

INTRINSIC CONNECTIONS BETWEEN FRONTO-PARIETAL NETWORK
DURING MENTAL ARITHMETIC TASKS

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DURING MENTAL ARITHMETIC TASKS

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*Specially dedicated to my beloved parents;
Zulkili bin Omar and Romlah Binti Abdullah, and my siblings
Who have encouraged me throughout my journey of education.
A warm thanks to all*

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In the name of Allah, the Most Beneficent, the Most Merciful
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ABSTRACT

Arithmetic knowledge are composed of several components, including procedural skill which are simple mathematics computation (MC) and complex mathematics computation, (MM), conceptual understanding and factual knowledge (FR). These components have been the basic references when conducting the neuroimaging study of cognitive arithmetic. Previous studies showed evidence of cortical activation of fronto-parietal regions with different intensity while performing various types of mental arithmetic problems. In addition, some studies have suggested that problem-size or difficulty can affect the activation of fronto-parietal regions. However, not much research has been done on effects of problem-size and arithmetic components in terms of their brain connectivity. Therefore this study was carried out to determine both empirical effects on the aspect of Functional Specialization (FS) and Effective Connectivity (EC) of fronto-parietal networks. In this study, functional Magnetic Resonance Imaging (fMRI) scans were performed on twenty-two ($n = 22$) healthy male participants. Each participant performed a series of arithmetic problems which presented in pseudorandom order. For each task, an arithmetic problem of true and false answers were presented in block stimulus paradigm within 30s followed by 30s rest. Participants made a judgement by pressing the handgrip button to indicate the wrong answer. Statistical Parametric mapping (SPM8) and Dynamic Causal Modelling (DCM10) were used to determine brain Functional Specialization (FS) and Effective Connectivity (EC). For each participant, a number of 56 EC models for PART I (Effects of Problem-Size) and 77 for PART II (Effects of arithmetic components) were constructed for each hemisphere to test the existence of couplings between Superior Parietal Lobule (SPL), insular, Inferior Occipital Gyrus (IOG) and Dorsolateral Prefrontal Cortex (DLPFC). These regions have been proved to be the key role in mental arithmetic and representing the fronto-parietal networks. The EC results show the existence of interactions between the regions of interest, but with different pattern of connectivity between hemispheres. In PART I, the SPL \rightarrow DLPFC connection during single-digit MM task was the only one that was significant (Posterior probability, $P < 0.90$) on the left hemisphere compared to other tasks. Meanwhile, the same connection, but on the right hemisphere was only significant during a MM task in PART II. This is due to both regions play important roles in fronto-parietal network, in which SPL is associated with number processing, while DLPFC is generally associated with working memory and task difficulty. Comparison study on MC and FR tasks where the answer can be directly retrieved from the memory, MM tasks were more complex, thus forcing the subject to retrieve, memorize and compute the answers at the same time. These findings indicated that both left and right hemispheres are involved in arithmetic processing. The results obtained from this study revealed that problem-size and arithmetic components do affect the EC between regions of interest despite their insignificantly difference in cortical activation.

