrating with each other. Brodmann’s cytoarchitectonic work in 1905 (Brodmann, 1905) and further reviewed in 1909 (Brodmann, 1909) compartmentalized the cortex into functionally separated areas, representing them with a unique number as shown for reference in Figure 2-1(B). Though functional segregation of the areas in the brain is not easy to demonstrate but it is one of the central themes in neuroscience.
Systematically, connectivity across different Brodmann’s areas emerged as a matter of interest. Nearby cortical areas in the brain are connected to each other through different kinds of lateral dendritic projections or short fiber connections. However, the distant areas in a hemisphere are connected to each other through bundle of major white fiber connections as illustrated in Figure 2-1 (C). Additionally, areas in the two hemispheres are also connected to each other through white fibers passing through Corpus Callosum, Anterior Commissure and Posterior Commissure. Many tasks like auditory, sensory, visual processing are accomplished because of information transfer between many areas in the brain.

Though many areas are involved in face recognition, but majority of the studies mainly found involvement of the structures in Occipital Lobe, Temporal Lobe, Parietal Lobe and Frontal lobe as discussed in the subsequent sections. The main white fibers connecting these lobes are Inferior Longitudinal Fasciculus, Superior Longitudinal Fasciculus, Inferior fronto-occipital Fasciculus, Uncinate Fasciculus as shown in different colors in Figure 2-1(C).
The complex process of face recognition involving many areas happens in the time range of hundreds of milliseconds. However, familiar faces can be recognized faster than unfamiliar faces. Repetition priming refers to the fact that a face is recognized faster if that same face has been seen previously (Bruce & Valentine, 1985); which is however dependent on the familiarity level of the person to the encountered face. If the faces are immediately preceded by the same face, the condition is called as primed; or if by a different face, it is unprimed. Priming of famous faces lead to faster reaction time, though it is also image dependent. Different images of the same person when used as prime and target could weaken the priming effect (Bruce & Valentine, 1985). Priming effects are more pronounced when same image is repeated compared to a different image (Eger, Schweinberger, Dolan, & Henson, 2005). Furthermore, priming effect for famous faces has also been found to be view dependent. Repetition priming therefore aims to
understand the phenomenon inside the brain that leads to altered processing of stimuli (visual recognition of faces). Priming could affect perception, memory, decision making and motor execution; and therefore has been a topic of research along with face recognition. In this context, different models of priming have been proposed.

2.3. Prior models of face recognition and priming

In this section, we will discuss a few of the most important face recognition models which are of anatomical, physiological and psychological importance, and could provide an overview of the face recognition and priming in the brain.

2.3.1. Functional models of face recognition and priming

Bruce & Young, (1986), developed a model for face recognition. The model is based on the fact that faces were cognitively processed through Face Recognition Units (FRUs). The FRUs get activated by the structural encoding of the faces to define its familiarity. When an FRU is sufficiently activated, it enables the subsequent access of semantic information. Semantic information about a person’s identity is stored in the Person Identity Notes (PINs). Recall of identity or semantic, resolves the feeling of knowing. However, it depends on the activation level of the FRUs to confirm if a face is recognized as familiar or not.

Another model based on similar framework is the interactive activation and competition (IAC) developed by Burton, Bruce, & Johnston, (1990); further modified by Burton, Bruce, & Hancock, (1999). In IAC model, activation spreads through a network made of a number of pools of processing units as shown in Fig 2-2. Five processing units are proposed, namely the feature units, the face recognition units (FRUs), the name recognition units (NRUs), the person identity nodes (PINs) and the semantic information units (SIUs). In the IAC model, PINs form
empty (without content) units that allow access to the semantic information stored in SIUs. Thus, PINs are the level of representation at which information from different stimulus types (e.g. faces, names) initially converge into a common representation. Finally, a successful identification of a famous face requires a match between FRUs, PINs and a person’s name.

Figure 2-2: Schematic representation that explains the interaction of various sub units in the IAC model (figure adapted from Burton et al., 1999).

When faces are primed, the link between FRUs and PINs get strengthened (Burton et al., 1999). This may happen because priming of a familiar or famous face cause the PINs to reach the threshold of activation earlier than the unprimed (Schweinberger, Pickering, Jentzsch, Burton, & Kaufmann, 2002). The link between NRUs and the PINs get strengthened when famous names are primed (Schweinberger et al., 2002). The surface topographic analysis of face and name priming study by Schweinberger et al., (2002), suggested that the underlying brain sources for face and name recognition could be similar at the level of PINs, though face and name recognition are predominant in the right and left hemispheres, respectively. However, how the
FRUs, PINs, and SIUs are established in which neuroanatomic areas of the brain and how they perform their respective role, still remains unclear.

2.3.2. Neuro-Anatomical model on face recognition

The neuroanatomical model on face recognition was introduced by Haxby et al., (2000) and further updated with additional areas by Haxby et al., (2011) as shown in Figure 2-3. It associates face recognition to a bilaterally distributed in both hemispheres of the human neural system. The model divides the face recognition areas into core and extended system. Facial information is processed by interactions within and between these subsystems.

![Figure 2-3: The updated neuro-anatomical model on face recognition by Haxby et al., (2011).](image)

The core system consists of three bilateral regions in Occipital, Temporal and visual cortex. These regions are the Occipital Lobe (OL), the Fusiform Gyrus (FG) and the Superior Temporal Sulcus (STS). The extended system consists of Mediotemporal Lobe (MTL), Anterior Temporal Lobe (ATL), and Prefrontal Cortex (PFC).
The role of those areas involved in face recognition has been traced from numerous studies based on MRI, ERP, MEG, PET etc. Since faces can be recognized from different facial features, therefore the areas in core and the extended systems are specialized in processing different aspects of faces as shown in figure 2-3. In the core system, OL especially the Occipital Face area (OFA) serves as the entry point of facial information to the brain and is involved in face perception. Identification of faces is done in the FG, especially the Fusiform Face area (FFA). STS is said to be involved in eye gaze and expression of face, which changes with facial movements. In the extended systems, PFC is more involved in attention and decision making. The Temporoparietal junction structures in MTL are involved in memory functions and in judging the familiarity with the perceived face, while ATL is involved in retrieval of biographical information about the perceived face. These areas, though being specialized for one function, are also involved in other functions of face recognition. Absence of clear boundaries between the roles of these areas creates difficulty in associating them as FRUs, PINs, SIUs and NRUs.

In the next section, we will discuss about interconnection between many of these areas that integrate to accomplish the task of face recognition.

2.3.3. Some earlier models on face network

Lot of research based on face recognition areas and their interconnectivity had been explored from fMRI based studies. Ishai, (2008) explored the effective network architecture of face recognition based on fMRI and dynamic causal model (DCM) as shown in Figure 2-4(A). The model assumed reciprocal connection among the visual, temporal, and prefrontal regions of each hemisphere. The model explored the change in effective connectivity across regions under different conditions when perceiving (1) emotional faces (change in connections
marked in yellow), (2) famous faces (change in connections marked in blue), (3) animated faces (change in connections marked in green), (4) low spatial frequency faces (change in connections marked in red), and (4) faces with more attention to its gaze (change in connections marked in orange).

Figure 2-4: (A) Face network adapted from the study of Ishai, (2008), reflecting changes in effective connectivity across different tasks marked in different colours. (B) Hierarchial face network adapted from the study of Zhen et al., (2013) reflecting functional connectivity of different areas involved in identification (blue), semantic processing (red) and expressions (green).

In another recent fMRI study by Zhen et al., (2013), a hierarchical model for face recognition was framed as shown in Figure 2-4(B) based on functional connectivity. In their cross subject study, specific areas responsible for identification of faces (marked in blue), semantic processing of faces (marked in red) and processing of facial expressions (marked in green) were shown. These sub-networks were divided on the basis of the strength of functional connectivity between these areas. It was found that the OL and the Infero-temporal areas in FG were mainly involved for identification, the MTL structures in Temporoparietal junctions were involved for
semantic processing and expressions, whereas frontal structures were involved for expressions only.

Two studies were made (Gschwind et al., 2011; Pyles et al., 2013) to derive white matter connectivity between the face responsive regions in OL and Temporal Lobe (regions derived from fMRI). These were to frame the diffusion tensor imaging (DTI) based face network as shown in Figure 2-5 (A) and (B). Both these studies concluded that (1) density of fiber connections in the right hemisphere were stronger than the left, and (2) connections to the STS from other face responsive regions were negligible for both hemispheres, even though STS has been included in the core system by the earlier model of Haxby et al., (2011).

**Figure 2-5:** Face network adapted from the studies of (A) Gschwind et al., (2011) and (B) Pyles et al., (2013). Width of connections refer to strength of fiber density in each hemisphere, reflecting higher density in right hemisphere, and negligible connectivity to STS.
2.4. Limitations of earlier works

The above literature gives us a more precise idea of different areas involved in face recognition and various available models which are designed to enhance our knowledge on this topic. However, these studies are mainly fMRI based. The non-invasive fMRI techniques is dependent on the blood oxygen-level-dependent contrast (BOLD). When areas in the brain are activated, they require more oxygenated blood. fMRI picks up this increased blood flow (BOLD) to pin point greater activity. Thus, fMRI is a measure related to blood flow in areas of the brain that lights up when a particular task is performed. This means, fMRI does not directly measure the neural activity of the areas, but indicate it indirectly. However, with its high spatial resolution, it can provide high location accuracy of the areas involved in processing of information.

In this aspect, the models mentioned above give us an understanding of the face network and the role of each area in face recognition, but being fMRI based, they have high spatial resolution and low temporal resolution (Bandettini, 2009). Since face recognition and priming are in the time range of hundreds of milliseconds, these models cannot provide enough understanding to the temporal dynamics of face recognition areas, and therefore cannot explain the temporal phenomena of priming (faster reaction time). A way out with LFP (local field potential) recordings can be suitable choice for obtaining the temporally resolved activities of the different areas of the brain, but being invasive they cannot readily be applied. Therefore, source models derived from temporally resolved non-invasive ERPs would be a good choice that might provide a deeper understanding of the dynamics of face recognition and priming. Though ERPs suffer from (1) volume conduction, i.e., spreading of electromagnetic signals across many sensors on the scalp from neuronal sources, and (2) choice of reference electrode, but they can
serve as a more direct measure of the underlying neural activity of the brain. ERPs are found to reflect a difference in amplitude and latencies of its components between primed and unprimed face recognition data (Herzmann & Sommer, 2010; Schweinberger et al., 2002). These components could serve as a valid indicators of sensory, cognitive, and motor processing. Inverse modelling of these ERP components is done by considering a model of the head, with equivalent current dipoles inside the brain approximating the outer ERP data. Dipoles at different time points especially for the peaks in the ERP data are localised at different areas of the brain.

2.5. Face recognition areas from ERPs

Previous works on source localization of face processing-related ERPs have revealed a number of brain systems involved. Around 100ms after stimulus onset, bilateral sources are active in the Inferior Occipital Lobe/Lingual Gyri (Mnatsakanian & Tarkka, 2004; Wong, Fung, McAlonan, & Chua, 2009) yielding the occipital positive-going visual evoked P1 component, which is a response of the peristriate cortex to any kind of visual stimuli (Tobimatsu & Celesia, 2006). In contrast, the next peak at 170ms (N170) is more prominent for faces as compared to other visual stimuli and has been localized in the Inferior Temporal Gyrus (Schweinberger et al., 2002) or in the Fusiform Gyrus (Deffke et al., 2007; Mnatsakanian & Tarkka, 2004; Wong et al., 2009). It has been suggested that the N170 component reflects the structural encoding of faces (for a review see Eimer, 2011) and is usually, neither affected by familiarity of the face (Bentin & Deouell, 2000; Eimer, 2000) nor by priming (Cooper, Harvey, Lavidor, & Schweinberger, 2007; Eimer, 2000).

Two other components of interest here are best seen in the so-called repetition priming paradigm as a difference between the ERPs to primed and unprimed faces. In such paradigms, there are usually two repetition effects - early repetition effect (ERE) and late repetition effect.
(LRE). The ERE or N250r was suggested to reflect the activation of structural face representations in memory (Schweinberger, 2011). It has its maximum around 250 to 300ms, and is positive at fronto-central and negative at occipito-temporal electrodes. Earlier studies reported larger repetition-related N250r responses for familiar than unfamiliar faces (Herzmann, Schweinberger, Sommer, & Jentzsch, 2004; Pfütze, Sommer, & Schweinberger, 2002). Schweinberger et al., (2002) and Bindemann, Burton, Leuthold, & Schweinberger, (2008) localized the sources of ERE/N250r in the ventral temporal area around Fusiform Gyrus. This area was further confirmed for repeated faces in a fMRI study by Eger, Schweinberger, Dolan, & Henson, (2005). In an magneto encephalography (MEG) study by Schweinberger, Kaufmann, Moratti, Keil, & Burton, (2007), the sources of M250r (thought to be equivalent to N250r in ERPs) were localized in inferior temporal/mid-Fusiform Gyrus area and in Cingulate Gyrus.

The ERE/N250r is followed by LRE or N400, a parietal positivity for ERPs to primed relative to unprimed faces between 300 – 600ms. The LRE was considered to reflect the activation of semantic knowledge about persons (Schweinberger, 2011, for a review) and was found to be enhanced for familiar relative to unfamiliar faces (Pfütze et al., 2002; Schweinberger et al., 2002). The LRE/N400 is therefore related to those aspects of semantic processing, which are triggered by familiar faces and not by unfamiliar faces. Neural sources of the LRE for faces have not yet been reported, although linguistic studies on the N400 in priming found sources at Superior and Inferior Temporal areas along with Prefrontal Cortex (Kutas & Federmeier, 2011; Lau, Phillips, & Poeppel, 2008).

Few works wherein further studies were made to elucidate the role of particular areas in processing differential aspects of facial information in each hemisphere will be discussed in the next section.
2.6. Lateralization of areas and their roles in face recognition

Face recognition has been found to be predominant in the right hemisphere, however, processing of facial information proceeds bilaterally in the two hemispheres (Bourne & Hole, 2006; Schweinberger, Sommer, & Stiller, 1994; Wang & Cottrell, 2012). Left and right hemispheric sources are specialized to process different types of facial information, with right FG being dominant and specialized for holistic face processing, and left FG being subordinate and specialized for facial feature-based processing (for review Bourne & Harris, 2008). However, faces are processed more on the basis of holistic information compared to feature based information (Collishaw & Hole, 2000).

On the same note but from a different perspective, Gainotti, (2007b) put forward the view that presentation of a famous face leads to spontaneous name retrieval and a sub-vocal naming process, which activates left fronto-temporal structures. The above perspectives indicate that sources in right and left hemispheres are specialized for processing different aspects in face- and person-related information.

It has been mentioned earlier that right FG is specialized for holistic face processing and left FG for processing based on facial features (Bourne & Harris, 2008; Rossion et al., 2000). Right FG (specifically FFA) was also found to be associated with face encoding and retrieval, while the left is associated with face encoding only (Prince, Dennis, & Cabeza, 2009). For MTL, nonverbal information like a face is processed predominantly in the right hemisphere (Coleshill et al., 2004; Crane & Milner, 2002; Gillespie, Bowen, & Foster, 2006; Lee, Yip, & Jones-Gotman, 2002; Moscovitch & McAndrews, 2002) and verbal information (like recall for language and words) is processed predominantly in the left (Coleshill et al., 2004; Moscovitch & McAndrews, 2002). Since most images contain both verbal and nonverbal information (like
famous faces do), bilateral activation of MTL is commonly found (for a review Kennepohl, Sziklas, Garver, Wagner, & Jones-Gotman, 2007). However, retrieval of famous names was found to mainly activate left MTL structures (Grabowski et al., 2001; Papagno et al., 2014). In PFC, as per the hemispheric encoding/retrieval asymmetry model (HERA), right PFC is more involved in episodic retrieval (Habib, Nyberg, & Tulving, 2003) and left PFC is more involved in semantic memory retrieval (Buckner & Petersen, 1996). However, during retrieval of famous names, the left frontal lobe was found to be strongly activated along with ATL and MTL structures (Papagno et al., 2014; Papagno et al., 2010; Pisoni, Vernice, Iasevoli, Cattaneo, & Papagno, 2015). In ATL, right ATL is the store house of episodic memories and specialized for famous face recognition, whereas, left ATL is more involved in naming of famous faces (for reviews see Olson, Plotzker, & Ezzyat, 2007). The lateralization perspective of the sources implies that holistic face identification and processing proceeds predominantly in the right, while information related to person’s identity retrieval from facial features is processed predominantly in the left, and the two processes might be running and coordinating with each other in parallel.

2.7. Summary

In this Chapter, we reviewed the importance of face recognition and previous works on areas and network of face recognition. Since impairments in face recognition happen due to deficits in the anatomical organization of areas in the brain or their interconnectivity, we provided an overview of the neuroanatomical architecture of the brain. Further, we discussed about the functional and neuroanatomical architecture of face recognition, priming as well as areas involved in this process. Earlier works on face recognition networks derived from fMRI, DCM and DTI were briefly described to provide an overview of works done in this arena.
Finally, we reviewed the major constraints of fMRI being used in these models. Models derived from fMRI have high spatial but low temporal resolution. Since face recognition and priming happen in the time range of hundreds of milliseconds, some earlier models are not enough to understand the temporal dynamics of face recognition and could not provide an explanation for the temporal phenomena of priming. In essence, we suggested that temporally resolved ERPs could be utilized to understand temporal dynamics of face recognition through source localization, as ERP components are a more direct measure of underlying neural activity. Furthermore, we overviewed the source localization areas traced in previous studies obtained from different components of a face ERP. Finally, we reviewed the lateralization perspective and role of the face processing areas.

In the next Chapter, we would discuss on research instruments that will be used subsequently as a tool in our integrated RIDE framework, for analyzing the ERP face recognition and priming data, which as expected, would improve our broad comprehension on face recognition network.
Chapter 3

Methodology of research

In this Chapter, we will introduce the basic methods adopted in this thesis that were included to constitute the integrated RIDE framework in three sections, namely (1) basics of EEG and ERP, (2) basics of source localization and, (3) basics of dynamic causal model. They form the building blocks of this integrative research framework and will be discussed sequentially. In the last section, application of the integrative research framework to face priming data relevant to our work will be made for consolidated understanding.

3.1. Basics of EEG and ERP

In this section, an overview of electroencephalography (EEG) and their use as event related potentials (ERPs) is introduced. Subsequently, the limitations of the conventional ERPs are discussed, and then overcoming of the limitations through the new technique RIDE is elaborated.