ABSTRAK

Pengetahuan arithmetik terdiri daripada beberapa komponen, termasuk kemahiran prosedural (pengiraan matematik mudah, (MC) dan pengetahuan matematik yang kompleks, (MM)), pemahaman konsep dan pengetahuan fakta (FR). Semua komponen ini telah menjadi rujukan asas apabila menjalankan kajian ke atas arithmetik kognitif menggunakan kaedah imbasan neuro. Kajian terdahulu telah membuktikan pengaktifan korteks *fronto-parietal* dengan keamatan yang berbeza semasa menjalankan pelbagai jenis masalah mental arithmetik. Beberapa kajian juga mencadangkan bahawa masalah saiz atau kesukaran boleh mempengaruhi pengaktifan *fronto-parietal*. Walau bagaimanapun, kurang penyelidikan yang telah dilakukan untuk menangani kesan masalah saiz dan pengiraan matematik dari segi hubungan efektif di dalam otak. Oleh itu, kajian ini dijalankan untuk menentukan kedua-dua kesan empirikal dari aspek pengkhususan kefungsiian (FS) dan hubungan efektif (EC) bagi rangkaian *fronto-parietal* semasa melakukan pengiraan matematik. Dalam kajian ini, imbasan pengimejan resonans magnet kefungsiian (fMRI) dilakukan ke atas dua puluh dua ($n=22$) subjek lelaki yang sihat. Setiap subjek perlu melakukan satu siri arithmetik yang dipersembahkan dalam susunan rawak. Bagi setiap arithmetik, jawapan yang betul dan salah telah dipamerkan dalam paradigma blok rangsangan. Subjek membuat pengiraan secara mental dan menekan butang bagi menunjukkan jawapan yang salah. Pemetaan Statistik Berparamater (SPM8) dan Pemodelan Dinamik Penyebab (DCM10) digunakan untuk menentukan sifat FS dan EC otak. Untuk setiap subjek, sejumlah 56 model EC bagi BAHAGIAN I (Kesan Masalah Saiz) dan 77 model bagi BAHAGIAN II (Kesan Komponen Arithmetik) dibina untuk setiap hemisfera bagi menguji kewujudan gandingan di antara Lobus Superior Parietal (SPL), Girus Inferior Osipital (IOG), Insular dan Korteks Dorsolateral Prefrontal (DLPFC). Kawasan korteks ini terbukti memainkan peranan utama dalam mental arithmetik dan mewakili rangkaian korteks *fronto-parietal*. Keputusan bagi EC menunjukkan kewujudan interaksi antara kawasan otak yang terlibat, tetapi dengan corak EC yang berbeza di antara hemisfera. Di BAHAGIAN I, hanya SPL→DLPFC pada hemisfera kiri yang bererti (Kebarangkalian posterior, $P<0.90$), iaitu ketika satu-digit MM berbanding arithmetik lain. Sementara itu, EC yang sama tetapi pada hemisfera kanan menunjukkan hubungan bererti semasa MM dalam BAHAGIAN II. Ini kerana, kedua-dua korteks memainkan peranan penting dalam rangkaian *fronto-parietal*, di mana SPL dikaitkan dengan pemprosesan nombor, dan DLPFC amnya dikaitkan dengan ingatan kerja dan kesukaran tugas. Berbanding dengan MC dan FR, MM adalah lebih kompleks, di mana subjek perlu mendapatkan semula pengetahuan fakta sedia ada, menghafal dan mengira jawapan pada masa yang sama. Penemuan menunjukkan bahawa kedua-dua hemisfera otak terlibat dalam pemprosesan arithmetik. Hasil kajian menunjukkan bahawa masalah saiz dan komponen arithmetik mempengaruhi EC antara kawasan pengaktifan dalam korteks *fronto-parietal* meskipun pengaktifan mempamerkan perbezaan yang tidak ketara

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LIST OF ABBREVIATIONS

ACC	-	Anterior Cingulate Cortex
AG	-	Angular Gyrus
AIC	-	Akaike's Information Criterion
BIC	-	Bayes's Information Criterion
BMA	-	Bayesian Model Averaging
BMS	-	Bayesian Model Selection
BOLD	-	Blood-Oxygenated Level Dependent
DCM	-	Dynamic Causal Modelling
DICOM	-	Digital Imaging and Communications in Medicine
DLPFC	-	Dorsolateral Prefrontal Cortex
DTI	-	Diffusion Tensor Imaging
EEG	-	Electroencephalography
EMG	-	Electromyography
EPI	-	Echo Planar Imaging
ERP	-	Event Related Potential
F	-	Negative-free Energy
FFX	-	Fixed Effect Analysis
fMRI	-	Functional Magnetic Resonance Imaging
fNIRS	-	Functional Near-Infrared Spectroscopy
FOV	-	Field Of View
FR	-	Facts Retrieval
FWER	-	Family-Wise Error Rate
GCM	-	Granger Causal Mapping
ICA	-	Independent Component Analysis
IOG	-	Inferior Occipital Gyrus

IPC	-	Intra-Parietal Cortex
MEG	-	Magnetoencephalography
MC	-	Simple Mathematics Computation
MD	-	Complex Mathematics Computation
MPR	-	Multi-Planar Reconstruction
MRI	-	Magnetic Resonance Imaging
MS	-	Multiple Sclerosis
MVAR	-	Multivariate Autoregressive Model
NMR	-	Nuclear Magnetic Resonance
PCA	-	Principal Component Analysis
PET	-	Positron Emission Tomography
PMA	-	Premotor Association Area
PPM	-	Posterior Probability Map
PSC	-	Percent Signal Change
RFT	-	Random Field Theory
RFX	-	Random Effect Analysis
ROIs	-	Region Of Interests
SEM	-	Structural Equation Modelling
SMA	-	Supplementary Motor Area
SPL	-	Superior Parietal Lobule
SPM	-	Statistical Parametric Mapping
TCM	-	Triple Code Model
VBM	-	Voxel-Based Morphometry
VFG	-	Visual Fusiform Gyrus
VOI	-	Voxel Of Interest
WICA	-	Within-condition Inter-regional Covariance Analysis

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CHAPTER 1

INTRODUCTION

In the first chapter, the scenario of mathematics in daily life as well as how neuroimaging research bridge the gap between neuroscience and mathematics education will be explained briefly under the first section of research background. Then, the problem statements of this work will be defined thoroughly followed by the contribution of this research in section three. In section four, a few research questions are listed. And as the objectives were lined up, the research scope will be drawn up as the boundary of the present study. At the end of this chapter, the research hypothesis is composed.

1.1 Introduction

One of the basic elements of mathematics are numbers. We use numbers almost daily to measure ordinary things such as height and weight, calculate daily expenses and even to estimate the education loan. In addition, numbers are used in various types of operations in mathematics such as ranking, counting and comparing quantities. Meanwhile, arithmetic knowledge comprises of several components, such as factual

knowledge, procedural skill, and conceptual understanding (Gilmore, 2006; Long, 2011). Generally, conceptual knowledge involves “knowing how”, which is composed of a network of relationships among pieces of information. Problems that are involved an inversed transformation (e.g. $10 + 4 - 4 = ?$) are used to measure the conceptual knowledge of arithmetic between addition and subtraction.

On the other hand, procedural knowledge can be defined as “knowing-how-to”, whereby composed of sets of procedures executed in a specific sequence and it primarily involves a standard arithmetic problem (e.g. $10 + 8 - 3 = ?$). Meanwhile, the cognitive number processing of arithmetic fact retrieval was proposed by McCloskey since three decades ago by verbally testing on dyscalculia patients (Dagenbach and McCloskey, 1992; McCloskey *et al.*, 1985). McCloskey (1985) also proposed that calculation involving multiplication and division encompassed of several calculation-specific processes.

These processes postulate the mechanisms for (1) retrieval of arithmetic facts (e.g., $6 \times 7 = 42$), (2) execution of calculation procedures, and (3) comprehension of operation signs (e.g., +, x) or words (e.g., plus). In conclusion, mental calculation can be described as a complex task that delineate an important component of higher order cognition that involves several fundamental cognitive activities. The specific processes involve covert production of numbers, execution of a calculated operation which is represented by arithmetic facts from a memorized table and storing data in working memory for further operations. This specific process is shown in Figure 1.1. Ashcraft (1992) in his review journal entitled, “Cognitive arithmetic: A review of data and theory” has proposed four important empirical effects which can influence the organization of a person’s knowledge of numbers and mathematics in the memory and the processes that can enable this knowledge to be accessed and applied in different settings. These engage the problem size/difficulty effects, error effects, relatedness effects and strategies of processing.

The problem-size effect has been described as a well-known phenomenon in mental arithmetic, in which the problem difficulty increases with the numerical size of the operands (Ashcraft, 1992). This shows that, the problem size effect is the most basic empirical effect in mental arithmetic studies, whereby as problems grow larger,

the process becomes more difficult. Taking this as a hypothesis, the first part of the current study was designed to observe the effect of problem size/difficulty on cortical activation as well as to how the information travel ipsilaterally between the regions. An inaugural study of mental arithmetic using neuroimaging modalities has been conducted about three decades ago by Roland and Friberg (1985). They measured the regional changes in cerebral blood flow, which was induced by different cognitive tasks, using single-photon emission tomography.