3.1.1. EEG

EEG (Electroencephalography) was first discovered in 1929 by Hans Berger (information from Wikipedia), who found that electrical activity of human brain could be measured by placing multiple electrodes on the scalp noninvasively as shown in Figure 3-1(a). EEG proved to be a useful tool for recording the fluctuations in neural activity of the brain. These fluctuations induce electric potential differences between the reference electrode and the chosen electrode. Such differences are sensed by the amplifier which amplifies the voltage and the signal is recorded as shown in Figure 3-1(b). The choice of the reference electrode is a controversial issue in EEG. It is therefore placed at a different position than the recording electrodes (earlobes or mastoids) or is taken to be the average of all recording electrodes. The electrodes for measuring EEG are located at a certain distance from each other depending on the number of electrodes used and the
spatial resolution required for the experiment. High spatial resolution can involve a dense array of up to 256 electrodes. Figure 3-1(c-e) shows the electrode location map of the international 10-20 system for EEG recording. The naming of the electrodes as shown in Figure 3-1(e) depends on the location in which they are placed over the scalp in the international 10-20 system (Pivik et al., 1993). The traces of EEG signal from these recording electrodes are stored in the computer for processing and analysis. A typical adult human EEG signal is about 10µV to 100µV (Aurlien et al., 2004). The fluctuation of EEG signal is supposed to be related to the activity of neuron populations of the cerebral cortex (Nunez & Srinivasan, 2006), although the exact source(s) of EEG is still in controversy (Buzsáki, Anastassiou, & Koch, 2012). EEG monitors the brain activity at a high temporal resolution (millisecond), which is very valuable for research on fast time scale properties of brain dynamics (Michel & Murray, 2012). Even in the resting state of human brain, the EEG signal often presents rhythmical patterns with several significant oscillation bands, each of which is closely associated with physiological and psychological significance (Klimesch, 1999; Schack, Vath, Petsche, Geissler, & Möller, 2002), and could also relate to certain kind of brain diseases (Babiloni et al., 2006; Jeong, 2004). Different bands of oscillations are found to be correlated and also modulate each other mutually (Canolty et al., 2006). The correlated brain activities across different brain regions measured by EEG are found to reflect a functional dynamic network, which initiated a new direction for brain study using the approaches of network analysis (Bullmore & Sporns, 2009). However, EEGs do suffer from some limitations. Firstly, EEGs represent the combined activity of thousands of neurons that needs to be synchronously triggered for significant deflection on the recording electrodes. Secondly, this synchronous triggering of many neuron travels through four different layers in the brain before reaching the scalp, and therefore are spread and diffused, thereby precision in
retrieving these sources actively is lost due to volume conduction. Thirdly, spatial resolution of EEG is not as high as fMRI. Fourthly, EEGs are a combination of neural signal. Associated noises accompanying them are difficult to be removed completely, making them tough to be filtered from the signal. To summarize, though EEGs suffer from few disadvantages, yet it is one of the most reliable, safe and non-invasive, temporally high-resolution measures of electrical activity across the dynamic brain system.

**Figure 3-1:** Illustrations of EEG recording. (a) Picture of EEG experiment on human participant. (b) Simplified schematic illustration of circuit for EEG measurement of the voltage between active and reference electrodes. (c-e) International 10-20 system of EEG electrode locations and naming (picture adapted from Malmivuo & Plonsey, 1995).

### 3.1.2. ERP

Event-related Potential (ERP) is a conventional and widely used method in neuroscience research based on the EEG data and was first recorded by (Davis & Davis, 1936). ERP is the average of a number of EEG single trials with respect to the same stimulus input as shown in
Figure 3-2(a). Usually subjects perform some tasks (e.g., face recognition) with or without response execution (e.g., button pressing). The stimulus for the task is presented repeatedly over several trials. When the epochs of different trials of EEG are realigned to the stimulus onset times and averaged as shown in Figure 3-2(b), a clear waveform with a series of peaks and troughs emerges as shown in Figure 3-2(c), which is called Event-related potential (ERP). Averaging of many single trial EEGs enhances the signal to noise ratio (Challis & Kitney, 1990) in the ERPs. The noise can then be minimized by appropriate filtering. The filtered ERP reveals the activity of cognitive processes because the waveform of ERP changes across different experimental conditions as illustrated in Figure 3-2(d). This averaging protocol has been extensively used in cognitive research. ERPs, therefore provide a non-invasive mean to understand the activity of the human brain when it perceives stimuli, makes decision or controls behavior (Picton, Lins, & Scherg, 1995).

**Figure 3-2:** Derivation of ERP from single trials of EEG: (a) Recording of EEG signal when the subject is performing a task; (b) Selected 30 single trial EEG from a single electrodes (PO8), aligned to onset of stimulus; (c) Stimulus-locked average ERP from the same electrode; (d) Illustration of the variation of waveform of average ERP across different conditions.
ERP is composed of many components as shown in Figure 3-3 and unless specified, the word ‘ERP’ or ‘conventional ERP’ refers to stimulus locked average ERP. Different components of ERP are defined according to their polarity, latency, functional relationship or underlying sources (Fabiani, Gratton, & Coles, 2000). For example, as shown in Figure 3-3, P3 or P300 is defined as the positive going component in ERP, normally observed in the time range of 270-320 ms of stimulus onset. Similarly, other ERP components of interest are P1/P100, N1/N170, MMN (Mismatch negativity), N400, P600 etc. Each of these components is found to be associated with a specific mental process (Luck & Kappenman, 2011) and show a huge variability across individuals, tasks or conditions. The latency of ERP components are supposed to reflect starting or accomplishing a specific mental process at the cost of time, while the amplitude reflects the processing strength.

**Figure 3-3:** Typical pattern of stimulus locked average ERP. Amplitude and latency of P3 or P300 component are defined as illustrated in the plot.

### 3.1.3. Limitations of ERP

As mentioned, ERPs are obtained from the average of many single trials corresponding to the stimulus onset time. This method of obtaining the ERP is based on the assumption that the
cognitive processing stage and the brain response activity in each single trial are constant when
the same stimulus is presented; however, only background noise fluctuates from trial to trial
(Glaser & Ruchkin, 1976). With averaging of sufficient number of trials, noise gets reduced, and
the signal to noise ratio enhances significantly. This ideal situation is presented in Figure 3-5(a)
where the latency of every trial approximately remains constant. However, in reality the
variability of the signal from trial to trial plays an important role (Kutas, McCarthy, & Donchin,
1977; Verleger, 1997) that may violate this assumption. For example, trial to trial fluctuation in
reaction time (RT) is shown in Figure 3-4. Similarly, the amplitude and latencies of ERP
components vary from trial to trial within a given experimental condition as shown in Figure 3-
5(b). When such intrinsically variable signals are averaged, it leads to an overlap between
adjacent components and to smearing of the time-variable components – broadening their shape
and diminishing their amplitude as shown in Figure 3-5(b).

**Figure 3-4:** Variability of ERP is shown as the single trial EEGs sorted by response time (white line)
from channel Pz of a selected single subject under one condition from a face recognition task (Herzmann
& Sommer, 2010).
**Figure 3-5:** Smearing of peaks due to averaging of single trial ERPs (a) In ideal situation: Each single trial of EEG consists of a wave shape - constant component and random noise. Averaging of these non-fluctuating single trial EEGs (marked in blue) leads to an ideal ERP (below the arrow). (b) In real situation: Each single trial of EEG consists of component that varies in its amplitude, latency, and morphology from trial to trial along with random noise (shown in three different colors above the arrow). Averaging of these trials as marked in black (below the arrow) is an improper smeared representation of an ERP. (Figure adapted from PhD thesis of Guang, 2013).

Furthermore, sub-components of ERP related to reaction time show variable latency with respect to stimulus onset, as has been found for P300 (for a review, see Verleger, 1997). In a simple case for simulation data, latency variable component may be affected by latency invariable components as shown in Figure 3-6. Stimulus (blue) and response (red) locked components are conventionally averaged (either to stimulus onset time or to reaction time). These are found to get intermixed by the shape of each other. This happens in reality when the stimulus evaluation-related process in fast speed trials gets intermixed with perception-related process in slow speed trials, and in the worst case, the components representing different processes may get mingled with each other completely. This could therefore be regarded as a challenge in interpretation of ERPs as an indicator of mental chronometry. It is thus desirable to develop new methods that would solve the predicament and enhance our perception from ERPs.
3.1.4. RIDE

Residue Iteration Decomposition (RIDE) is a technique developed at the Department of Physics, Centre of Nonlinear studies, Hong Kong Baptist University in collaboration with Department of Psychology, Humboldt University, Germany by Ouyang et al., (2011), for solving the predicament of smearing and temporal overlapping of components in ERPs. RIDE uses the temporal decomposition technique to segregate the ERP into a few component clusters. This is based on classical model of brain processing that divides the response of the brain to external stimulus input into three basic stages of cognition – perception, central and motor action (named as sandwich model by Hurley, 2002) as shown in Figure 3-7(a). Each of these stages requires different mental processes (Masaki, Wild-wall, Sangals, & Sommer, 2004; McCarthy & Donchin, 1981) as shown in Figure 3-7(c) which varies with time as shown in Figure 3-7(b), leading to variation in the overall reaction time across different trials. RIDE utilizes this information of latency variability across single trials of ERP sub-components (Figure 3-7(b)) to decompose ERPs into three different component clusters S, C and R as shown in equation (1),

Figure 3-6: Overlap of different ERP components locked to different time events. (a) Simulated single trials data with stimulus-locked (blue) and response-locked (red) components; (b) Stimulus-locked average ERP; (c) Response-locked average ERP. (Figure adapted from PhD thesis of Guang, 2013).
$EEG_i(t) = S(t) + C(t - \tau_i) + R(t - RT_i) + \xi_i$ \hspace{1cm} (Eq-1)

where $i$ denotes the trial index, $\tau_i$ denotes the latency of C-component, $RT_i$ is the latency of R-component ($R$ is assumed to be reaction time (RT) -locked) and $\xi_i$ is the noise accompanying each trial.

The significance of the three component clusters are (1) a stimulus-locked component cluster named ‘S’, indicates neural processes like visual perception or structural encoding, unrelated to the response speed; (2) a reaction time (RT) locked component cluster named ‘R’, indicates motor-related processes; and (3) an intermediate component cluster named ‘C’, mainly attributed by latency-variable processes, indicates central cognitive processes, such as stimulus evaluation or response selection. RIDE has been repeatedly shown to sharpen the distinction between different ERP components across different experimental paradigms (Ouyang et al., 2011; Ouyang, Schacht, Zhou, & Sommer, 2013; Rostami et al., 2015; Stürmer, Ouyang, Zhou, Boldt, & Sommer, 2013; Verleger, Metzner, Ouyang, Śmigasiewicz, & Zhou, 2014; Wang, Ouyang, Zhou, & Wang, 2015).
Figure 3-7: Representation of mixing and smearing of different mental processes. (a) Assumed model of mental processing with basic components. (b) Realizations of responses in brain for different trials. (c) The latency distribution of time for accomplishing each process.

3.1.5. RIDE derived ERPs (RERPs)

The ERPs obtained from combination of S, C, and R components of RIDE are termed as RIDE derived ERPs (RERPs). Below is a brief overview of the iterative procedure followed by RIDE algorithm to separate the ERP into stimulus locked S, median latency locked C, and median reaction time locked R components:

1) Firstly, the single trial latency of C component was estimated by cross-correlation between ERP and single trial waveforms;

2) Then; Initially $S = C = R = 0$ was set;

3) C and R component were then subtracted from the single trials and all single trials were synchronized to stimulus onset to get the median waveform for S;
4) S and R component were then subtracted from the single trials and all single trials were synchronized to single trial latency for C to get the median waveform for C;

5) Finally in the same manner, S and C components were subtracted from the single trials and all single trials were synchronized to response onset to get the median waveform for R;

6) Step (3) to (5) were iterated until they converged;

7) Again, the single trial latency of C was re-estimated by the cross-correlation between C and single trials after removal of S and R components from them.

8) At last, steps (2)-(7) were further iterated until the outer convergence was achieved.

More details about the algorithms applied here can be found in Ouyang et al. (2015a). The RIDE procedures are done on all electrodes so that the RIDE components across the scalp at a given time point can form a surface topographic pattern.

An important option of RIDE is reconstructing ERPs after compensating for latency variability (Fig. 3-8). After separating ERPs into three component clusters with different latency variability (Fig. 3-8, left and middle panels), we can synchronize each cluster according to their single trial latencies and locate them at their most probable (median) latency and summate them into a latency-synchronized waveform, yielding a reconstructed ERP (RERP) (Fig.3-8, right panel). The RERP represents a waveform that is corrected for smearing and is most representative of single trials and might provide a better insight of cognitive (sub-) processes in mental chronometry.

Trial to trial variability of ERP is an important consideration when evaluating cerebral function (Picton et al., 1995) and cannot be ignored when brain mechanisms are to be explored. Peaks get smeared due to variability of these signals. Peaks represent some particular activity in the brain, and since different generator are active at the same latency, the peak may result from
superposition of different electromagnetic fields generated by the collective potentials of these neural sources (Picton et al., 1995). RERPs are better than conventional ERPs as they take into account the trial to trial variability of single trials. This rectifies the smearing effect and increases the amplitudes of late components (Ouyang et al., 2015a, 2015b). An example of sharper peaks in RERPs has been provided in Figure 3-9 for the face priming ERP data obtained from the work of Herzmann & Sommer, (2010). RERPs on the same dataset have been obtained from the work of Ouyang et al., (2011). Sharper peaks are encircled for both primed and unprimed famous face condition in ERP and RERP data, respectively. This enhancement in RERPs could provide more concrete overview of the neural sources when source localization will be performed on them. We anticipate that benefits of RIDE at surface level could also be generalized to source level.

Figure 3-8: Illustration of RIDE decomposition and reconstruction of ERP. **Left:** The blue, red and green components represent S, C and R component clusters time-locked to stimuli, non-locked and locked to the responses. In the conventional stimulus-locked average ERP (bottom), the latency-variable late components are smeared and mixed. **Middle:** RIDE separates the three component clusters. **Right:** RIDE resynchronizes all component clusters to their own latency and locates each component at the median latency and then reconstructs ERP by summation to obtain the RERP (bottom), which recovers the components likely to be observable in single trials.
Figure 3-9: Illustration of RIDE effects on the ERP waveforms by correcting latency variability. ERP (blue) and RERP (red) waveforms are compared for electrodes Fz (left, A, C) and Cz (right, B, D) for primed (A, B) and unprimed (C, D) famous faces. Sharper peaks (encircled) are found in the late components in case of RERP data, which are supposed to facilitate source localization in late windows.

3.2. Basics of source localization

In this section, we will discuss activity of neural sources as equivalent current dipoles and the role of dipolar sources in multilayered structure of human head. Further, different source localization techniques and need for focal source localization will be elaborated. In that aspect, the basics of BESA as a software tool for focal source analysis would be explored. Finally, the use of source waveforms as an important index relevant to our study will be stressed.
3.2.1. Dipoles in the head

High temporal resolution of EEGs/ERPs makes them a first-rate tool for estimating the neural activities in the brain (Gevins, 1998). Imaging the electrical activity of the brain from ERPs during sensory-motor or cognitive task consists in estimating the underlying sources in cerebral space and time. For this, a physical model of neural current sources is approximated by a current dipole (Figure 3-10(a)) which is considered to be a correct approximation for synchronous activation of a population of $10^6$ cortical macro-columns of pyramidal cells (Gloor, 1985). These dipoles in the brain are created due to neuronal current flow between the excitatory and the inhibitory neurons. A dipole is considered to be a simplistic assumption of the time varying flow of current happening in the neuronal cells of the brain, however contributions are also due to monopoles, quadruples and octapoles (Nunez & Srinivasan, 2006). Areas up to 3 cm in diameter can be accurately modeled by a single equivalent dipole (Nunez & Srinivasan, 2006). Maxwell’s equations are then used to calculate the electric (and magnetic) field on the surface of the scalp formed due to these dipoles. The current dipoles are approximated for their location (equivalent center of the modeled gray matter patch measured similar to x, y, z coordinates of a sphere) and orientation (net direction of the modeled post-synaptic neuronal current, perpendicular to the surface of the modeled gray matter patch measured in similar to angles $\theta$, $\varphi$, $\psi$ of a sphere). Numerous current dipoles can be represented by an equivalent current dipole as shown in Figure 3-10(b). The sources can be tangential, radial or oblique as shown in Figure 3-10. Magnetoencephalography (MEG) can detect tangential dipoles whereas EEG source localization can detect tangential, radial and deep sources (Michel & Murray, 2012). The computation requires taking into account the head geometry and the conductivity properties of the head tissues.
Figure 3-10: Numerous dipoles (a) can be represented accurately by an equivalent dipole shown in (b). The orientation of the dipoles in the cortex can be radial, tangential or oblique. (Figure adapted from Scherg, 2010).

The human head is a multilayered structure composed of the scalp, skull, cerebrospinal fluid (csf), and the brain with different conductivity and anisotropy across different layers. In that aspect, different head models based on Boundary Element Method (Meijs, Weier, Peters, & Van Oosterom, 1989) and Finite Element Method (Haueisen, Ramon, Czapski, & Eiselt, 1995; Marin, Guerin, Baillet, Garnero, & Meunier, 1998) are employed to increase the accuracy in the design of the head models. However, these layers are also modeled as concentric spheres with homogenous conductivity for a simplistic head model. The influence of head geometry and the conductivities (for details on conductivity values refer Fernández-Corazza, Von-Ellenrieder, & Muravchik, 2011) have been widely investigated (Haueisen et al., 1995; Marin et al., 1998). However, in case where prior information about head geometry is not known, standard ellipsoidal head model could be an optimal choice.
3.2.2. Spatio-temporal model fit

Two types of source localization could be performed on the EEG/ERP data, namely, (1) Focal Source Localization or Discrete Source Localization and, (2) Distributed Source Localization. Focal source models assume a small number of dipoles (with dipole moments) with fewer degrees of freedom compared to EEG sensors that can account for the variation in the observed EEG/ERP data (Scherg & Von Cramon, 1986). This data reduction technique from EEG multisensor space to a few dipole moments in the source space is implemented by BESA (Grech et al., 2008). Distributed source models assume that the source locations are numerous and distributed across a given cortical surface (Hauk, 2004). The purpose of this technique is to determine strength and orientation of the active sources with a common assumption of L1 or L2 minimum norm. This technique is implemented in LORETA, sLORETA, VARETA, S-MAP, ST-MAP, LAURA, SSLOFO etc. Though, both techniques of source localization have their own merits and demerits, it usually depends on the kind of research one is interested in and the way the results will be utilized for understanding the scope of the experiment. For example, the crosstalk between the sources in distributed source models is very high and their activity is also smeared, which makes it tough to distinguish between different nearby active brain regions compared to solutions obtained from focal source models where nearby active areas are distinct (Hoechstetter, Berg, & Scherg, 2010). However, the source images can be generated more easily with predefined source model in distributed source localization whereas focal source solution requires a high amount of user’s interaction (Hoechstetter et al., 2010). If considerable precision is taken in the choice of parameters, the accuracy of both techniques is almost similar (Baillet et al., 2001). On the other hand, if the research demands require a temporal analysis of the source waveforms (SWF), then focal source models will be beneficial compared to distributed source
models and vice versa, when a spatial analysis in source localization is more important than temporal analysis.