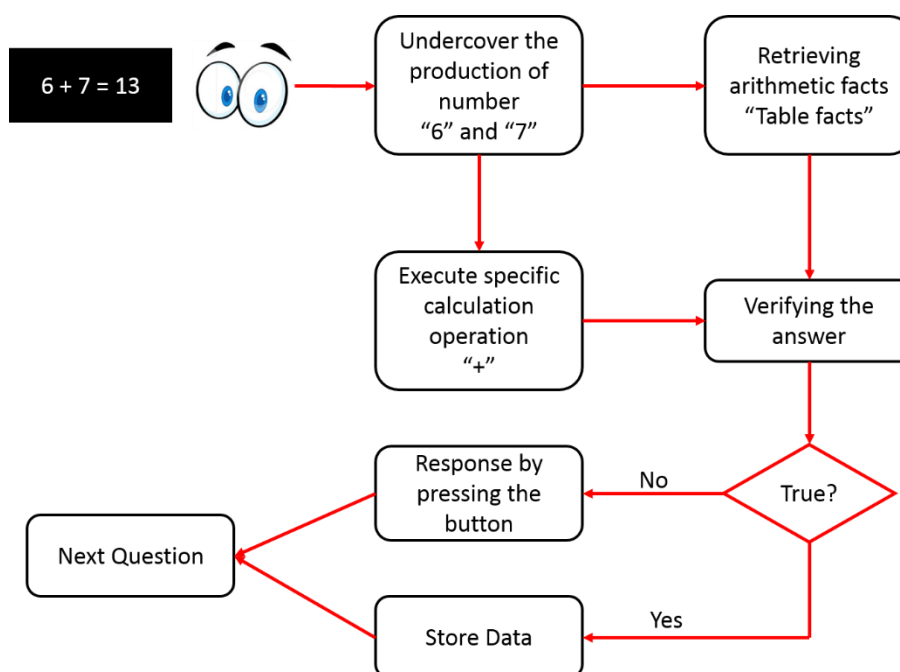


Figure 1.1 The cognitive process on calculation-specific processing for the mental arithmetic (Dagenbach and McCloskey, 1992; McCloskey *et al.*, 1985)

A serial of subtraction problems used in arithmetic tasks has specifically activated the Angular Gyrus (AG) bilaterally. Upon this study, a number of significant neuropsychological studies have evolved over the last three decades, which concentrated on the cognitive mapping of number processing and calculation (Arsalidou and Taylor, 2011; Zamarian *et al.*, 2009). This shows that in the last 30

years, the rapid development of brain imaging techniques has helped the identification of the neuro-anatomical brain areas supporting arithmetic functions more precisely.

Networks of brain regions are responsible for the different functions executed during arithmetic problem solving. However, based on the number of steps they require, this arithmetic decision has posed various numbers of cognitive demands, differently. Numerous neuroimaging studies focus on arithmetic processing using single-step arithmetic problems (e.g., $3 + 4$, $5 - 2$) which are composed of one-digit or a combination of one and two-digit numbers (Fehr *et al.*, 2007). Besides, it also includes the manipulation of numbers in successive operations (e.g., $4 - 3 + 6$) (V Menon *et al.*, 2000) or even solving integration problems (Ambady *et al.*, 2009). Evidence from neuroimaging studies indicates that the neural substrate of arithmetic processes are composed of the cingulate cortex, parietal cortex (including intra-parietal sulcus and inferior parietal lobule), lateral prefrontal cortex, insula and occipital cortex (Eickhoff *et al.*, 2009; Kong *et al.*, 2005). These areas are proved to be the main region in mental arithmetic.

The involvement of prefrontal cortex in the brain activity has been linked to one of the cognitive functions such as working memory (Yoo *et al.*, 2012), with considerable emphasis on its role in monitoring or manipulating information, as required in arithmetic tasks. Researchers who study numerical processing and computation perceive that difficult arithmetic tasks require more working memory resources than simple tasks (Fehr *et al.*, 2007; Kong *et al.*, 2005).

Practically, it is suggested that the three parietal circuits (Stanislas Dehaene *et al.*, 2003a) are involved in arithmetic processing. The bilateral horizontal intraparietal sulcus/superior parietal lobule, which is one of the three parietal circuits is thought to be the domain-specific for arithmetical processing. Meanwhile, the other two regions, involving the left AG verbal system and the posterior parietal attention system are most probably shared with other cognitive domains. One of these parietal, which is the superior parietal lobule (SPL) bolster the attention, spatial working memory and visuo-spatial processes.

These processes are pertinent to numerical processing. Specifically, these three parietal regions are also known as Triple Code Model (TCM) (Stanislas Dehaene *et al.*, 2003a; Schmithorst and Brown, 2004). TCM model predicts that numbers are handled in three numerical surface format: (1) a visual Arabic code portrayed by a series of digits (brought on the activation of bilateral activity in inferior ventral occipital-temporal areas), (2) an analogic quantity and magnitude code (generated activity in the left inferior parietal areas, which underlies quantity and magnitude judgement) and (3) verbal code represented by words (prompted the initiation of the left perisylvian areas). Inside this system, simple-digit calculations can be tackled either through a direct route utilizing operands (e.g., 3×5) transcoded into a verbal code (three times five), which would inspire the rote memory of this operation, or through an indirect semantic route in which the operands represent quantities in which semantical meaningful manipulations can be performed.

As for subtraction problem, the indirect route is regularly taken when rote memory for a problem is inaccessible. Therefore, Dehaene and Cohen (1996; 2003a) contended that addition and multiplication depend generally on rote verbal memory (direct route), while subtraction depends for the most part on quantitative manipulations (indirect route), and that these two processes are reflected in the brain as two main cortical systems for calculations.

The involvement of frontal, central-parietal (or temporal) and parietal components have been described in numerous fMRI and ERP studies regarding addition and subtraction (Burbaud *et al.*, 1999, 2000; Chochon *et al.*, 1999; Cowell *et al.*, 2000; S. Dehaene, 1999; Rickard *et al.*, 2000; S M Rivera *et al.*, 2005; Stanescu-Cosson *et al.*, 2000; L. Zago *et al.*, 2001; Rocha *et al.*, 2005). These widespread areas are included in arithmetic calculations and have been articulated in the previous studies. All authors have focused on both the left frontal and parietal areas as common and critical components of the arithmetic brain.

Some of these authors have recommended that the frontal regions are greatly involved in the more difficult calculations (Anderson *et al.*, 2011; Bongard and Nieder, 2010; V. Menon *et al.*, 2000; Rypma and D'Esposito, 1999; Yu *et al.*, 2012) while the temporal region is generally hypothesized as having a bilateral distribution in

arithmetic computations, its activity is depicted as for the most part reliant on the type of calculation and problem size (Chochon *et al.*, 1999; Cowell *et al.*, 2000; S. Dehaene, 1999; Rickard *et al.*, 2000; Stanescu-Cosson *et al.*, 2000). Whereas, some authors have additionally alluded to other visual and verbal components related to arithmetic calculation (Cowell *et al.*, 2000; S. Dehaene, 1999).

In concomitant to the increasing numbers of cortical activation study on mental arithmetic, the focus began to shift from blobology to connectivity. The aboriginal study of connectivity underlying number processing has been conducted by Yiyuang Tang and colleagues (2006). They have developed a functional connectivity of visuo-premotor association network of simple addition task by comparing the effects of culture on brain activities. The focus on connectivity underlying different types of mental arithmetic began to increase in a small number despite the increasing numbers of connectivity studies in other areas. This research study has been extensively used to observe and discover brain connectivity focusing more on cognitive brain function such as language, auditory, visual, working memory etc.

However, the effective connectivity underlying multiplication network has been discovered for the past five years using Multivariate Granger Causality method (Krueger *et al.*, 2011). Other brain connectivity underlying mental arithmetic were also conducted using DTI fiber tractography (Tsang *et al.*, 2009), functional connectivity (Emerson and Cantlon, 2012; Park *et al.*, 2013), and Fiber Tract (Open DX)(Klein *et al.*, 2013).

Despite the importance of number processing in daily life and numerous findings on the development of its underlying brain regions, little is known about the effective connectivity underlying number processing between fronto-parietal networks, unlike in other basic cognitive functions, such as auditory system. The ability to observe brain functions as well as brain connectivity that exists between the network during number processing via mental calculation enables us to study the changes in circuitry during different complexity (effect of problem size) and different operators (procedural knowledge vs. fact retrieval), thus it may help to improve effective teaching strategies.