Since, our focus of current research was to establish whether the benefits of RIDE (enhanced peaks in RERP) at surface level generalize to source level, therefore, choice of focal source localization fits appropriately for comparison between conventional ERP and RERP. Therefore, we will particularly discuss about focal source localization and BESA in more detail, as it was employed for source localization in our study.

3.2.3. Focal source localization

Linear superposition of a few dipoles are responsible for scalp topographies across various time points of an EEG/ERP recording as shown in Figure 3-11. Source localization methods search the best dipole position(s) and orientation(s) to explain data based on scalp topographies. After a certain number of dipoles are fixed \textit{a priori}, the estimation is guided by non-linear minimization of a cost function. Two standard approaches are made for approximating the number of dipoles, namely (1) the whole period is analyzed at once with an increasing number of dipoles. New dipoles are added as long as explained variance considerably increases; (2) the period is analyzed sequentially over peaks (Snyder, 1991) and new dipoles are added for each additional time window if further activity remains unexplained. Application of these methods are mostly on spherical head models which constitute the lead fields (Figure 3-11) for fast calculation of the forward solution for a given dipole position and orientation.

Dipole fit methods and more particularly the BESA implementation has proved to be powerful exploration tools for many cognitive and clinical studies (Ebersole, 1994; Scherg & Von Cramon, 1986). BESA assumes a realistic lead field matrix by considering various head models, of which a four shell ellipsoidal head model replicating a realistic human head is widely
accepted. It consists of brain, scalp, bone and cerebrospinal fluids having thickness of 85mm, 6mm, 7mm, and 1mm with average conductivity of .33 S, .33 S, .0042 S and 1 S respectively.

**Linear superposition:** \[ d(t) = L \cdot s(t) + n(t) \]

\[
\begin{align*}
data &= \text{model (Leadfields)} \times \text{source activities} + \text{noise}
\end{align*}
\]

**Figure 3-11:** Illustration shows how lead field matrix and source activity can be calculated from a given dipole obtained from scalp topography. (Figure adapted from Scherg & Berg, 2010).

**3.2.4. Basics of BESA**

The BESA (Brain Electrical Source Analysis software) source modeling considers a time window to fit a dipole that is supposed to be stable in location with fixed or varying orientation. After a time window of interest has been selected from the peaks in the data or from the scalp topographic maps, principal component analysis (PCA) of the selected time window is done. The time length of the selected time window is varied such that the decomposition of the data is dominated by a single PCA component. Then a guess of the number of sources to be fitted on that data is made looking at the scalp topographic map. A distributed topographic map on the scalp indicates bilateral activation of both hemispheres. In that aspect, symmetrical fitting of the dipoles across two hemispheres of the brain is a choice. This could also be made in BESA usually when a priori information about bilateral activation of the hemispheres is known, like
source localizing the auditory or face recognition data. The location and orientation of the sources could be obtained in many coordinate systems; however standard systems like talairach or MNI are internationally accepted. Once the sources are fixed, the source estimation is guided through minimization of cost functions that is weighted combination of 4 fit criteria, as mentioned below:

1) A criterion of Residual Variance (RV) in the data: this is the amount of signal that remains unexplained for a chosen time window of fit by the current source model. This criterion is defined as the following ratio:

\[ RV = 100 \times \frac{\langle \| V(:,t) - \hat{V}(;t) \| \rangle}{V(:,t)} \% \]  

(Eq-2)

Where \( V(:,t) \) are the measured potentials at instant \( t \), \( \hat{V}(;t) \) are the reconstructed potentials for a given source model according to the assumed model of the head, and \( \langle \| a(t) \| \rangle \) is the time average of the 2-norm of the time-varying vector \( a(t) \).

2) A variance criterion that increases when the sources tend to be active outside of their \textit{a Priori} time interval of activation. When the RV increases to a high extent outside their fitting interval, a need for the next dipole pairs could be experienced by the user.

3) An energy criterion that avoids the interaction between two sources when a large amplitude of the waveform of one source is compensated by a large amplitude on the waveform of the second source, giving rise to small amplitude on the surface of the scalp.

4) A separation criterion that encourages solutions in which, as few sources as possible, are simultaneously active for a time window. This is done by maintaining the regularization constant to 1%.
Though minimization of the cost function is a priority while performing source localization in BESA, the user needs to be aware of few points:

1. Reaching minimum RV is not the sole criteria: The first approach in source localization attempts to reach a point of minimum RV. This approach might seem attractive but is in fact really hazardous if it is done with only this criterion in mind. The RV criterion gives little credit to the rest of the sensors as they have little contribution quantitatively to the global signal power and could lead to spurious and unrealistic source localization. So the user must consult the scalp topographic maps.

2. Scalp topographic maps: Scalp topography takes all the sensors into account and is a good way to estimate and make a choice for bilateral or symmetrical distribution of sources across the two hemispheres. They also guide whether minimum RV solutions may be trusted by visualizing the topography of the reconstructed potential maps on the scalp as well as comparing them to the original ones. Fortunately, over-fitted solutions tend to produce potential maps on the scalp that may deviate from the original and could give an index of the poor accuracy of the current solution.

In conclusion, dipole fitting in a sphere model can give precious indications about the regions that are likely to be active. However, precise localization of the sources for anatomical registration should be processed with extreme care. This is especially the case when considering the minimum RV as the only quantitative guiding criterion. Important aspects like stability of the fitted source solution across time, their physiological plausibility, and similarity of the scalp potential map with the original one have to play a central role in the source fitting strategy.
3.2.5. **Source waveforms (SWFs)**

The source waveforms (SWFs) thus obtained after inverse operation of the EEG/ERP data is an indicator of the reconstructed brain activity (Scherg & Berg, 2010) as shown in Figure 3-12. The source waveforms are the inverse operations of the lead field matrix with the outer EEG/ERP data. The inverse operator acts like a spatial filter that deblurs the measured waveform (Scherg & Picton, 1991). The source waveform thus obtained is a measure of varying dipole moments over time as shown in Figure 3-12.

**Figure 3-12**: Illustration shows the inverse operation of the outer EEG/ERP data to obtain the source waveforms or the dipole moments of the sources for the selected time period (Figure adapted from Scherg & Berg, 2010).

The SWFs are a very important measure as they reflect the activity in the brain. They are superior to outer EEG data because (1) they do not suffer from volume conduction and, (2) the reference electrode also has no influence on its activity (Michel & Murray, 2012). Being non-invasive and with high spatiotemporal resolution, SWFs could become a suitable tool for effective connectivity analysis. They could reveal the robust picture of the working mechanism.
of the brain when causal influence of one source on the other could be determined through dynamic causal modeling (DCM)

3.3. Basics of Dynamic causal model (DCM)

In this section, we will discuss briefly about the structure of the cortex and different kinds of connection possible from a cortical source in the brain. Subsequently, we will discuss about the role of these connections in outlining hypothesis-driven models from our data. Finally, we will discuss about comparison among different hypothesis-driven models, emphasizing selection of the preferred model.

3.3.1. Basics of cortical structure and underlying dynamics of DCM

Brain is a complex structure kept inside the cranium covered by four layers namely the cerebrospinal fluid, the arachnoid, the pia and the dura matter. Underneath these four layers, lies the cortical structure, divided into columns or voxels of volume $1\text{mm}^3$. Each column is further divided into 6 layers constituting millions of neurons of different shapes and density, having inhibitory or excitatory behavior. This 6-layer structure of a cortical column was skillfully described by Jansen & Rit, (1995). The Jansen model often said as first order neuro-mass model (NMM) emulates the MEG/EEG activity of a cortical source using three neuronal subpopulations. A miniature model has been shown in Fig. 3-13(A) for our understanding. NMM shows population of excitatory pyramidal (output) cells receiving inputs from inhibitory and excitatory populations of inter-neurons, via intrinsic connections (thin solid black lines in Fig 3-13 (A)). Within this model, excitatory inter-neurons can be regarded as spiny stellate cells found predominantly in layer 4 that receive forward connections (thick solid black lines in Fig 3-
Excitatory pyramidal cells and inhibitory inter-neurons occupy a granular layer and receive backward (dashed solid black lines in Fig 3-13 (A)) and lateral inputs (grey lines in Fig 3-13 (A)). Anatomically, though inhibitory neurons are less in number compared to excitatory neurons but their effect is influential as the inhibitory synapses are nearer to the cell body. The excitatory and inhibitory neurons lead to dipolar behavior of an area inside the brain. The cortico-cortical connections connecting different lobules within the same hemispheres are known as association fibers or white matter connectivity.

Figure 3-13: Schematics of (A) first order neuro-mass model designed by Jansen and Rit, 1995 along with their interaction with other cortical areas via intrinsic and 3 types of extrinsic connections. (B) the differential equations governing each subpopulation in the cortex. (Figure adapted from David et al., 2006).

Dynamic causal model (DCM) for ERPs, David et al., (2006) employs the neuro-mass model (NMM) as explained above. This model uses the concept of effective connectivity and
measures the influence of one source on the other (Friston, 2011). In DCM, brain is considered as a deterministic non-linear dynamic system that is subject to inputs and production of outputs (Friston, Harrison, & Penny, 2003). Each cortical structure in this system is governed by a set of differential equations [for details refer, David et al., (2006); also shown in Fig. 3-13(B)] connected intrinsically and also connected extrinsically through forward, backward or lateral connection as shown in Fig. 3-13(A) and (B).

3.3.2. Model construction

The DCM analysis on the source data involving the Bayesian framework could be done using the software toolbox SPM8 (http://www.fil.ion.ucl.ac.uk/spm/) Physiologically plausible sources defined with interconnectivity patterns are responsible for the generation of EEG (David, Harrison, & Friston, 2005; David et al., 2006). In this aspect, forward connections are driving, run from lower level to higher level areas, whereas backward connections are both driving and modulatory, run from higher to lower areas (Friston, 2005). Modulatory backward connections are the connections that could modulate the responsiveness to another input and play a big role in hierarchical designing of different generative models in DCM. Designing of the models based on forward, backward or lateral connection requires an in-depth knowledge of anatomy and physiology of the areas in the brain in which the sources got localized. White fiber connectivity between sources plays an important role in the design of connections between different sources. The generative models are hypothesis driven (for details, refer to Stephan et al., 2010) based on Bayes rules and certain model parametric approximation or measurement (David et al., 2005; Stephan, Tittgemeyer, Knösche, Moran, & Friston, 2009), where each model explains the data (outer ERP, Inner SWF, fMRI, PET etc.) based on expectation maximization algorithm (an
iterative scheme that estimates conditional expectations and maximum likelihoods of model parameters minimizing the free energy) detailed in (David et al., 2005). In short, this causal scheme minimizes the difference between observed and expected data based on \textit{a priori} information (Friston, 2005). Different models, with or without particular connections between two sources could be outlined that could well explain the data. Therefore, a criterion for selecting the goodness of fit of each model on the data is an important part of DCM.

3.3.3. Model selection and comparison

DCM accesses two quantities from a model, namely (1) Model Evidence $p(y \mid m)$: probability of a model ($m$) given the data ($y$), a parameter used to compare model fitting across different models using Bayesian model comparison (Penny, Stephan, Mechelli, & Friston, 2004). Bayesian model comparison accounts for the accuracy and complexity of the model to finalize the preferred model. In the worst case, where two models have the same accuracy, model with simpler network architecture wins. (2) Model parameters ($\Theta$): it defines the connectivity parameters of a given model (Stephan, Penny, Daunizeau, Moran, & Friston, 2009). The model parameters are obtained from the Bayesian model average (BMA), which estimates the modulatory effects of the experimental input over model parameters. The posterior mean ($m$Eps) and standard deviation of each connection in the preferred model or the not-preferred could be obtained from the DCM framework as a marker of coupling strength between two regions that modulates across different experimental conditions. A detailed description of the framework used to model the source data can be found in David et al., (2006); Pinotsis, Moran, & Friston, (2012).

When outlining models with SWFs, ERP neural mass model and LFP spatial model could be selected over the chosen stimulus time interval. The location coordinates of the obtained sources
in MNI needs to be filled up and the time window for which SWFs need to be modeled has to be mentioned. Finally, different models can be outlined, fitted and compared using the Bayesian model comparison in SPM framework. For details, SPM8 manual can be referred by the user (http://www.fil.ion.ucl.ac.uk/spm/). Integration of ERPs/RERPs, BESA source localization and DCM framework together can be a powerful tool to investigate the working mechanism of the brain from temporally resolved scalp data. If RERP SWFs are better than ERP SWFs in any experimental paradigm, then use of RERP with this integrated framework can provide deeper insights to our understanding of the brain functions.

3.4. Overview of the integrated framework

In the previous sections, we have explained each of the elements that are integrated together to form a common framework for our research. Here, we provide a brief illustration of the integrated framework with application to our work, along with an example from the RERP data of a single subject taken from the study of Herzmann & Sommer, (2010). The results shown here on individual subject face priming data will be relevant to our work later but will provide a consolidated understanding of the developed framework. The RERP data was obtained from the face priming ERP data of Herzmann & Sommer, (2010) on which RIDE was applied from RIDE tool box (http://cns.hkbu.edu.hk/RIDE.htm). RIDE separates the ERP data into three component clusters S, C, and R; realigns them to their respective latency, and then adjoins them back to obtain the RERPs. RERPs have been shown above to be better than ERPs (Fig. 3-9). The surface topographic view of the RERP data has been shown in Figure 3-14.
Source localization was done with BESA 6.0. For this, the framework modified the RERP data in the format accepted by BESA. A choice of filtering the data could be made by the user, if the data has lot of noise in it. However, current data set has been properly preprocessed and filtering was not required. A four shell ellipsoidal head model (as mentioned previously) was considered for localizing the four pair of sources for a time window of 0-350ms as shown in Figure 3-15. The regularization constant was kept at 1%. Regularization constant is a parameter that balances the crosstalk between the sources and is conventionally kept at 1%.

The dipoles were fitted at the latency of 100 ms, 170 ms, 230 ms and 320 ms such that the residual variance (RV) of the data reduces to 1.86 %. The sources were numbered as 1, 2, 3, and 4 on each hemisphere according to the order in which they were localized serially. Their precise location (x, y, z) in terms of Talairach or MNI coordinates could be obtained from BESA. The source waveform (SWF) is the fluctuating dipole moment that is obtained after fitting the dipolar sources to the RERP data.
The SWFs are exported from BESA to MATLAB. Our framework further arranged the SWFs in the format required for DCM analysis, to be done through the Bayesian framework of SPM8 (http://www.fil.ion.ucl.ac.uk/spm/). Though different options of processing the SWFs could be selected from SPM8, however, our integrated framework had been tested, only for the ERP neuro mass model and LFP spatial model.

The influence of network architecture from one source on the other could then be evaluated by outlining different hypothesis driven model of the sources. However, for the following illustration, we outlined two arbitrary network architectures (ignoring hypothetical dictum) on the obtained SWFs as shown in Figure 3-16 (A) and (B). The architecture in Figure 3-16 (A) had only forward connection and therefore named as Forward (F) model. Similarly, Figure 3-16 (B) had backward connections along with forward connections and therefore named as Forward Backward (FB) model.
Figure 3-16: Schematic representation of (A) Forward (F) DCM model with forward connections (solid lines), (B) Forward-Backward (FB) DCM model with backward connections (dashed lines) along with forward connections. Extrinsic input to the system enters via Source 1.

From the prior information available through physiological measurements, DCM predicts the response of each source as shown for the two models in Figure 3-17 (A) and (B). The causal scheme minimized the difference between observed and predicted data. DCM assumes the extrinsic input to be Gaussian that enters the system through source 1. In the DCM model (Figure 3-17 (A) and (B)), the solid blue lines show the predicted response and dashed blue lines represent the observed SWF data obtained from BESA. It can be seen that the F model fits better to the observed response. The two models can then be compared for their goodness of fit through an iterative scheme (mentioned above) and have been shown in Figure 3-17 (C). As can be seen that the model exceedance probability of the F model is higher (> .8) than that of FB model, and therefore F model is regarded as a “preferred” model out of the two outlined models. The posterior mean of the models was then calculated from DCM to understand the effective network architecture and the causal influence of one source to the others.
The above integrated framework will be implemented in our subsequent chapters to compare the RIDE derived ERPs and conventional ERPs, as well as to understand the working mechanism of the brain when faces are recognized and primed.

**Figure 3-17:** Graphical representation of the observed (dashed blue lines) and predicted (solid blue lines) activity of the sources from (A) F model, (B) FB model. The comparison of the goodness of fit in terms of model exceedance probability of F and FB model is shown in (C).
3.5. Summary

In this Chapter, we discussed the basic elements of this research work and gave a brief overview and illustration of the integrated framework. The basic elements comprise of three sections, namely (1) Basics of EEG and ERP, (2) Basics of source localization and, (3) Basics of dynamic causal model.

In the first section, the art of obtaining EEG from the scalp and conventional averaging of these single trial EEGs to obtain ERPs are discussed. Though conventionally averaged ERPs provide a good insight of the brain activity, their late components suffer from smeared peaks due to the latency variability in single trial EEGs. The smearing problem could be addressed by reconstructing the ERPs after latency synchronization with the Residue Iteration Decomposition (RIDE) method. RIDE was found to increase the amplitudes of the late components of the scalp-recorded ERPs across different experimental paradigms. In this aspect, the algorithm for extracting RIDE derived ERPs (RERPs) from conventional ERPs was discussed. As RERPs perform better on scalp, we expect them to perform better also at the cerebral space when source localization is done on them.

In the second section, the source localization technique is discussed with particular attention to focal source localization. Focal source localization was done through BESA in our study and therefore the principles of BESA are discussed in particular. We mentioned the care one must take to perform source localization with discrete dipoles so as to avoid over-fitting to the outer scalp data. Next, the procedure to obtain source waveforms as reflection of brain activity is discussed. The source waveforms are advantageous compared to outer scalp ERPs as they do not suffer from the problem of volume conduction and reference electrode. Extracting
SWFs using BESA and utilizing them to understand the causal influence of one source on the other could provide a robust picture of the brain mechanism.

In the third section, we briefly discussed about the dynamic causal model employed through the SPM framework. We discussed how the framework approximates each cortical source based on real anatomy. The logic behind the interconnectivity of one source with others through forward, backward or lateral connections is mentioned. We thereafter reviewed how different hypothesis driven models could be outlined from the knowledge of anatomy and physiology of the brain. Different models could then be compared and their goodness of fit could become the selection criteria for the preferred model from the entire family of outlined models.

In the last section, we provided an integrated form of the framework by combining the sections above. A brief overview of the integrated framework and its working mechanism had been outlined, taking individual subject ERP data as a benchmark representation from the work of Herzmann & Sommer, (2010). A detailed implementation and discussion of the framework will be done in the subsequent chapters.
Chapter 4

Data Acquisition and RIDE analysis

In this Chapter, we will introduce the Herzmann & Sommer, (2010) experiment for ERP data acquisition of face priming on famous faces. Subsequently, we will overview the work of Ouyan et al., (2011), claiming RIDE’s improvement over scalp topography on the same data set compared to conventional ERP. Finally, we will point out the benefits of RIDE at scalp/electrode level that could facilitate better source localization of RERPs.

4.1. Experiment and conventional ERPs

EEG data of 21 participants performing familiarity judgments about primed (PF) and unprimed (UF) famous faces was recorded by Herzmann & Sommer, (2010). They performed the experiment with 23 participants (15 women and 8 men) making familiarity judgments about famous, unfamiliar, and experimentally learned faces. However, in our study we only considered the data from famous faces. The participants were 23 student volunteers of Humboldt University aged between 18 to 33 (Mean= 23.7 years SD= 3.5 years). According to the adapted version of the Edinburgh Handedness Inventory (Oldfield, 1971), the participants were strongly right-handed (M=+80.1, range=53 to 100) and also reported normal or corrected-to-normal visual acuity. The familiarity level to the famous faces were judged from a questionnaire received in prior by participants with 62 sets of famous faces (e.g. actors, politicians, and sportsperson). The questionnaires had the images inbuilt of the celebrities along with the names, which were later used in their priming experiment. Details of the images used in the experiment can be found from Herzmann & Sommer, (2010).
Prior to the experiment (in the design phase of the experiment) participants rated the probability of recognizing the celebrity in the second session using a seven point scale (ranging from 1= “I will definitely recognize this person.” to 7= “I will definitely not recognize this person”). For famous face recognition, those 20 faces were selected for each participant which had the highest ratings (always between 1 and 3) in the priming experiment. A viewing distance of 1 m was kept between participant and the screen, where stimuli were presented at the center of a light gray monitor.

All faces had neutral expressions or weak smiles (teeth being unexposed) and were without beards or glasses. External features were excluded by fitting all portraits into a vertical oval frame 259 by 388 pixels (7.0 by 10.2 cm; 4.0° by 5.8° of visual angle) leaving only the face up to the hairline as shown in Figure 4-1.

![Figure 4-1](image)

**Figure 4-1:** Figure adapted from the study of Herzmann & Sommer, (2010) representing an unprimed condition about how a target face known previously, preceded by an unfamiliar prime face.

Every stimulus was preceded either by a different face or by the same face (unprimed vs. primed conditions) as shown in Figure 4-1. EEG data was recorded with 64 sintered Ag/AgCl
electrodes mounted in an electrode cap (Easy-Cap\textsuperscript{TM}) with electrode TP\textsubscript{9} as common reference and electrode AF\textsubscript{z} as ground. Participants had to indicate the target familiarity by pressing keys with their index fingers. The assignment of familiar and unfamiliar stimuli to left and right hands was counterbalanced across participants. Only 21 of the original data sets could be included because the data sets of two participants contained too many artifacts.

EEG data was preprocessed as follows: From the continuous record, epochs of 1100 ms were derived starting 100 ms before the onset of the target face. Trials with ocular (blink or saccades) and non-ocular artifacts (defined as voltage steps exceeding 50 $\mu$V/ms or a difference of more than 100 $\mu$V in an interval of 200 ms) and incorrect behavioral responses were discarded. EEG were aligned to a 100 ms baseline before target onset, digitally low-pass filtered at 30 Hz with zero phase shift, and recalculated to average reference. Data sets for famous faces contained between 40 and 60 trials. Conventional ERPs were obtained by averaging the experimental trials synchronized to stimulus onset. However in the present study, only primed famous (PF) and unprimed famous (UF) face EEG data was used. The RT (reaction time) facilitation of priming reflect significantly longer RT, $t(20) = 7.2; p < 0.001$, for UF condition ($M = 611$ ms; SD = 57.2 ms) compared to PF condition ($M = 472.9$ ms; SD = 63.3 ms) (for details, refer Herzmann & Sommer, 2010).

4.2. Conventional ERP and their components

Herzmann & Sommer, (2010) found four ERP components important in their analysis. They are (1) P100: a positive going deflection around 80-150 ms pronounced over Pz electrode; (2) N170: negative going deflection around 150-200 ms pronounced over TP\textsubscript{10} and PO\textsubscript{10}; (3) Early repetition effect (ERE): the difference wave (primed minus unprimed) starting around 200 ms and lasting until 400 ms, with electrical negativity at temporal electrodes (e.g. TP\textsubscript{10}) and a
positivity at fronto-central electrodes (e.g. Fz), and (4) Late repetition effect (LRE): the
difference wave with parieto-central positivity (e.g. Pz) around 250 -500 ms.

Herzmann & Sommer, (2010), further divided each of the ERE and LRE period into two
more sub categories based on the Global Map Dissimilarity (GMD) as shown in Fig 4-2. GMD
compared two conditions by subtracting topographic map of one condition from the other to
determine the time periods (microstates) when topographic map landscapes remain quasi-stable,
and then change quickly to another. The GMD identified four microstates of the repetition
effects. They are (1) ERE1 (260-315 ms) (2) ERE2 (315-350 ms) (3) LRE1 (350-420 ms), and (4)
LRE2 (420-500 ms). They concluded that priming effects in the ERP of famous faces started
from 250 ms (ERE) and continued until 500 ms (LRE).

4.3. Previous RIDE analysis

Residue iteration decomposition (RIDE) decomposes the ERP into three
subcomponent clusters S, C, and R. The S component is stimulus-locked and indicates visual
perception and structural encoding. The latency variable C component is associated with central
cognitive process like decision-making, and response-locked R component reflects the motor
described above. From the perspective of RIDE, it is concluded that S and C component account
for the processing of facial information, and R component account for processing of motor action.

Ouyang et al., (2011), analyzed the topographic map of conventional ERP, and S and
C components of RIDE. Surface topographic analysis of scalp data provides information about
the active cerebral sources in the brain (Michel et al., 2004). Surface topographic map of the
ERE and LRE period for conventional ERPs indicates that ERE and LRE get intermixed with
each other, resulting in a blurred topography across the scalp as shown in Figure 4-2 (ERP) for
LRE1. Furthermore, the late part of LRE is demonstrated to be a result of latency shift between primed and unprimed condition and this latency variability also leads to a blurred topography as shown in Figure 4-2 (ERP) for LRE2. RIDE components S and C could clearly distinguish the surface topography for each of the ERE and LRE periods as shown in Figure 4-2 (S) and (C). This reflects that different cerebral sources are active during the different periods of repetition effects with S resembling to the topography of ERE period, and C resembling to the topography of LRE period (parieto-occipital positivity), respectively (for details, refer to Ouyang et al., 2011).

In short, RIDE was able to distinguish between the priming effects more clearly than conventional ERPs. This clearly reflects the potential of RIDEs to allow distinct identification of the underlying sources for ERE and LRE period. LRE however, often confused as an artifact of latency shift between primed and unprimed components, was shown to have distinct cerebral sources through the surface topographic map of C component of RIDE.
Figure 4-2: First row shows the repetition priming effect on the scalp topographic map of ERP components for different time windows (ERE1, ERE2, LRE1, and LRE2). Similarly, the second and third row reflects the same for S and C of RIDE respectively (Figure adapted from Ouyang et al., 2011).

4.4. RIDE derived ERPs (RERPs)

In the previous section, components of RIDE were found to provide distinct scalp topography for the effects of priming. RERPs are a reconstruction of the ERPs from the combination of S, C and R components after correcting the latency variability, i.e., locking/aligning each component to its most probable latency across single trials. This means S component is locked to stimulus onset, R is locked to the most probable (median value) of the reaction time and C is locked to the most probable latency of C across the single trials. We hypothesize that RERPs should facilitate better source localization compared to ERPs because of the topographic benefits it has over the scalp (shown in 4-2). Our work therefore encompasses the benefit of reconstructing the RERPs from ERPs and is illustrated in Figure 4-3 and 4-4.
Figure 4-3 shows the intra-conditional advantage of RERP over ERP whereas Figure 4-4 shows the impact on inter-conditional (PF and UF) advantage of RERP over ERP. In Figure 4-3, latency correction leads to enhancement of the amplitudes of the later components as illustrated at electrodes Fz and Cz for primed and unprimed famous faces. In all figures, sharper peaks (encircled) were found in RERPs (red curve) mainly in the later components compared to the ERP data (blue curve). This sharpening of amplitudes should facilitate source localization in the late time windows for the RERP data as compared to the ERP data.

Figure 4-4(A) shows the waveforms of conventional ERP for primed (PF) and unprimed famous (UF) faces for electrode Pz. There was a difference in latency and amplitude between the primed and unprimed famous faces. When the latency jitter was corrected in RERPs [Fig. 4-4(B)], the amplitudes were enhanced in the two conditions, which change the conditional effects in the sensor space. We expect that such changes would be reflected also in the source activity.

When a standard way of source localization is adopted using the sequential source fitting strategy (localizing the sources from the peaks in the data from earlier to late times), the benefits of RERP over the scalp (shown in Figure 4-3 and 4-4) could also manifest in source space. In reference to this context, the following Chapter is framed to elaborate source localization analysis of RERP and ERP for the same dataset.
Figure 4-3: Illustration of RIDE effects on the ERP waveforms by correcting latency variability. ERP (blue) and RERP (red) waveforms are compared for electrodes Fz (left, A, C) and Cz (right, B, D) for primed (A, B) and unprimed (C, D) famous faces. Sharper peaks (encircled) are found in the late components in case of RERP data, which are supposed to facilitate source localization in late windows.
**Figure 4-4:** Illustration of change of condition effects by RIDE. Time courses of ERP (A) and RERP (B) at the Pz electrode are compared across the primed and unprimed conditions. Correcting the latency variability by RIDE for the RERP data leads to sharper peaks and can change the conditional effects as shown in B.

### 4.5. Summary

In this Chapter, we discussed the EEG experimental procedure of Herzmann & Sommer, (2010) performed on 23 subjects to obtain the primed and unprimed famous face ERP data. Repetition effects of priming for famous faces in the ERP data were seen to start from 250 ms and continue until 500 ms, commonly classified as ERE and LRE. Herzmann & Sommer, (2010) further divided each of the ERE and the LRE period into ERE1, ERE2, LRE1, and LRE2.

Ouyang et al., (2011) analyzed the surface topographic map of all the ERE and the LRE periods for conventional ERP, and for S and C components of RIDE. RIDE was able to distinguish between the priming effects more clearly than conventional ERPs. This achievement of RIDE over conventional ERP clearly indicates that the underlying neural sources could be distinctively separated by RIDE components, whereas these sources remain blurred and hidden in the conventional ERPs.
Furthermore, we reviewed the intra-conditional and inter-conditional advantage of RERPs over ERPs on the same dataset. We hypothesize that RERPs could broaden the scope of source localization analysis compared to ERPs, especially for the late components. The subsequent chapter will deal with source localization from the perspectives of the advantages that RERPs could have over ERPs.
Chapter 5

Implementation, Results, and Discussion

Part I: Source localization

In this Chapter, we will discuss implementation of data on source localization of ERP for face priming which was primarily reproduced from the study of Herzmann & Sommer, (2010), as well as RERP, reconstructed from the RIDE components in Ouyang et al., (2011). We will thrash out source implementation in ERP and RERP source models separately. Results depicting feasibility of source localization of both models and a comparison there of, on priming effects in source activity of ERP and RERP derived sources for various time windows of interest. In the closing stage, we will interpret the results in terms of role the sources might play in face recognition and priming. In the process, we might launch advantages of RIDE at source level.

5.1. Implementation of source localization

Sources of conventional ERPs and RERPs were modeled with Brain Electrical Source Analysis (BESA v.6.0, MEGIS Software GmbH, Munich, Germany; Scherg & Berg, 1995). A 4-shell ellipsoidal head was used to model the brain activity in a 0 to 800 ms time window. The regularization constant (a parameter used to reduce the interaction between sources) was set to 1%.

Scalp topography, an important parameter for source localization, has been shown in Figure 5-1(A) and (B), for ERPs and RERPs in both primed (PF) and unprimed (UF) famous face conditions respectively. Scalp topographies of both ERP and RERP show an even distribution of potential across two hemispheres until 600 ms, suggesting mirror- symmetric sources in the hemispheres. This helps us to assume bilateral sources in our source localization
approach for both ERP and RERP data. After 600 ms the topographic map gets more lateralized to the right, however, the potential distribution still remains spread across both hemispheres, suggesting continuation of bilateral activity for face recognition. This is in consistence with other studies which suggest face recognition to be bilateral but predominant in the right hemisphere (Bourne & Hole, 2006; Schweinberger et al., 1994; Wang & Cottrell, 2012). Another interesting observation can be made if minutely observed, that the difference between ERP and RERP scalp topography start to vary after 240ms. In RERPs the distribution gets sharper compared to ERPs, which facilitates better identification of neural sources. This is because of the sharper peaks in RERP data. Finally, source localization started with creating a master source model, based on ERPs averaged across the PF and UF conditions encompassing all 21 subjects (Hoechstetter et al., 2001; Wong, Fung, McAlonan, & Chua, 2009), as shown in Figure 5-1 (A) (represented as GA). A separate master source model was derived for RERP data (Figure 5-1 (B) averaged in the same way as the ERPs.

Sequential fitting strategy for source localization is a standard way for localizing sources in the brain. We followed the same strategy for source localization of our ERP and RERP data. Since RERPs had de-blurred sharp peaks (shown in previous chapter, Figures 4-3,4) compared to conventional ERPs, it is expected to provide better output for source localization. In sequential source fitting, time windows at the peaks are selected such that the spatial principal component analysis (PCA) is governed primarily by one component. Bilateral sources are localized in that peak interval such that the residual variance (RV) reduces to an acceptable level. A constant check is kept back on the physiological plausibility of the pairs of dipoles fitted sequentially over time. Dipoles are obtained at latencies of P100, N170, ERE, LRE and at 700ms. The result of the
final fitting across whole period of 0-800 ms reached a residual variance below 10% (Mnatsakanian & Tarkka, 2004; Wong et al., 2009).

**Figure 5-1:** Surface topographical map average across 21 subjects for Prime Famous (PF), Unprimed Famous (UF), and their grand average (GA) of both the conditions are reflected for (A) Conventional ERP and (B) RERP.

**5.2. Results of source localization**

Hemispheric views of the two source models on the 4-shell ellipsoidal head are shown in Figure 5-2 (A) and (B) for ERP and RERP source models, respectively, with the sources being marked in numbers for the left hemisphere. For grand average (GA) of conventional ERPs, five bilateral pairs of sources were obtained, giving a residual variance (RV) of 3.32%. In comparison, grand
average (GA) of RERP master source model, yielded six bilateral dipole pairs with a RV of 3.18%.

Figure 5-2: Overview of master source models in two hemispheres obtained from BESA 6.0 for (A) Conventional ERPs and (B) RERPs.

The seed intervals of the peaks, as mentioned in Table 5-1, are obtained from ERP and RERP sources. The latencies at which these sources are obtained has been classified into same time windows (as mentioned in Chapter 4) by Herzmann & Sommer, (2010). The Talairach coordinates of all (left hemisphere) sources for both ERP and RERP signals are also given in Table 5-1. The Brodmann’s areas (BA) of the sources are also listed in the Table. To check for similarity in the location coordinates for both ERP and RERP sources, the Euclidean distance
between a given source in ERP model and the corresponding source in RERP model (if present) was calculated.

The sources for P100 at 110 ms were located in BA 19 of the Occipital Lobe (Sources 1 in Fig. 5-2(A) and 5-2(B)) at almost identical locations for ERP and RERP source models. The N170 component was localized for both ERP and RERP in the Fusiform Gyrus or BA 37 at well similar coordinates (Sources 2 in Fig. 5-2(A) and (B)). Activities in the ERE time window (280-300ms) were located in BA 30 in the Mediotemporal Lobe (MTL) and were very close to each other for both ERPs and RERPs (Sources 3 in Fig. 5-2(A) and (B)). Even though the ERE period was classified into two time windows, 260-315ms (ERE1), and 315-350ms (ERE2), according to sensor space properties (Herzmann & Sommer, 2010), dipole localization suggested only a single pair of dipoles within the MTL with residual variance below 2-3% for these two windows. Adding more sources would have led to over fitting in the ERE period and hence may lead to erroneous solutions. Sources in the LRE period were located in the Prefrontal Cortex (PFC) and the Anterior Temporal Lobe (ATL). For activity around 370-390ms (LRE1), the sources were localized in Prefrontal Cortex (Sources 4 in Fig. 5-2(A) and 5-2(B)). However, distance of the two source solutions for ERP and RERP differed by more than 1 cm, with sources in BA10 and BA9, respectively. The second pair of sources accounting for the LRE2 (480-500ms) was localized in BA 38 or ATL, quite similar for ERPs and RERPs (Sources 5 in Fig. 5-2(A) and (B)). The final sources accounting for response-related components were only obtained for the RERP model and localized in the Premotor Cortex (BA6) (Source 6 in Fig. 5-2 (B)).
### Table 5-1: Source Localizations of grand average ERPs and RERPs (master source models). Only left hemispheric coordinates are given.

<table>
<thead>
<tr>
<th>Serial Order</th>
<th>Seed interval (ms); Component</th>
<th>Source Locations (x, y, z) in mm; Brodmann Areas</th>
<th>Region</th>
<th>Euclidean distance between ERP and RERP Sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>110-120; P1</td>
<td>-38,-70,-4; BA19</td>
<td>ERP</td>
<td>RERP</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-37,-70,-5; BA19</td>
<td></td>
<td>1.4 mm</td>
</tr>
<tr>
<td>2</td>
<td>160-170; N170</td>
<td>-40,-52,-15; BA37</td>
<td></td>
<td>Fusiform Gyrus</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-40,-49,-16; BA37</td>
<td></td>
<td>3.2 mm</td>
</tr>
<tr>
<td>3</td>
<td>280-300; “ERE”</td>
<td>-15,-45,1; BA30</td>
<td></td>
<td>Medio-Temporal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-15,-42,1; BA30</td>
<td></td>
<td>3.6 mm</td>
</tr>
<tr>
<td>4</td>
<td>370-390; “LRE1”</td>
<td>-23,47,15; BA10</td>
<td></td>
<td>Prefrontal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-14,48,22; BA9</td>
<td></td>
<td>11.4 mm</td>
</tr>
<tr>
<td>5</td>
<td>480-500; “LRE2”</td>
<td>-34,4,-15; BA38</td>
<td></td>
<td>Anterior Temporal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-32,5,-17; BA38</td>
<td></td>
<td>3.0 mm</td>
</tr>
<tr>
<td>6</td>
<td>680-700</td>
<td>-----</td>
<td></td>
<td>Premotor</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-28,-10,46; BA6</td>
<td></td>
<td>----</td>
</tr>
</tbody>
</table>

#### 5.3. Source waveform (SWF) analysis

The master source models consisted of a set of dipole locations and orientations for ERPs and RERPs. The locations and orientations of the number of dipoles in each master source models were applied per force on the jackknife averages for the corresponding signal type and each condition. Jackknife averaging is an iterative process of omitting one participant data from the grand average per iteration. Similarly, in our data set, from the grand average of 21 participants, a jackknife average is obtained by omitting one of the participants iteratively in turn, so that, on inclusion of the grand mean, there remains 21 jackknife averages in total. The variation of residual variance (RV) was recorded on every jackknife average of each condition of each model. For conventional ERPs, the mean ± standard deviation of RV were 6.23 ± 2.87 % and 7.18 ± 3.13 % for the primed and unprimed condition, respectively; for the RERPs the corresponding numbers were 6.85 ± 4.71 % and 6.62 ± 3.86 %, respectively. The range of the
variation in RV across all participants for both conditions indicates good feasibility of the master model for both ERP and RERP.