In addition, neuroscience approach may add to open deliberation by demonstrating that diverse neural circuits are included in the procedural knowledge and the retrieval of arithmetic facts as an aftereffect of the present study upheld by past discoveries. Therefore, to the author's knowledge, this is the first study giving proof that different complexity (problem size) and different successive operators significantly affect the fronto-parietal networks attained from functional Magnetic Resonance Imaging (fMRI) and Dynamic Causal Modelling (DCM) Analysis.

In this study, the functional specialization, activation intensity and effective connectivity for two mental arithmetic tasks encompasses the effect of problem-size (Results presented in *Chapter 4: Effect of Problem Size*) and the impact of arithmetic components (Results presented in *Chapter 5: Effect of Arithmetic Knowledge*) were conducted with twenty-two healthy participants. The functional specialization of the brain is based on the tasks involving different types of arithmetic problems given during the fMRI experiments. The fMRI data collected from this study will be analysed using Statistical Parametric Mapping (SPM) method.

SPM is a statistical methodology of Random Field Theory (RFT) that is used to make inferences about the topological features of statistical processes that are continuous functions of space or time and it is typically used to distinguish regionally particular impact in neuroimaging data to describe functional anatomy and disease-related changes (K. J. Friston *et al.*, 1995). Functional data obtained from the experiment needs to be matched with standard anatomical space to associate the activation with the brain regions. Next, parameter estimation will be conducted using general linear model to specify the statistical models which represent the haemodynamic response of the tasks. Then, the statistical inference is made based on the Gaussian Random Field Theory and this step is known as functional specialization.

To obtain the analysis of functional integration, the percentage signal change (PSC) analysis on the region of interests (ROIs) is conducted. The purpose of this analysis is to explore the data, which involves various types of stimulus or tasks (Mohammad, 2012). Besides, the analyses will focus only on the brain regions that are dependent on the given task. The signal changes are defined as relative signal changes

in the brain regions. To analyse the effective connectivity between regions of interest, the dynamic causal modelling (DCM) is used.

DCM posits a causal model whereby neuronal activity in a given region induces changes in neuronal activity in different areas, by means of interregional connections, and in its own particular activity, through self-connections. A DCM is fitted to data by tuning the neuro-dynamic and haemodynamic parameters so as to minimize the error between predicted and observed fMRI time series. A few models are constructed by specializing the activated brain regions, which refer to the different mental arithmetic tasks. These models will be fitted with the measured BOLD signals. Therefore, the intrinsic connection between regions and how they are influenced by the experiment-context can be obtained.

Then, all models are analysed using Bayesian Model Selection (BMS) and Bayesian Model Averaging (BMA). BMS is a powerful technique in deciding the most likely, among a set of contending hypotheses of the mechanisms that generate the observed data (K.E. Stephan *et al.*, 2009). Whereas, BMA is used to produce the average network structure of the winning models (Will D. Penny *et al.*, 2010).

1.2 Problem Statements

Either in natural phenomenon or technologies arising around us, mathematics is used extensively as it expresses itself everywhere and in almost every facet of life. This scenario supports the fact that mathematics is the language of science and engineering. Besides, mathematics is defined as the science of numbers, and as a matter of fact human being did not invent mathematics concepts instead, we discovered them. Uniquely, the language of mathematics is in numbers. Not Malay, English or Japanese language.

In the present study, both specialization and integration analysis proposed in neuroimaging study were conducted in order to deeply understand how the brain regions are involved in mathematics working memory response between fronto-parietal networks under different approach of mathematical tasks. Study on functional specialization focuses on the region activated during mental arithmetic task has been reported numerously. Detail on neuroscience of learning arithmetic based on fMRI evidence has been summarized by Zamarian *et al.* (2009). However, little is known about functional integration analysis which focuses more on “How the brain interact to one another during certain tasks (Stevens, 2009)” especially in the field of learning arithmetic.