By enforcing the dipole locations and orientations to the jackknife averages of ERP and RERP data, we obtained source waveforms (SWFs) for all the 21 jackknife averages. The source waveform is the fluctuating dipole moment over time obtained by inverse modelling of ERP and RERP data with a realistic 4 shell ellipsoidal head model. The 21 SWFs obtained from each condition of each model allowed for statistical analysis of experimental effects in the source space. The experimental effect is the change in condition due to repetition priming of the famous faces.

To statistically test the repetition priming effects in the sources, we applied appropriate corrections for jacknifing procedure on repeated measures ANOVA (Ulrich & Miller, 2001), and two-tailed t-tests (Miller, Patterson, & Ulrich, 1998). Both statistical measures were applied to SWF amplitudes in 6 time windows (1) 170-260 ms (Early window), (2) 260-315 ms (ERE1), (3) 315-350 ms (ERE2), (4) 350-420 ms (LRE1) (5) 420-500 ms, (LRE2), and (6) Late window of 500-700 ms. Except for the early and late windows, the time windows 260-315 ms, 315-350 ms, 350-420 ms and 420-500 ms had been identified as four microstates of priming effects in the ERPs by Herzmann & Sommer,(2010) (also mentioned in chapter 3). We added two further windows (170-260 ms and 500-700 ms) to see if priming contributions in the sources would be present in these earlier and late stages of processing. The time period before 170 ms was not considered in the present study as it is attributed mainly to vision (P100 component) and structural encoding of faces (N170 component) which are usually unaffected by priming (Herzmann & Sommer, 2007; Schweinberger et al., 2002).
5.4. Priming effects in SWFs

Source waves were divided into six time windows and priming effects in each window were assessed according to two statistical measures of ANOVA with repeated measures on factors priming (primed, unprimed) and signal type (ERP, RERP) and post-hoc $t$-tests of priming in each signal if the interaction had been significant. To visualize the results of these tests, three levels of significance were distinguished $p<.05$, $p<.01$ and $p<.001$ and shown in green, blue, and red, respectively (Fig.5-3). We will summarize the priming effects in each source and compare the ERP and RERP source priming effects for four prominent sources as shown in Figure 5-3. Table 5-2 presents an overview of the statistical results.

**Occipital Lobe and Fusiform Gyrus (FG)**

Priming effects in source activity originating in Occipital Lobe (Source 1) were found neither in ERP nor in RERP source models. Priming effects in the right FG (Source 2) started in the ERE2 (315-350 ms) window and lasted until the LRE2 (420-500 ms) window as shown in Figure 5-3(A). Priming effects during the ERE2 and LRE1 (350-420 ms) time windows were similar in ERP and RERP source models. However, the priming effect was extended in the LRE2 time window in the RERP source model. In the left FG, priming effects were confined to the LRE1 window without much difference between ERP and RERP source models.

**Mediotemporal Lobe (MTL)**

Priming effects in the right MTL (Source 3) started in the LRE1 window and continued until the LRE2 window. In both windows, priming effects were stronger in the RERP
source model. Priming effect in left MTL started from LRE2 window for RERP source model only, but was present in the late window of 500-700 ms for both ERP and RERP source models. In this late window, priming effect was stronger in RERP as compared to ERP source model. In short, the RERP source model enhanced and extended the priming activity in the MTL source (Fig. 5-3(B)).

**Prefrontal Cortex (PFC)**

Priming effect found in right PFC (Source 4) at LRE2 window (420-500 ms) was similar in ERP and RERP source models. However, strong priming effects in right PFC during LRE1 (350-420 ms) and late window of 500-700 ms were only found in RERP source model. The RERP source model has extended priming effects in right PFC. In left PFC, for LRE2 (315-350 ms), priming was stronger in RERP source model. However, ERP source model was found to have an extended priming effect in time window of LRE1 (350-420 ms) (Fig. 5-3(C)).

**Anterior Temporal Lobe (ATL)**

Priming effects in left and right ATL are shown in Figure 6D for both ERP and RERP source models. In right ATL (Source 5), priming effects started from ERE2 and continued during LRE1 (350-420 ms) interval. During ERE2 priming effects were similar in both ERP and RERP source models. However, for LRE1 window, priming effect was stronger in RERP source model. In left ATL, priming effects for ERP source model started from ERE2 (315-350 ms) and continued until LRE2 (420-500 ms). However, for RERP source model priming effect started only from LRE1 (350-420 ms) but continued until late window of 500-700 ms. The pattern of priming effect was similar in both ERP and RERP source models, with priming effects being shifted to later time point in RERP model (Fig.5-3(D)). During the ERE2 window, priming was found only in ERP source model. During LRE1 and LRE2 windows, priming was stronger in
ERP source model. However, during last window of 500-700 ms, strong priming effect was found only in RERP source model.

**Premotor Cortex (PMC)**

The PMC source was found only for RERP model as RERP reconstructs the reaction time-locked R component, which is smeared in stimulus-locked ERP. Hence, RERP source model could not be compared with ERP source model for this source, thereby restricting application of ANOVA with repeated measures. However t-test was performed on this source. Interestingly, left PMC source showed a priming effect in late time window of 500-700ms with \((t>3, p<.01)\) and right PMC was found to have an earlier priming window of 350-420 ms \((t>3, p<.01)\).
Table 5-2: Priming effects in source space within selected time windows.

<table>
<thead>
<tr>
<th>Brain Source</th>
<th>Factor (df)</th>
<th>70-260</th>
<th>260-315 (ERE1)</th>
<th>315-350 (ERE2)</th>
<th>350-420 (LRE1)</th>
<th>420-500 (LRE2)</th>
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<tr>
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<td></td>
<td>5.5*</td>
<td>8.3**</td>
</tr>
</tbody>
</table>

Notes: FG = Fusiform Gyrus; MTL = Mediotemporal Lobe; PFC = Prefrontal Cortex, ATL= Anterior temporal Lobe; * = p < .05; ** = p < .01; *** = p < .001; ns= not significant. If the interaction between priming and signal type is significant, the lines below show the results of post hoc $t$-tests for priming in each signal type.
Figure 5-3: Source waveforms and priming effects were derived from ERP and RERP signals. Priming effects were tested in selected time windows and significance is indicated by coloring (green: $p<.05$, blue: $p<.01$; red: $p<.001$; $p$-values are corrected for jackknifing but uncorrected for multiple testing). Dipolar strength of all sources was within the range of ±150 nAm. (A) Left and right Fusiform Gyrus (B) Left and right Mediotemporal Lobe. (C) Left and right Prefrontal Cortex. (D) Left and right Anterior Temporal Lobe.
5.5. Discussion

Rationale behind this study was to localize neuroanatomically the priming effects in ERPs elicited by famous faces with dipole source modelling and to explore possible advantages of RIDE-reconstructed RERPs over conventional ERPs in a data set from a familiarity decision task for famous and unfamiliar faces with identity priming (Herzmann & Sommer, 2010). Interestingly, we took a somewhat different approach from previous studies (Bindemann et al., 2008; Schweinberger et al., 2002) towards localizing face priming effects. Rather than using difference in waves for localizing sources of priming effects, we started out from un subtracted averaged ERPs and RERPs for primed and unprimed conditions. A further distinction of present approach is the employment of jackknife averages, allowing a statistical assessment of priming effects in source waveforms in time windows of interest. We expected to replicate the sources for ERE/N250r and explore sources of following effects in LRE/N400 latency range.

5.5.1. Source localization

Both ERP and RERP-derived models consistently indicated source for P1 component peaking at 110 ms in Occipital Lobe. The same source for P1 component was also reported, by other studies for face-elicited ERPs (Mnatsakanian & Tarkka, 2004; Wong et al., 2009). The P1 marks the processing of any visual input into peri-striate areas of the cortex (Tobimatsu & Celesia, 2006) although there are also reports about a sensitivity of the P100 for faces (Dering, Martin, Moro, Pegna, & Thierry, 2011; Desjardins & Segalowitz, 2013) or eyes (Doi, Sawada, & Masataka, 2007).

For both ERP- and RERP-based models, peak for N170 was found in Fusiform Gyrus. Similar loci for N170 in ventral and lateral occipito-temporal cortices have been reported (Deffke et al., 2007; Mnatsakanian & Tarkka, 2004; Wong et al., 2009). The N170 has been
suggested to indicate the structural encoding of faces (Eimer, 2011) and interpretation of stimulus configurations as faces (Rossion, 2014).

The source for seed interval 280-300 ms was found in BA 30/ MTL with similar location coordinates for both ERP and RERP models. Similar MTL sources for face-elicited ERPs during this time period were also found by Mnatsakanian & Tarkka, (2004). Since equivalent dipoles act as center of mass capturing activity from neighboring areas (Scherg, 1990) the dipole localized at BA 30 in our study may reflect activity of several MTL structures. In line with this suggestion, Barbeau et al., (2008) also found strong activity to famous faces in intracranial recordings from MTL structures including posterior parahippocampal gyrus, perihinal cortex, medial temporal pole and hippocampal formation after 250 ms of stimulus onset.

For seed interval around 370-390 ms, we located a pair of sources in the Prefrontal Cortex (PFC). A distance of about 11.5 mm was found between the two source models, with RERP sources localized at BA9 and ERP source model at BA10. The relatively big difference in location of this source in two models may have occurred because of latency correction in RERP, which sharpens the peaks and topographies in late components, thereby changing the source configurations. BA9 and BA10 in lateral Prefrontal Cortex are functionally correlated (Fuster, 1988). Prefrontal Cortex is responsible for tasks requiring memory retrieval, executive control of behavior, attention and decision-making (Miller & Cohen, 2001; Posner, Sheese, Odludaş, & Tang, 2006).

A further pair of sources accounting for activity in the seed interval 480-500ms was localized in BA38 or Anterior Temporal Lobe (ATL). ATL has been found to have strong white matter connectivity with both the mid-Fusiform Gyrus and Inferior Occipital Gyrus (IOG) (Pyles et al., 2013). Rogers et al., (2004) considered ATL to be a semantic hub with connections to PFC
and other temporal visual processing areas. Collins & Olson, (2014) speculated the face network to be bilaterally extended from IOG to ATL, with facial representations at low level areas to become increasingly complex and abstract as perceptual information progresses along this network towards ATL, instantiating the final stage of face recognition. Lesions in ATL are related to problems with famous face recognition, face imagery, configural face processing, or more general, person-based semantic dementia (Busigny, Robaye, Dricot, & Rossion, 2009; Gainotti, 2007a; Williams, Savage, & Halmagyi, 2006).

Last source obtained only for RERP source model for activity around 700 ms was localized in Premotor Cortex or BA6. In conventional stimulus-locked ERPs, the R-component cluster is strongly smeared. This source therefore, can only be localized from response-locked ERPs or RERPs where the R component cluster has been synchronized at the most probable reaction time.

5.5.2. Localizing priming effects

After localizing the sources from different seed windows, source waveforms across whole epoch were obtained for each source; jackknifing allowed to test whether source waveforms significantly differed in strength between primed and unprimed conditions and whether priming effects differed for ERPs and RERPs. Table 5-2 and Figure 5-4 provide overviews of the results.
Several observations stand out. Firstly, priming effects did not start before 315 ms post stimulus. This is roughly in line with reports of priming effects in sensor space although a bit late, considering the reports of Herzmann & Sommer (2010), who found a significant effect in the ERE1 window between 260 and 315 ms for the same dataset (as mentioned in Chapter 4). This delay may be due to conservative nature of the correction procedure for jackknifing averages. Second, there was no priming effect in waveforms of the Occipital Lobe. This was to be expected because priming effects for early visual processes are usually weak or absent. Third, in all other sources there were priming effects in time windows after 315 ms. These priming effects strongly overlap in time, which is what one would expect from a system with several parallel streams. Fourth, although the above observations are true for both ERP and RERP-derived source waveforms, there seems to be a general difference between sources based on these two signal types.
Two-way ANOVA conducted for ERP- and RERP- derived source activity reflected priming effects in these late sources, which were frequently more pronounced in RERPs than ERPs (Table 5-2). The latency-corrected RERPs show enhanced amplitudes in the late components, extending and enhancing the priming effects in these late sources. However, RERP-derived sources seemed to be not only stronger and longer lasting than in ERPs, there also seemed to be a general trend towards more or stronger priming effects in the right hemisphere in RERPs. This is especially clear in Figure 5-4. Of course, a right-hemispheric dominance for face processing is what one would expect and is in accordance with similar finding from others (Schweinberger et al., 1994; Wang & Cottrell, 2012). In contrast, the effects based on the ERP analysis were more symmetrically distributed. Hence, it seems that the chances of finding late priming effects in (right-hemispheric) source space are higher with RERPs derived from the RIDE method compared to the conventional ERPs.

Interesting ending observation is that the priming effects in sources of the left hemisphere were mostly in the late time windows of 420-500 ms and 500-700 ms (Fig. 5-4(A), for both ERP and RERP source models), whereas the priming effects in the sources of the right hemisphere started mostly in the early time windows ranging from 315-350 ms and 350-420 ms (Fig. 5-4(B)). This indicates that processing of faces in the left hemisphere may require prior processing in the right hemisphere (Verosky & Turk-Browne, 2012).

In the following, we will discuss priming effects in different sources. In some of these cases, we can indeed relate to previous findings from ERP studies. In other cases, there are no comparable ERP data but findings from repetition suppression in fMRI studies do exist.
**Priming in the Fusiform Gyrus**

Priming effects in right FG were similar in both ERP and RERP models—lasting from 315 to 420 ms in ERP and from 315 to 500 ms in the RERP source model. In the left FG a priming effect was restricted to the 350 - 420 ms interval. The FG source showed no significant difference between ERP and RERP source models except for the late LRE2 interval where priming was present in the RERP- but not in ERP-derived source. This robust priming in the FG conforms to previous finding that the ERE/N250r is mainly present in the stimulus-locked S-component cluster (Ouyang et al., 2011).

Though lacking temporal resolution, repetition suppression in fMRI has been found in mid-Fusiform Gyrus for familiar faces (Eger, Schweinberger, Dolan, & Henson, 2005; Henson, Shallice, Gorno-Tempini, & Dolan, 2002), however, direct comparability would be localization studies of face priming effects in ERPs. Schweinberger et al., (2002) and Bindemann et al., (2008) located the N250r during a time window just before 300 ms in the Fusiform Gyrus. Although their coordinates for the N250r seem to be more lateral and somewhat more anterior than the coordinates of the Fusiform Gyrus source in the present study, one should keep in mind two aspects that impede a precise comparison of the findings. Whereas the present dipole solutions were based on grand average ERPs and RERPs, Schweinberger et al., (2002) and Bindemann et al., (2008) had localized the N250r/ERE effects in difference waves between primed and unprimed conditions. Although difference waves may seem to provide purest priming effect, they may be subject to additional noise relative to unsubtracted ERPs and can be ambiguous because it is hard to disentangle contributions of amplitude and latency differences. Second, in the present data a priming effect in the time window of the ERE/N250r was seen not only in the FG but also in the ATL (see next section). Hence, any differences in position within
the FG might be due to variations in the number of dipoles in the particular solution as equivalent dipoles can capture activity from neighboring areas. Nevertheless, we may conclude that there is (partial) convergence in localizing an early priming effect in the Fusiform Gyrus.

**Priming in the Anterior Temporal Lobe**

Figure 5-4 suggests that the pattern of priming effect in the right ATL is consistent in both ERP and RERP source models in time windows ERE2 and LRE1. The ATL is considered to process representations of a person’s identity, name, and biographical information (Haxby, Hoffman, & Gobbini, 2002). Kriegeskorte, Formisano, Sorger, & Goebel, (2007) suggested that the ATL identifies faces that are detected by Fusiform Face area (FFA) and sends feedback to FFA. This is in line with the present priming effects starting more or less simultaneously in the right FG and right ATL during the time window of ERE2, suggesting parallel processing or close feedback loops in the brain during face recognition. Priming effects (ERE2 to LRE1) in the right ATL obtained from both ERP and RERP source models also signify their involvement in retrieving person-specific information and the feeling of familiarity (Gainotti, 2006) with the presented faces.

The pattern of priming effect in the left ATL was also similar in both ERP and RERP source model but the effect was late in time. The priming effect from the ERP source model were in the time periods of LRE1 and LRE2, but for the RERP source model it was shifted towards the time periods of LRE2 to late 500-700 ms window. These late left-ATL priming effects (LRE2) might be due to its role in the retrieval of name-specific information (Gainotti, 2006).
Priming in the Mediotemporal lobe

From Figure 5-4, a priming effect in the MTL can be seen to be extended in RERP source model for two time windows (LRE1 for right and LRE2 for left). This extension of priming effect in the RERP MTL source was seen for time windows which are earlier than for the ERP source model. This relatively late priming effect may signify the role that MTL likely plays in semantic retrieval. This is in agreement with the fMRI studies by Elfgren et al., (2006) and Zhen et al., (2013), who suggested the strong role of the human MTL structures in semantics and in recognition of famous faces. Priming effect in this source at BA 30 is in accordance with fMRI study which also found decreased activation in the Parahippocampal place area when familiar faces are repeated (Mur, Ruff, Bodurka, Bandettini, & Kriegeskorte, 2010).

Priming in the Prefrontal Cortex

Similarly, enhanced and extended priming effects were also seen in PFC from RERP source model as shown in Figure5-4. The right PFC showed a strong priming effect in the LRE1, the LRE2, and in the late window of 500-700 ms (RERP model, see Fig. 7B). Priming effects in LRE1 and in late window of 500-700 ms were absent in ERP source model. The priming effect at LRE1 possibly indicates a role of right PFC in memory retrieval starting from 350 ms onward. PFC plays an important role in visual working memory (Sarnthein, Petsche, Rappelsberger, Shaw, & Von Stein, 1998), when there is competition between alternative action representations (D’Esposito & Postle, 2015). However, visual working memory for faces seems to relate more to late rather than early processing stages (Meinhardt-Injac, Persike, & Berti, 2013). Moreover, interaction between the Inferotemporal regions, MTL, and PFC was found to be crucial for various working memory tasks (Axmacher, Schmitz, Wagner, Elger, & Fell, 2008). The priming effect in the late window may also indicate role of right PFC incognitive
control employed in the service of responding in familiarity decision task (Goldman-Rakic, 1987; Levy & Wagner, 2011). Robust repetition suppression for famous faces has been found in the Prefrontal Cortex (Eger et al., 2005; Sugiura, Mano, Sasaki, & Sadato, 2011).

**Priming in the Premotor cortex**

Though comparative analysis with the ERP model could not be done for the source in PMC, the RERP source model indicated that the right Premotor Cortex contributed to priming during the LRE1 window and the left PMC contributed during the late window of 500-700 ms. The early effect in right PMC is consistent with the fact that the Premotor Cortex contains visually responsive cells (Boussaoud, Barth, & Wise, 1993; Fogassi et al., 1992) and the late priming effect in left PMC indicates its role in motor planning and has been suggested to be specialized for the visual guidance of forelimb movements (Kurata, 1989). Cisek & Kalaska, (2010) and Rizzolatti, Fogassi, & Gallese, (2002) found Premotor Cortex to have both motor and cognitive abilities.

**5.6. Summary**

In this Chapter, we discussed implementation of source localization on ERP data and on RERP data of face priming obtained from the study of Herzmann and Sommer, 2010 and Ouyang et al., 2011, respectively. Separate source models for ERP and RERP data were obtained on the grand average of 21 subjects across the two conditions (PF and UF). With ERP source model, 5 sources were obtained at Occipital Lobe (OL), Fusiform Gyrus (FG), medio temporal Lobe (MTL), Prefrontal Cortex (PFC) and Anterior Temporal Lobe (ATL). RERP source model allowed localization of one extra source at Premotor Cortex (PMC) along with OL, FG, MTL, PFC and ATL.
The SWFs were obtained from the jackknifing procedure applied to the source data (ERP and RERP) on which respective source models were imposed by force. The variation of RV across the 21 jackknife averages of ERP and RERP reflected acceptable source localization. Priming effects in the source waveformss (SWFs) of both ERP and RERP source models were statistically tested with two way ANOVA with repeated measures on priming factors (primed, unprimed) and signal type (ERP, RERP); and with post-hoc two tailed t-test on the six time windows namely Early window, ERE1, ERE2, LRE1, LRE2 and Late window.

The pattern of priming provided lot of information about face recognition in the brain. In general, the present findings support the notion that priming effects for famous faces are heterogeneous, starting with the activation of face representations stored in memory. In sensor space, this is reflected in the N250r or ERE. In the source space, this effect can be localized in the FG. However, in the present data it was found that, at the same time there is also activation of semantic knowledge about person as reflected in the priming effect in the right ATL. While the FG activation appears to be short-lasting, the ATL activation continues, with MTL and the PFC getting more involved chronologically. From the hemispheric point of view about processing of faces in the brain, the pattern of priming provided important understanding that faces are processed early in predominant manner in the right hemisphere than in the left.

Overall, the present analysis has shown the advantages of RERPs over ERPs in modeling of the brain sources. This advantage– as to be expected – are most pronounced for late rather than early effects. The sources obtained from the late components namely MTL, PFC, and ATL show pronounced priming effects in RERPs compared to ERP source model. Numerous studies of face recognition assert face processing to be predominant in the right hemisphere and that too was confirmed in our study with RERP sources model only. Additionally, priming
effects in the source space are temporally resolved in comparison to repetition suppression or repetition enhancement phenomenon observed through fMRI, and therefore, face network created from them could reveal the temporal dynamics of face processing in the brain.

In the subsequent Chapter, since our study is primarily on face recognition and priming, advantages of RERP derived sources over ERP would be the driving force for selecting RERP sources to underline the causal architecture and to facilitate better insight of face processing network in the brain.
Chapter 6

Implementation, Result and Discussion

Part II: DCM Effective Network for Face Recognition and Priming.

In the previous chapter, we have shown that RERPs are advantageous than conventional ERPs for the sources obtained from the late components (>250 ms). Therefore, in this chapter, we will only use RERPs to obtain causal network architecture of face recognition and priming on each hemisphere using dynamic causal model (DCM). Results depicting model fit and network properties will be presented to provide an understanding of the priming on model architecture preference. The brain behavior relationship will be tested by associating each model of left and right hemisphere to the reaction time (RT) performance of individual subjects preferring the given model. In the last part, we will discuss the role of effective interconnections between sources in each hemisphere and their overall contribution to face recognition and priming.

6.1. Implementation of DCM

In this section, we will emphasize implementation of outlined DCM models on the RERPs. Though the models could also be outlined on ERPs, however RERPs were found to be advantageous over ERPs in the source space (Chapter 5). Improved surface topographies of late components through RIDE were shown to amplify source dynamics, especially for late components (> 250ms). Source activity obtained from RERPs was found to be superior in capturing priming effects in the source space compared to that obtained from ERPs, especially for source activity obtained from late components like MTL, PFC, and ATL. This improvement in late component sources is important from the perspectives of DCM. It has been suggested that
late ERP components are augmented by backward connections, and reflect a re-entry of dynamics into hierarchically lower processing areas (David et al., 2005).

The first step taken before implementing the DCM models was to project the sources obtained in Chapter 5 on individual subject data. In Chapter 5, we elaborated source location and priming effects in sources on the jackknife averages. Jackknife average, though provides an overview of source localization accuracy for the group; however, they do not find a suitable application in DCM, which estimates the goodness of fit of each model on individual subject data. In that perspective, we will subdivide this section into few parts concerning source localization, SWF analysis, DCM model construction, and DCM connection parameters.

6.1.1. Source localization

The strategy of obtaining sources for RERPs is same as discussed in Chapter 5. However, here sources are obtained only for the period from 0-500 ms, which are localized bilaterally in a temporal order at Occipital Lobe (OL), Fusiform Gyrus (FG), Mediotemporal Lobe (MTL), and Anterior Temporal Lobe (ATL). The precise coordinates of sources and seed interval in which they were sequentially obtained are mentioned in Table 5-1 in Chapter 5. In the current study, the residual variance (RV) of the RERP master source model with five bilateral pair of sources is found to be 3.82%.

6.1.2. Source waveform (SWF) analysis

Locations and orientations of master source model were fitted per force to individual-participant RERP data of each condition (PF and UF) to obtain source waveforms (SWFs). Mean ± standard deviation of RV for fitted RERP master source model on 21 subjects was 5.47 ± 2.36 % and 6.68 ± 2.73 % for primed (PF) and unprimed (UF) conditions, respectively.
Statistical testing of repetition priming effects in SWFs of all sources was done with two tailed $t$ test. The statistical measure were applied to SWFs amplitudes in 6 time windows: 80-170, 170-260 (Early), 260-315 (ERE1), 315-350 (ERE2), 350-420 (LRE1) and, 420-500 (LRE2) ms. Details on importance of the 5 time windows from 170 ms to 500 ms have been discussed in previous chapters. In the present study, an extra window (80-170 ms) was added for analysing repetition effect after 80 ms due to consideration in DCM in which Gaussian input enters the brain system after 60 ms of stimulus onset (David et al., 2006), an approximations based on electrode recording studies in visual and inferotemporal cortex (Hirsch et al., 2002).

6.1.3. Priming effects in the SWFs

As mentioned above, SWFs in the present study (obtained from individual participant) were divided into six time windows. Priming effects in each window were analysed for significance ($p < .05$) using two tailed $t$-tests ($t$ values> 2) for each source.

Priming effects in the OL source of both hemispheres were absent for all time windows. In left FG, priming effects started from 315 ms and continued until 420 ms. Similarly, in right FG, they started at 260 ms and continued until 500 ms. In the left MTL, priming effects started at 350 ms and continued until 500 ms. Similarly, in the right MTL, they were present between 315 to 500 ms. Priming effects in left PFC started from 315 ms and continued until 420 ms. Similarly, priming effects in right PFC started from 315 ms and continued until 500 ms. In the left ATL, priming effects started at 260 ms and continued until 420 ms. Similarly, priming effects in right ATL started from 260 ms and continued until 500 ms.

Similar to analysis in Chapter 5, the current analysis also found no priming effects in OL source. DCM models are outlined with backward connections based on this observation.
6.1.4. DCM- model construction

Priming of famous faces lead to faster reaction time (RT). Behavioural results in terms of RT for present data also confirm the same. A quick review of RT facilitation by priming of famous faces supports the RT facilitation of priming. The RT was significantly longer, $t(20) = 7.2; p< .001$, for UF condition ($M = 611$ ms; $SD = 57.2$) compared to PF condition ($M = 472.9$ ms; $SD = 63.3$).

In order to understand priming effects in performance (RT) at the level of brain mechanisms, it is important to understand what priming does to neural face recognition network. In this aspect, using source locations and source waveforms obtained (in previous sections), different hypothesis based generative models are delineated, in consistence with anatomy and physiology of the brain (Friston, 2005).

The anatomical structure of two outlined hypothesis driven DCM models is mainly based on white matter connections (Schmahmann et al., 2007). For most of the areas found in our study, white matter connections are present across them. This was also reported in works from face recognition based Diffusion tensor imaging (DTI) studies by Pyles et al., (2013), and Gschwind et al., (2011). The schematics of two outlined DCM models, namely Forward (F) and Forward-Backward (FB) for each hemisphere, with exogenous visual input, considered to be entering the brain system through Occipital Lobe (Chen, Henson, Stephan, Kilner, & Friston, 2009) have been shown in Figure 6-1. Forward connections follow temporal ordering of sources derived from early to late segments in RERPs, that is, from OL to ATL. This temporal sequencing of information flow is an edge that ERP source localization has over fMRI.

Outline of DCM models was based on most probable structural connectivity underlying face recognition areas (Stephan et al., 2010). In this respect, four white fiber tracts
seem to connect face recognition systems. These are depicted in Fig. 2-1 (Chapter 2) and are illustrated as follows: (1) *Inferior Longitudinal Fasciculus* connecting OL, FG, and ATL structures (Schmahmann et al., 2007), which was also verified for face recognition in DTI studies by Pyles et al., (2013) and Gschwind et al., (2011). Forward connections in F model from OL to MTL, FG, and ATL have therefore been outlined. (2) *Inferior Fronto-Occipital Fasciculus* connecting FG, ATL, and PFC (Catani, Jones, Donato, & ffytche, 2003; Schmahmann et al., 2007), motivating forward connections from FG to ATL and PFC in Fig. 6-1. In addition, forward connection from FG to ATL has been found to be important for face identification (Kriegeskorte, Formisano, Sorger, & Goebel, 2007). Synchronized activity between FG and PFC during famous face recognition suggests direct connections between these areas (Barbeau et al., 2008). (3) *Superior Longitudinal Fasciculus* connecting MTL structures with PFC (ffytche & Catani, 2005; Martino et al., 2011; Schmahmann et al., 2007) directing forward connection from MTL to PFC into outline of the proposed models. Previous studies found interactions between IT regions (FG), MTL, and PFC to be crucial for various visual working memory tasks (Axmacher et al., 2008). (4) *Uncinate Fasciculus*, mainly connecting PFC and ATL, in line with flow of information based on temporal ordering of source localization. The Uncinate Fasciculus further extends through middle longitudinal fasciculus to connect MTL and ATL structures in the brain (Catani, Howard, Pajevic, & Jones, 2002; Papagno et al., 2014; Schmahmann et al., 2007), providing sufficient clues for forward connections from MTL to ATL. Removal of Uncinate Fasciculus in patients has been reported to impair naming and recognition of famous faces (Papagno et al., 2010; Yang, Susilo, & Duchaine, 2014).

Regarding directions of forward connections, we considered ATL localized as last sources in 0-500 ms as apex of the model and forward flow of information moves from
earlier areas to ATL acting as higher processing area (Fig. 6-1 (A)). Rogers et al., (2004) also considered ATL as the semantic hub with connections to PFC and other visual processing areas. Binney, Parker, & Ralph, (2012) claimed that anatomical organization of ATL is designed such that it serves as a hub for information convergence from different input modalities emerging from frontal, parietal, temporal, and limbic regions. Collins & Olson,(2014) speculated face network to be bilaterally extended from IOG (Inferior Occipital Gyrus, part of OL) to ATL, with facial representations at low level areas to become increasingly complex and abstract as perceptual information progresses along this network towards ATL, instantiating the final stages of face recognition. The sequential localization of sources from OL to ATL in our data is consistent with this suggestion.

Bi-directionality of white fiber connections in same hemisphere is plausible for serving forward projections of sensory information to higher cognitive areas and top down modulation from higher areas to early perceptual areas (Yvert, Perrone-Bertolotti, Baciu, & David, 2012). Therefore, in FB model (Fig.6-1(B)); backward connections have been involved across FG, MTL, PFC, and ATL. The logic behind backward connections was based on predictive coding hypothesis of repetition suppression and priming.

Predictive processing models act as a systematic bridge between perception, cognition and action by bringing them together within a common framework. Predictive coding assumes that each source in brain is capable of predicting next state in an economic way by minimizing its prediction errors (Clark, 2003). Prediction error is the divergence of an observed state from expected state (Schultz & Dickinson, 2000). Minimizing prediction error is the driving force behind quick recognition, inference and action-selection. Predictive coding considers forward flow of sensory information as conveying of prediction error, and backward flow of
information as conveying the prediction (for review, Rauss & Pourtois, 2013). When faces are repeatedly presented, predictability is increased and prediction error gets reduced (Clark, 2013). This implies top-down modulation from higher level on lower level areas to actively suppress predicted category responses (Friston, 2005). In this regard, backward connections being modulatory, generate predictions of lower level responses, fit appropriately to the causal structure of predictive coding in the Bayesian framework of DCM (Friston, 2005; Bastos et al., 2012). Ewbank et al., (2011), found backward top-down modulations to play a critical role in repetition suppression, when identical images are repeated. PFC, an area found activated for stimulus repetition tasks (for review Horner, 2012) has backward connections to lower level areas when visual memory has an influence on visual responses (Furl, 2015). In view of justifications and findings of above mentioned studies, backward connections are outlined across those areas where priming effects have been found in current study, that is, ATL, PFC, MTL and FG. Absence of priming effect in OL suggests no backward connection to this area. Backward connections are therefore directed from a higher to the areas found lower to it (according to temporal ordering of sources based on ERP components and time segments) with the exception for OL source as shown by dashed lines in Fig.6-1(B).
6.1.5. DCM – connection parameters

Two DCM models were fitted on source activity of each hemisphere for each condition (PF or UF) for 21 participants to obtain the Bayesian model average (BMA). BMA estimates the modulatory effects of experimental input over model parameters (Stephan et al., 2010). Comparison of parameter estimates between primed and unprimed conditions is based on the model chosen at individual and group level, and reflects the coupling changes across two conditions. The most preferred model contributes largely to single posterior density for entire group, a step that allows Bayesian inference at group level. The Bayesian inference can also identify significant changes in connectivity between conditions. In this respect, posterior means (mEps) and standard deviation SDs (sEps) were calculated for each connection for both preferred and not-preferred models of two conditions. A two-tailed t-test marks significantly different connections ($p < .05$) in BMA for UF relative to PF condition. This step leads to indications of
physiological processes that could change the coupling in models across primed and unprimed conditions (Stephan, 2004).

6.2. Results

In this section, we will initially discuss preferred and not-preferred models for each condition (PF and UF) in each hemisphere in terms of model exceedance probability. Subsequently reaction time performance of priming will be associated to preferred and not-preferred model in each hemisphere to understand the underpinnings of brain behaviour relationship. Finally, connections important for face recognition and priming in each hemisphere will be analysed and highlighted.

6.2.1. Preferred model

Bayesian model selection (BMS) was applied to determine the most plausible model (Stephan et al., 2009); wherein model exceedance probability shows that a particular model is more likely than other model considered. For this, SWFs of each of 21 participants were inverted on two outlined DCM models (F and FB) for each hemisphere across both conditions (PF and UF). BMS with random effects was chosen both at individual and group levels (Stephan et al., 2010), and model exceedance probability was observed at both individual and group levels. The preferred model with higher model exceedance probability compared to other model shows better balance between model accuracy (i.e. goodness of fit) and model complexity. The model exceedance probability at group level is shown in Figure 6-2. The FB model was better fitting (preferred) model for PF condition in both right and left hemispheres with 62% of participants preferring this model (exceedance probability> .6). Similarly, for UF condition, same percentage of participants preferred FB model for right hemisphere (exceedance probability> .6). However,
in left hemisphere of UF condition, F model was preferred model with 67% of participants opting for this model over FB model (exceedance probability> .6).

### Figure 6-2: Graphs showing model exceedance probabilities of F and FB models fitted within each hemisphere (Hem) for two priming conditions (PF and UF).

#### 6.2.2. Brain-Behaviour relationship

An analysis of association between RT and model preference in each hemisphere for each condition was performed to see brain-behaviour relationship. Figure 6-3(A) and 3(B) depicts model selection (red square for F model and blue circle for FB model) and mean as well as and standard deviation (SD) of RT (marked on y axis) of participants preferring the model for each condition (marked on x axis) for left and right hemisphere, respectively. For left hemisphere (Fig. 6-3(A)), participants that preferred the FB model showed faster RTs compared to participants preferring F model, in spite of both models showing similar priming effects in RT. In right
hemisphere (Fig. 6-3(B)), the RTs of participants preferring F or FB model overlapped each other for both PF and UF condition, again, both models showed similar priming effects in RT. This indicates that in right hemisphere for both conditions, participants irrespective of their overall RT could prefer any of the F or FB models, i.e. model type preference was related neither to overall RT nor to the priming effect.

![Figure 6-3](image_url)

**Figure 6-3:** Illustrations of (A) relation of individual mean reaction time with the type of model preferred (red square for F model and blue circle for FB model) in left hemisphere for PF and UF conditions. (B) same as A for right hemisphere.

To affirm that FB model in left hemisphere is the key contributing factor of fast RTs but not a significant contributor to priming across the group of participants, irrespective of model choice in right hemisphere, we presented graphically the number of participants preferring F or FB models in each hemisphere and their RT (mean ± SD) in Figure 6-4. Here, y coordinate reflects mean RT (±SD), and x coordinate reflects four categories of model choice in the two
hemispheres. The four categories are (1) LF-RF: Preference for F model in both left and right hemisphere; (2) LF-RFB: Preference for F model in left but FB model in right hemisphere; (3) RF-LFB: Preference for F model in right but FB model in left hemisphere, and (4) LFB-RFB: Preference for FB model in both hemispheres. The number of participants falling in each category of model choice is provided as well. The UF and PF conditions are shown in blue and red, respectively. Shorter RTs were found in both priming conditions for category LFB-RF and LFB-RFB. The results confirm that participants preferring FB model in left hemisphere, irrespective of model choice in right hemisphere (F or FB), had faster RTs across both PF and UF conditions. On the other hand, we note that for groups of participants preferring either F or FB model in left hemisphere, there are similar performance effects due to priming: the RT is about 110 ms shorter in PF than in UF condition (Figs. 6-3 and 6-4).

**Figure 6-4:** Mean reaction time (±SD) of number of participants with specific preferred-model combinations across hemispheres (L, R = left and right hemisphere; F, FB = forward only vs. forward-backward model) for each condition (PF or UF). The number of participants for a given category is indicated next to error bar.
6.2.3. DCM - connection parameters

In the final steps, we assessed the strengths of connections within F and FB network models for left and right hemispheres, as well as primed and unprimed conditions. Though DCM studies typically focus only on preferred models at group level, analysis of not-preferred models, for example, F model in PF condition in both hemispheres; or FB in UF in left hemisphere; for this work can be justified with three reasons. (1) The difference between the model exceedance probabilities of preferred and not-preferred models in each hemisphere is not remarkably different. (2) There are about 1/3 participants that opt for not-preferred model in each condition (Fig. 6-2). (3) There are differences in performance (RT) for participants opting not-preferred model in left hemisphere; though in both hemispheres, models (F and FB), and conditions (PF and UF) respectively, displayed priming effects in RT (Fig. 6-3 (A) and (B)). The modulation of connectivity was checked for significance by means of two-tailed t-tests performed on the posterior mean data of all 21 participants (including both preferred and not-preferred models).

Intra-conditional effects were tested for connections with one node in common to identify the dominant link when compared to other links of this node. For the forward connections, four nodes were considered as sending nodes and two-tailed t-tests were performed pairwise for every possible combination of connections in that subgroup. A connection from a subgroup was considered to be dominant when it won over \( p < .05 \) all the other connections in the subgroup. (1) OL subgroup: Outgoing connections from OL node (i.e. OL-FG, OL-MTL and OL-ATL) with three possible pairwise combinations of connections on which t-test were done. (2) FG subgroup: Outgoing connection from FG node (FG-MTL, FG-PFC and FG-ATL) with three similar possible combinations. (3) MTL subgroup: Outgoing from MTL node (MTL-ATL,
MTL-PFC) with only 1 possible comparison. (4) ATL subgroup: Incoming connection to ATL (OL-ATL, FG-ATL, MTL-ATL and PFC-ATL) with 6 possible pairwise combinations. In order to assess single PFC→ATL connection, which otherwise could not be assessed statistically from sending node PFC, incoming connections of ATL were considered for comparison with other forward connections.

Similarly, for the backward connections, three common nodes were considered and the subgroups are (1) FG subgroup: Incoming connections to FG (MTL-FG, PFC-FG, ATL-FG) with 3 possible combinations; (2) MTL subgroup: Incoming connections to MTL (ATL-MTL and PFC-MTL) with 1 possible comparison; and (3) ATL subgroup: Outgoing connections from ATL (ATL-FG, ATL-MTL, and ATL-PFC) with 3 possible combinations. In order to assess single ATL→PFC connection, which otherwise could not be assessed statistically from receiving node PFC, outgoing connections of ATL were considered for comparison with other backward connections, analogous to the case of forward connections, as narrated above.

For condition in which value of posterior mean was found to be significantly higher than others, such connections significant ($p < .05$) in subgroup are indicated with a ¥ symbol in Tables 6-1 and 6-2. In general, a connection that was significantly dominant in one subgroup was also found to be dominant when considered in another subgroup. None of the node showed evidence of parallel processing, as every node with incoming (outgoing) connections had only one prominently dominant connection for both F and FB models.

In order to assess connections that are influenced by *inter-conditional effects*, i.e. priming, significance *across priming conditions* was tested for every connection in each hemisphere. Thus, priming effects on connection strength were tested for each link of a given model in a given hemisphere. For example, F model of UF condition in left hemisphere is
compared with the F model of PF condition (in left hemisphere only), even though the latter is a
not-preferred model at group level. First we tested FB models in each condition (priming) and
hemisphere (Table 6-1), and then, for priming effects in F models (Table 6-2). For considering
increase in connection strength, connections that were found to be significantly ($p < .05$)
stronger in a given priming condition are marked with a * symbol. Connections that were
significantly higher in one priming condition than in other, were also found to be significantly
dominant (relative to the other connections of a source) within that condition (intra-conditional).
These were marked with ¥* symbols. Figure 6-5 graphically depicts the results presented in
Tables 6-1 and 6-2 with FB models (A, B, C, D) and F models (E, F, G, H) shown for each
hemisphere and priming condition.
Table 6-1: Forward-Backward (FB models): Bayesian model average on posterior means and standard deviation (mean ± SD) of input and modulation estimates of all connections across PF and UF conditions, and within each condition for source waveforms of the entire 21 participants.

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¥ = dominant connection at a given node; * = connections that are stronger in a given priming condition than in other condition, ¥* = connections that both dominant at a given node and stronger in a priming condition than in other condition.
Table 6-2: Forward (F) models: Bayesian model average on posterior means and standard deviation (mean ± SD) of input and modulation estimates of all connections across PF and UF conditions, and within each condition for source waveforms of the entire 21 participants.

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<td>OL-MTL</td>
<td>0.08± 0.02</td>
<td>0.06 ± 0.01</td>
<td>0.04± 0.03</td>
<td>0.04± 0.01</td>
</tr>
<tr>
<td>OL-ATL</td>
<td>0.06± 0.01</td>
<td>0.04 ± 0.01</td>
<td>0.04± 0.03</td>
<td>0.05± 0.02</td>
</tr>
<tr>
<td>FG-MTL</td>
<td>0.08 ± 0.02*</td>
<td>0.06± 0.03</td>
<td>0.17± 0.02*</td>
<td>0.20± 0.02*</td>
</tr>
<tr>
<td>FG-PFC</td>
<td>0.03± 0.01</td>
<td>0.11 ± 0.03**</td>
<td>0.04± 0.02</td>
<td>0.11 ± 0.04*</td>
</tr>
<tr>
<td>FG-ATL</td>
<td>-0.04 ± 0.02</td>
<td>-0.02 ± 0.02</td>
<td>0.01± 0.01</td>
<td>0.00± 0.03</td>
</tr>
<tr>
<td>MTL-PFC</td>
<td>0.03± 0.03</td>
<td>0.02 ± 0.03</td>
<td>0.15± 0.02*</td>
<td>0.16 ± 0.04*</td>
</tr>
<tr>
<td>MTL-ATL</td>
<td>-0.06± 0.01</td>
<td>-0.04 ± 0.02</td>
<td>-0.00± 0.01</td>
<td>-0.01± 0.02</td>
</tr>
<tr>
<td>PFC-ATL</td>
<td>0.14± 0.01*</td>
<td>0.12 ± 0.01*</td>
<td>0.17± 0.03*</td>
<td>0.20± 0.02*</td>
</tr>
<tr>
<td>Extrinsic Input to OL</td>
<td>-0.04 ± 0.13</td>
<td>-0.04 ± 0.13</td>
<td>0.03± 0.00</td>
<td>0.03± 0.00</td>
</tr>
</tbody>
</table>

¥ = dominant connection at a given node; * = connections that are stronger in a given priming condition than in the other condition, ¥* = connections that both dominant at a given node and stronger in a priming condition than in the other condition.
6.3. Discussion

The overall objective of this study was to relate behavioural performance (RT) in a face familiarity task with repetition priming to underlying effective network architecture using time-resolved latency-corrected RERPs to understand the brain behaviour relationship. Towards this endeavour, we applied DCM modelling in each hemisphere on the source waveforms obtained from latency corrected RERPs. The motivation to apply DCM on SWFs was based on their independence of effects of volume conduction and choice of reference electrode (Michel & Murray, 2012). In Chapter 5, for the same dataset, RERP source activity was found to be better than ERP source activity by enhancing and extending the localization of priming effects in source space, especially for sources (MTL, PFC and ATL) obtained for late RERP components.
Source localization of RERPs also allowed us to obtain the direction of information flow from the temporal order of sources, enabling us to distinguish forward and backward connections. Since, late ERP components influence the backward connectivity and mark re-entry of dynamics from higher processing areas to lower processing areas (David et al., 2005), RERP-derived sources might suit better for purpose of DCM modelling, especially when models include backward connections.

Employing RERP-based, chronometrically ordered sources, two DCM models, Forward (F) and Forward-Backward (FB) (Fig. 6-1) were defined, based on known underlying anatomical projections and predictive coding hypothesis, following the priming effects in sources mentioned above. The models were then fitted to RERP source activities of each hemisphere and evaluated for their goodness of fit at individual and group levels as shown in Fig. 6-2. Using these models, we specifically addressed following questions:

1. Is priming related to a general preference for FB models?
2. Can priming effects be related to changes in strength of specific connections?
3. Are these changes specific to the cerebral hemispheres?

Before we turn to the results related to these questions, we will discuss relationship of our results to previous views about face processing networks.

6.3.1. The face processing network

Forward connections: - In both F and FB models (Fig. 6-5A-H), forward connections from OL to FG are strong (high posterior mean) for both PF and UF conditions and for both hemispheres; but they are stronger in the right hemisphere (posterior mean = .24 and .18 for FB and F models, respectively) than in the left (posterior mean = .17 and .15 for FB and F models, respectively; see Tables 6-1 and 6-2). This is consistent with previous DTI studies for face
recognition where right hemispheric fibre connections of the face processing network were stronger and denser than in the left (Geschwind et al., 2011; Pyles et al., 2013; Tavor et al., 2014). Similarly, with posterior means ranging between 0.10 to 0.25, forward connection from PFC to ATL was also found dominant for two conditions in both left and right hemispheres, and in both F and FB models. Anatomically, this connection is mainly through Uncinate Fasciculus (Olson, McCoy, Klobusicky, & Ross, 2013). Functionally, this connection serves an important role for face familiarity information, with right PFC providing input to right ATL (Simmons, Reddish, Bellgowan, & Martin, 2009). The right ATL is said to generate face familiarity feeling and right frontal cortex has the role of monitoring it (Gainotti, 2007a). Similarly, the connection in the left is responsible for recognition and retrieval of famous names (Collins & Olson, 2014; Olson et al., 2007). This connection therefore plays a major role in face recognition when familiar identities are involved.

**Backward connections:** - In the right hemisphere, significant backward connectivity was found between ATL and FG for both priming conditions in the preferred FB models (Fig.6-5 B and D). This supports the fMRI findings of Kriegeskorte et al., (2007), who suggested that ATL identifies face that are detected by FG, which in turn sends feedback to FG for proper identification of the face. In left hemisphere, there was also significant backward connectivity from ATL to PFC shown for PF condition (Fig. 6-5A). This connection was also dominant in UF condition for participants who opted for (not-preferred) FB model (Fig. 5C). Since in both PF and UF conditions, participants preferring FB model in left hemisphere were faster in overall RT (Fig 6-3A), this backward connection from ATL to PFC appears to be a main contributor to the global facilitation of response speed.
6.3.2. Is priming related to a general preference for FB models?

In line with a common assumption that priming might foster preference for backward connections, we tested whether preferred model at group level might give FB an edge over F model in the priming condition. At group level, we found that FB model was preferred in right hemisphere for both PF and UF conditions, independent of priming. However, in left hemisphere, FB model was preferred for PF condition, whereas for UF condition the F model was preferred. This difference in preference of FB model in PF condition and F model in UF condition for left hemisphere indicates that priming has a tendency to activate backward connections and top down processing, which appears to be consistent with works elsewhere (Ewbank et al., 2011; Horner, 2012). However, model preference for FB was about 62%, that is, there were at least 1/3 of participants who preferred F model in primed condition. Conversely, there were about 1/3 of participants who preferred FB model in unprimed condition. Thus, in left hemisphere, relationship between priming and backward connections appears to be complex.

A further investigation was made at individual level within each condition (PF or UF), in order to assess if models with backward connections make a difference in performance (RT). We associated RT of participants to the model they preferred individually in each hemisphere (left and right), and in each condition (PF and UF) (Figs. 6-3A and B). We found that participants preferring FB model in left hemisphere reflected an overall fastness in in RTs, independent of PF and UF conditions (Fig. 6-3(A)), but such a linkage was absent in right hemisphere (Fig. 6-3B). It important to note that priming effect in RTs was of similar magnitude and independent of F or FB model preference in either hemisphere. Hence, at individual level a preference for FB model cannot be a determining factor or a correlate of priming effect. However, backward connections in left hemisphere appears to be in relation with global and sizeable speed-up of
overall RT. Bias towards left hemisphere to facilitate faster reaction time through preference of FB model, irrespective of model preference in right hemisphere is illustrated in Figure 6-4. This demonstrates distinct differences in RT between primed and unprimed conditions, irrespective of any preference of model in two hemispheres. Such unexpected finding will be discussed in section 6.3.4.

To sum up, at group level, there seems to be a somewhat better fit for FB models, however, it is difficult to relate this difference in fit to the size of priming effect. Hence, underpinnings of priming effects, irrespective of relative model fit in FB and F models would be dealt independently.

6.3.3. Connection strength modulations responsible for priming effects?

Rather than considering only preferred models, as common in DCM, we analysed connection strengths in all models, whether preferred at group level or not. Thus, for inter-conditional (priming) effects we compared the conditions within each model type (e.g. F model) and hemisphere, irrespective of whether that model was preferred or not at group level. Inspection Figure 6-5, which is an illustration of results presented in Tables 6-1 and 6-2, furnishes following crucial observations. (1) In both left and right hemispheres, irrespective of F or FB models being preferred, priming strengthens forward connections from FG to PFC. (2) In FB models, priming strengthens backward connections from PFC to FG in both hemispheres. (3) The pathway from FG via MTL to PFC, modulated by priming is hemisphere-specific. In right hemisphere, this pathway is stronger in UF than PF (Fig. 6-5D), and in left hemisphere, it is weaker in UF than PF (Fig. 6-5A). We will discuss these observations in turn in the following parts.
**Forward and backward connections between FG and PFC:** Regardless of model preference, and of hemisphere, priming strengthened forward connections between FG and PFC, and also strengthened backward connections between these structures in FB models. The modulation in connection between FG and PFC when famous faces are perceived was also found by Ishai, (2008). When famous faces are perceived, FG is responsible for face encoding (for review, Ghuman et al., 2014) and PFC is responsible for memory and decision-making (for review, refer to Euston, Gruber, & McNaughton, 2012). The increase in strength of posterior means for both forward and backward connections in PF compared to UF reflects importance of this connection in priming. This is in agreement with the IAC model (Burton, Bruce, & Hancock, 1999; Burton, Bruce, & Johnston, 1990), which emphasises on strengthening of the link between FRU and PINs due to priming. Hence, if one accepts localization of FRUs in FG as suggested by Eger et al., (2005), present findings may indicate that activation of FRUs (in FG) by perception of a known face is transmitted better or faster to the decision making system in PFC during the priming process, when FG is continued to stay activated. However, strengthening of information transmission from FG to PFC is evidently not the only effect of priming, as shown by hemisphere-specific effects in the long route from FG via MTL to PFC, which would be discussed next.

**Hemisphere-specific modulation of connections from FG over MTL to PFC:** In left hemisphere, for FB model, two forward connections were significantly stronger in primed than in unprimed condition, namely the connection from FG to MTL and from MTL to PFC (Fig. 6-5A). Both connections are also dominant (marked with a star in Fig. 6-5A). These connections provide an understanding of the way left hemisphere processes facial information. When famous faces are perceived, left FG, being specialized for recognition of facial features (Rossion et al.,
possibly activates biographical and semantic information in left MTL (Kennepohl et al., 2007) and left PFC (Buckner & Petersen, 1996), respectively. For PF condition, two routes are strengthened, namely a shorter route with forward and backward connections from FG to PFC, and a longer route from FG to PFC via MTL. Altogether, priming in left hemisphere activates all possible routes of information transfer from FG to PFC.

In right hemisphere, for the FB models, connections dominant within UF condition and significantly stronger than PF condition are from FG to MTL and from MTL to PFC (Fig.6-5D). The change in connectivity patterns by priming indicates that when famous faces are perceived, information proceeds from FG to PFC via MTL (Fig.6-5D). When faces are primed, direct connection between FG and PFC is strengthened as in left hemisphere; however information flow from FG via MTL to PFC is diminished as shown in Fig.6-5B.

In essence, the following picture of repetition priming effects for famous faces on connections within face network emerges. (1) Priming strengthens forward and – if modelled – backward connections between FRUs in FG and decision making systems in PFC. (2) Priming shifts involvement of MTL in two hemispheres to a clear dominance of left MTL. While involvement of MTL in right hemisphere is weakened by priming, that of left MTL, is strengthened. This may be explained by different functions of left and right MTL. As suggested by Grabowski et al.,(2001); Papagno et al., (2014), left MTL is involved in name retrieval. Increasing involvement of left MTL might indicate improved access or stronger involvement of name access after repeated encounter and its contribution to decision making. Likewise, decreased activity in right FG → MTL → PFC pathway might indicate a short-circuiting of the pathway from FRUs via PINs to familiarity decision system.
Though F models exhibited similar priming effect as FB models (Fig 6-3B), there was no difference in RT between F and FB models within each priming condition. This indicates that presence of backward connections in FB model in right hemisphere does not contribute significantly in speeding up response time.

6.3.4. Global speed-up when FB model is preferred in left hemisphere

Contrary to right hemisphere, a priming-independent speeding up in RT was observed (Fig 6-3(A)), when FB model was preferred in left hemisphere, irrespective of priming condition. A backward connection that is common in FB models in both conditions is from ATL to PFC (Fig. 6-5(A) and (C)). Thus, this connection appears to be responsible for fast response in participants preferring FB models, irrespective of priming conditions.

Left PFC, found as a node for backward connections (ATL to PFC in both conditions), therefore, appears to have an important role in facilitating RT. Nee et al., (2013) found left PFC to be involved in executive functioning and post retrieval selection. This indicates that in the present familiarity judgment task, left PFC will be involved in retrieval of a person’s semantic knowledge, including biographical facts, in order to select proper response. This accuracy in decision making may be facilitated by backward connections from ATL to PFC causing faster RTs for participants in both UF and PF conditions. Left ATL is specialized for naming of famous faces (Collins & Olson, 2014; Olson et al., 2007) and is connected to PFC by Uncinate Fasciculus, removal of which has been found to significantly impair naming capability for famous faces in patients (Papagno et al., 2014; Papagno et al., 2010). According to these results, one might speculate that naming – although it is not required in present familiarity decision task – might be an important ingredient to processing speed independent of priming.
6.3.5. Open question and limitations

From the current study, effects of priming in connection parameters between sources was in accordance to the observed priming effects in their source waveforms, except for ATL source. Connections from ATL (both left and right) did not reflect any priming effects. Tsukiura, Suzuki, Shigemune, & Mochizuki-Kawai, (2008) found left ATL to mediate association between names and person related semantic information; and right ATL to mediate association between faces and person related semantic information in memory. Since, in our study famous faces were used, possibly, connections mediating from ATL got strongly involved for both primed and unprimed conditions, without a clear difference between conditions due to a ceiling effect.

Although relatively small sample size, constraints of present models, and absence of inter-hemispheric connections in this study may limit its credibility; however, it represents a novel perspective for our understanding of the brain-behaviour relationship in face priming. Further investigation with a family of models might overcome the limitations and confirm hemispheric specificity of priming effect in relation to backward connections and response times.

6.4. Summary

This Chapter was primarily aimed to understand priming effects in performance (faster RT) at the level of brain mechanisms. For this, it was important to understand what priming does to the neural face recognition network. Two hypothesised models (F and FB) for each hemisphere, mimicking anatomical and physiological structure of the brain were outlined in DCM from chronometrically ordered sources obtained at Occipital Lobe, Fusiform Gyrus, Mediotemporal lobe, Prefrontal Cortex, and Anterior Temporal lobe. The models were fitted to individual subject source waveforms (SWFs) obtained from RERPs. RERPs were advantageous
in capturing priming effects in sources obtained from late components. Late components augment backward connections, and reflect a re-entry of dynamics into hierarchically lower processing areas.

Delineating backward connections in FB model was based on predictive coding hypothesis which relies on calculated priming effects in sources for various time windows. Absence of priming effects in Occipital Lobe suggested no backward connection to this source. The models (F and FB) were then observed for their goodness of fit on each hemisphere. FB model was found to be preferred for both hemispheres in PF condition, whereas in UF condition, FB was preferred model for right hemisphere, and F was preferred model for left hemisphere. The reaction time (RT) performance of every subject in both conditions (PF and UF) were then associated with type of model preferred by each individual in each hemisphere to understand the brain behaviour relationship. Only the left hemisphere reflected that, despite of any preferred model at group level (FB for PF, and F for UF), subjects with faster RT in both conditions preferred FB model.

The posterior means representing connection strength between sources were then evaluated on models for each hemisphere in both conditions. It provided information regarding connections that are important for face recognition, and connections that are modulated by priming in each hemisphere (Figure 6-5).

In general, results are consistent with previous suggestions that facilitation of information in face priming might involve processing in both left and right hemispheric sources. Holistic face identification and processing is predominantly running in right hemisphere, but is coordinating with left hemisphere for retrieval of information related to person’s identity from facial features perceived by it. In concern to our main question regarding the underpinnings of
repetition priming effects for famous faces, the common notion that priming would be related to a preference for backward connections found only weak support. In concrete, priming can be related to strengthening (or higher efficiency) of connections between system that processes face structure and their memory representations (FG), and controlling decisions (here, about face familiarity) and response selections (PFC). Furthermore when FB models are considered, there is also a feedback connection between these two systems (PFC \rightarrow FG) and an additional involvement of the MTL (memory system) via forward connections. Interestingly, the priming-related opposite modulations of connectivity paths and neural source of MTL emphasised the functional aspects of left and right MTL in face priming. Additionally, irrespective of priming, feedback connection from ATL to PFC in left hemisphere seems to be of functional relevance for global speed-up of responses.
Chapter 7

Summary and Prospects

7.1. Summary

Event-related potentials (ERPs) are widely used measures of brain activity in humans due to their excellent temporal resolution, noninvasiveness, and validity as indicators of sensory, cognitive, and motor processes. Conventionally, ERPs are obtained from averaging of several single trial EEGs locked to a time marker (in general, stimulus onset time). Single trials of EEGs have latency invariant and latency variable components in them. Latency variable components are commonly found during late time periods (> 250 ms). Conventional averaging of latency variable components smears the waveforms of conventional ERPs, giving rise to blurred scalp topography for late components. This creates ambiguities in their potential to understand the underlying mechanism of the brain.

Residue Iteration decomposition (RIDE), was a technique developed by Ouyang et al., (2011) to reduce smearing present in conventional ERPs, so as to reveal a clearer picture of the scalp topographic distribution. RIDE uses an iterative scheme to separate the ERP into component clusters having different latencies, and then realigning them to their respective most probable latency. By integrating latency corrected components, RIDE derived ERPs (RERPs) are obtained. When RIDE is applied to scalp-recorded ERPs, amplitudes of late components often increase (Ouyang et al., 2015a, 2015b). Such advantage of RIDE over conventional ERP on surface of the head has given it a platform to be applied across different experimental paradigms.

This thesis aims to extend RIDE from outer scalp space to inner source space dynamics of the brain. The motivation was to develop an integrated framework that could extend RIDE
toolbox (http://cns.hkbu.edu.hk/RIDE.htm) as a complete package to provide substantial understanding on working mechanism of the brain. As a benchmark, we took priming ERP data on famous faces (from the study of Herzmann & Sommer, 2010), and RERP data (from Ouyang et al., 2011). Ouyang et al., (2011) found improvements in scalp topography after application of RIDE. The choice for exploring face priming ERP and RERP data in source space gives two-folded benefits. On one hand, we examine and establish advantages of RERP over ERP in source space; and during this process we create framework that could extend the applicability of RIDE toolbox. On the other hand, benefits obtained from analyzing the face ERP/RERP data inside the brain will provide insight on dynamics of different working mechanism during face recognition and priming. Research on face recognition are very important as they can provide understanding of the dynamics of areas inside the brain, and based on that, remedial or compensatory trainings by clinicians could be designed as a part of neurorehabilitation for patients suffering from disorder in face recognition (for details, refer to Bate & Bennetts, 2014).

Various models of face processing have been designed based on areas found promising during the process of face recognition. However majority of face recognition studies that define the face recognition network are based on fMRI having low temporal resolution. FMRI therefore restrains our understanding of the face processing network.

Since, face recognition happen in the range of few hundreds of milliseconds, variation in amplitude and latency of ERP components, especially with change across conditions (e.g. priming), is a more direct measure of activity on underlying neural sources. Inverse modelling of ERP data can provide information about underlying neural generators of ERP. Conventional ERPs suffering from blurred topography and lack of distinct peaks in late components, limit our
abilities to discern sources. RERPs prove to be advantageous in this aspect due to their latency corrected enhancement in the peaks.

In this thesis, an integrated framework prepares data for source localization, performed through BESA 6.0 on primed famous (PF) and unprimed famous (UF) ERP and RERP data. Two master source models (ERP and RERP) were created on the grand average data of two conditions (PF and UF) for 21 subjects. Source localization work was done to obtain sources that have physiological plausibility and can give optimum residual variance. Sources were localized bilaterally at Occipital Lobe (OL), Fusiform Gyrus (FG), Mediotemporal lobe (MTL) and Anterior Temporal lobe (ATL) for both ERP and RERP models. However, an additional source at Premotor Cortex (PMC) was localized for RERP source model only, as RERP could integrate motor components in them. Sources obtained were in conformity with studies of others. Source waveforms (SWFs) were obtained by applying respective source models on the jackknife averages of subjects of each condition in ERP and RERP data. Priming effects were then measured in six time windows for SWFs obtained from both ERP and RERP model, of which four time windows were pre-specified from the study of Herzmann & Sommer, (2010). As per expectations, RERP source model was able to capture priming effects in SWFs more efficiently than ERP source model, especially for late component sources (MTL, PFC, and ATL). Extended and enhanced pattern of priming effects in RERP sources revealed important information about the possible role each source plays in face recognition and priming. Overlapping in priming effects of different sources were observed at various time windows. This reflects the joint effort of early and late sources in face processing (e.g. role of FG and ATL), and supports the notion of parallel processing of information in these sources. Consistent with studies of others (Verosky & Turk-Browne, 2012), early priming effects were seen in the right hemisphere and late priming
effects in the left hemisphere. This indicates that processing of faces in left hemisphere may
require prior processing in right hemisphere. In addition, predominance of right hemisphere in
face recognition was only reflected from priming pattern of RERP source model, and not the
ERP source model. Importance of right hemispheric dominance in face recognition has also been
reported by others (Schweinberger et al., 1994; Wang & Cottrell, 2012). RIDE reconstructed
ERPs therefore promise a more comprehensive understanding of time-resolved dynamics sources
play during face recognition, especially the late sources.

Considering better prospects that RERPs provide in source localization, we further
decided to encompass effective connectivity analysis into our integrated framework. When
neural system is perturbed due to external stimulus (e.g. viewing a face), neural activity spreads
across anatomical sources. Causal influence of one source on the other can be estimated by
effective connectivity employing dynamic causal model (DCM).

Physiological and temporal limitation compromises fMRIs capability of estimating effective
connectivity from the data (David et al., 2008). Hence, RERPs/ERPs hold an edge over fMRI
when source localization is done on them. Temporal sequence in which sources are obtained
during source localization of RERPs is beneficial to infer the information flow during face
processing. This guides the hypothesis to outline the causal architecture of network model in our
study. Compared to ERPs, RERPs are beneficial for DCM as RERPs reinforce the effects of late
components and their sources. Late components augment backward connections, and reflect re-
entry of dynamics from higher areas to lower areas (David et al., 2005). In our integrated
framework, the causal architecture was delineated from SWFs obtained from RERPs.
From statistical parametric mapping (SPM) toolbox, DCM was deployed in the integrated framework. Since DCM analysis is based on individual SWFs, therefore, RERP source model was fitted on individual subject data of each condition (PF and UF).

Two hypotheses based generative models were outlined for each hemisphere, one with forward connection (F model) and one with forward – backward (FB model) connections. Our approach considered SWFs of left and right hemispheres separately, and then fitted each model on SWFs, in order to estimate the hemispheric contribution in face recognition and priming.

Two models (F and FB) were then observed for their goodness of fit on each hemisphere. At group level, in right hemisphere, FB model was preferred over F model in both primed (PF) and unprimed (UF) conditions. However, in left hemisphere, FB model was preferred in PF condition and F model was preferred in UF condition. This indicates that causal architecture changes with priming in left hemisphere. However, when priming effects were analysed at individual level for model preference of each hemisphere, the common notion that priming would be related to a preference for FB model found only weak support. Since in DCM models, experimental factors (e.g. priming) could change connection parameters or causal architecture (difference in F and FB model preference in left hemisphere), or both. Hence, evaluation was done for connections between sources of each hemisphere for all preferred and not-preferred models.

From the perspectives of network topology some interesting results were observed. It was found that priming strengthens forward connections between FG and PFC in F models of both hemispheres. In FB models of both hemispheres, priming strengthens both forward and backward connections between two sources PFC and FG. This indicated that priming can be related on strengthening of connections between system that processes face structure and their
memory representations in FG, and controlling decisions (here, about face familiarity) and response selections in PFC.

Another interesting result was found in the way priming affects the route FG→MTL→PFC in each hemisphere. In right hemisphere, this pathway is stronger in UF than PF, and in left hemisphere, it is weaker in UF than PF. This indicates that involvement of MTL in right hemisphere is weakened by priming, and that of left MTL is strengthened. The findings shed light on the different functional aspects of left and right MTL, and emphasize on name retrieval aspects of left MTL (Grabowski et al., 2001; Papagno et al., 2014).

A global speed up in response time was found only in left hemisphere for participant preferring FB model of both PF and UF condition. Backward connections (ATL→PFC) in the left play a big role in speeding up the response time. The findings support the strong role left PFC has in executive functioning and post retrieval selection as found in the study of Nee et al., (2013). Left ATL is specialized for naming of famous faces (Collins & Olson, 2014; Olson et al., 2007) and is connected to PFC by Uncinate Fasciculus, removal of which has been found to significantly impair naming capability for famous faces (Papagno et al., 2014; Papagno et al., 2010). Independent of priming, this finding indicated that though naming is not required in the familiarity decision task of the present study, but still it is an important ingredient in processing the response speed.

7.2. Advantages of the present work

The present work extended the toolbox of RIDE to understand the source dynamics and processing of information in the brain from the latency corrected ERPs (RERPs) derived from RIDE. A recent review article by Olivares, Iglesias, & Saavedra, (2015), foresees an integrated system to be developed either from ERPs which are free from traditional defects (one of which is
due to latency) or from single trial EEGs, that could advance our understanding of the working mechanism of the brain, especially when faces are processed. RIDE along with this extended framework shows progressive advantage to the future of ERP studies that the authors envisioned in their review paper.

The framework compared the conventional ERPs and RERPs in the source space for a face priming data. This ERP dataset was obtained from the work of Herzmann & Sommer, (2010), on which, Ouyang et al., (2011) showed the benefits of RIDE on the scalp surface. We extended the work in the source space and overviewed the benefits of RIDE in the priming effects obtained from the source waveforms (SWFs). Conventionally, these effects are judged only for scalp potentials (ERPs). However, due to RIDE, better SWFs facilitated our judgements on priming effects in the source space, especially in late sources. It seems, current work is a pioneering attempt to estimate priming effects in the source space from both ERPs and RERPs. The work established the advantages of RERPs over conventional ERPs in the source space. The framework confirmed the SWFs of RERPs as a better choice for modelling the source dynamics.

In this perspective, SWFs from RERP were used to define the causal architecture of the face processing and priming network. The behavioural performance (RT) was correlated to the network architecture. To our knowledge, this is the first study that correlates behavioural performance (RT) of face priming for each condition (PF and UF) with network architecture derived from the temporally resolved sources obtained from latency corrected RERPs. Our study reflected that priming in the two hemispheres strengthens the route in which information travels from FG to PFC. The study also reflected the role of backward connections in the left hemisphere to facilitate to speed up the global response. The study also explored hemispheric specificity of priming.
Beauty of the current works lies in obtaining a temporally resolved cohesive architecture of sources and their working mechanism from the integrated framework based on RERPs. This framework can thus be used in other experimental paradigms.

7.3. Limitations of the work

Though our work presented promising results by integrating several aspect of analysis and modelling of ERPs, there are still some limitations. The limitations of work can broadly be divided into two categories, namely (1) limitations of the integrated framework, and (2) limitations in the available data. We will discuss about the two categories in separate sections. It was not the primary aim of this thesis to address these limitations.

7.3.1. Limitations of the integrated framework

The limitations of the integrated framework lie in the limitations of: RIDE, source localization through BESA, and connectivity analysis through DCM. We will overview the limitations in the following.

Ouyang et al., (2011) discussed the limitations of RIDE which can be due to (A) noise and artifacts: Too much noise or too many artifacts can affect the correctness of RIDE results, and therefore pre-processing the data and inclusion of sufficient number of trials is important. (B) Latency variability: since RIDE separates ERP into components with relatively independent latency variability, narrower distribution of latency could create ambiguity in their separation. And (C) the assumption: RIDE assumes linear superposition of different component clusters, which may bias the result when strong nonlinear interaction between component clusters appears.

Source localization also suffers from limitations (Scherg & Picton, 1991), of which the most important are the following. (A) Uniqueness in solution: Dipolar solutions are not unique. A dipole could change its location and orientation. This poses a severe problem for temporally
resolved ERPs and restricts their spatial localization. Therefore, care must be taken during source localization to reach optimum value of its residual variance. Prior knowledge of anatomy and physiology of the brain is very important in dipolar source localization. (B) Noise in the data can increase the possibility of getting non unique solutions. Pre-processing of the data is therefore important for reproducibility of the obtained source solution.

In similar manner, DCM analysis too has various limitations, of which the most important was pointed out in the work of Chicharro & Ledberg, (2012). They claimed that brain being a complex, self-organised system is not only affected by external perturbation, but also has its own internal dynamics before perturbation, which influences its working phenomenon. Furthermore, the subsystems in the brain are bidirectional, and therefore, the effective cause-and-effect relationships are not enough to explain causal architecture of the brain. Inclusion of natural causal effects is therefore imperative in DCM.

7.3.2. Limitations in the available data

The face priming ERP and RERP data provide an in-depth understanding of the face processing system in the brain. However, there are few constraints in the work. (A) Small sample size: The data set has only 21 participants. Larger sample size could give more concrete solutions to the current analysis, especially when comparing the different preferred models within conditions. (B) Electrode system: Only 64 electrodes were used to obtain the ERP data. Increase in the number of electrodes would facilitate better source localization and increases the precision in SWFs. (C) Gaussian input through OL: DCM assumes the external perturbation to the system to be Gaussian. In reality, the input could be different and accompanied with noise. Assuming visual processing to start from OL is another consideration of the study, as many studies have found processing of visual input in the retina of human eye. And (D) Hemispheric
separation: The source waveforms obtained and the network derived in the current work were separated bilaterally into each hemisphere. In reality, the two hemispheres work in unison and are interlinked to each other through white matter fibres. So far in our study, inter-hemisphere connections are not considered.

7.4. Future perspectives

Based on the current work, the framework and the future research could be propelled in a few important directions. (A) Distributed source localization: Same as discrete source localization done in our work, the framework could also employ the distributed source localization algorithms like LORETA, sLORETA, LAURA etc. The sharper peaks due to RIDE might facilitate accurate and focussed views of distributed sources. Another possibility could be the use of orthogonally aligned discrete regional sources. Regional sources can provide dipole moments in three directions and therefore can be more precise than the normal discrete dipoles used in the current work. (B) Auxiliary statistical analysis: auxiliary application of statistics like 2 or 3 way ANOVA with main and interaction effects between models and hemispheres could be also applied to obtain more systematic understanding of the network topology and parameters of DCM. This could serve as an additional confirmation to the results obtained in the research work. (C) Frequency domain analysis: until now, the extended framework is confined to the analysis in the time domain. However, frequency transformation of RIDE may augment the approach. Different models based on time–frequency analysis could then be integrated with RIDE data. This can provide information regarding the alpha, beta, gamma and theta band oscillations in the brain. Synchronization of oscillations between areas could provide different clues. In that respect, frequency based induced response DCM models (Chen et al., 2009) could also be employed in RIDE data. (D) Clinical analysis: The framework could be functionally integrated with other
experimental modalities like fMRI, PET for use in clinical applications. Diagnostic improvements in ERP through RIDE with the extended framework could provide clues regarding the impairments in the areas and their interconnection in patients. The dynamics understood in the present face recognition study could be utilised in future for designing neurorehabilitation techniques for patients suffering from face recognition disorders (for details, refer Bate & Bennetts, 2014).

7.5. General Conclusion

With application of an extended framework of RIDE with source localization and DCM, much more extensive knowledge of face processing and priming was obtained in this thesis. The work represents a pioneering perspective towards understanding of face recognition and priming. This framework could be applied to other experimental paradigms. Non-invasiveness, better temporal resolution and finally, consistence of the results with other studies reflect the merit of this framework. Therefore, future works based on this framework would contribute to usher frontier of research in many aspects of cognitive neurosciences.
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