The distribution of previous studies, which analysed and observed the mental arithmetic performance on brain activity through different fields of study is shown in Figure 1.2. Therefore, the present study will clearly discuss activated fronto-parietal network across different mathematical tasks and how the brain works during these tasks. Thus, this present study will bridge the gap between experimental psychological study of working memory with education (mental arithmetic) and neuroscience study (the fronto-parietal activation and connectivity) in order to draw out a better understanding of mental arithmetic processing within the brain on normal subjects.

At the end of this study, the outcome can be made as a reference baseline of disconnected brain network of dyscalculia (the disability of doing mathematics) subjects while doing the same mental arithmetic study. Thus, a clear distinction of fronto-parietal connectivity between normal and dyscalculia subjects could be justified in the future. Therefore, it is hoped that through this study, researchers could develop more effective teaching method of basic mathematics learning (e.g., mental arithmetic) for dyscalculia subject as well as lower performance subjects in such a way that can help them survive in the real world since basic mathematical calculation is a vital component in life.

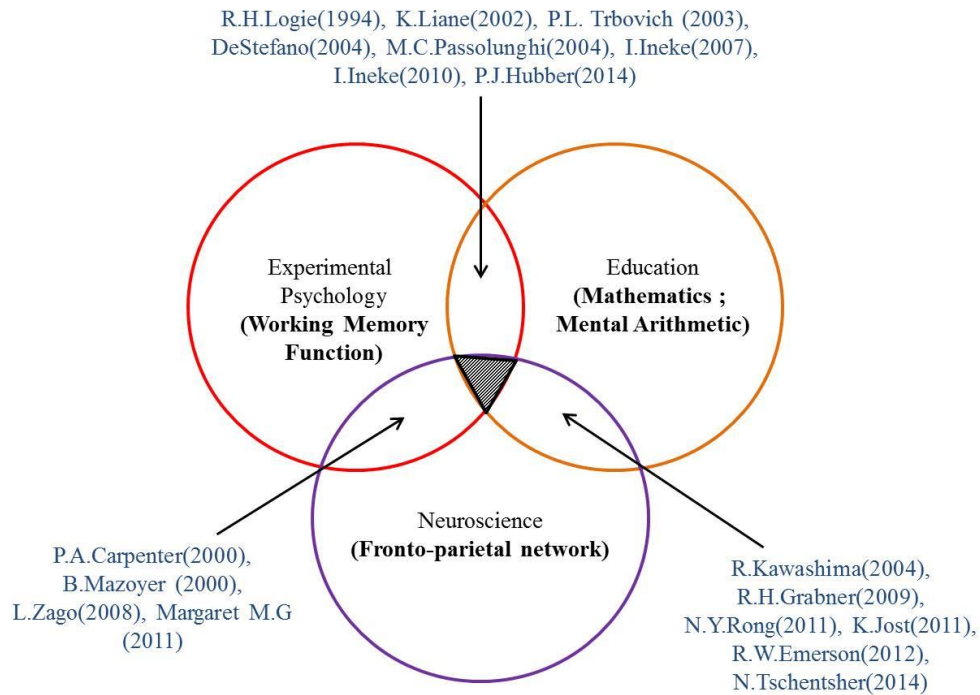


Figure 1.2 The distribution of previous study conducted on mental arithmetic tasks through different fields of study

1.3 Research Questions

There are several questions that arose during this study:

- a. Which part of the brain is involved in arithmetic processing?
- b. How are these regions connected with one another during arithmetic processing?
- c. Does problem-size/ difficulty affect arithmetic processing? And how?

1.4 Research Objectives

The present research study was conducted in order to bridge the gap that exists between neuroscience and education. Generally, this study was conducted in order to analyse the functional specialization and integration under two different chapters. Chapter 4 focuses on the effects of problem-size, which is indicated by single- and double-digit problems, while Chapter 5 concentrates on the effects of mathematics components during mental arithmetic tasks, which encompass procedural and factual knowledge. There are several objectives that this study hopes to achieve, which are:

- i. Identifying the functional specialization in the brain regions
- ii. Comparing the percentage of signal change on the four regions of interests (ROIs), which comprise of IOG, SPL, DLPFC and insular for both left and right hemispheres
- iii. Determining the structure of effective connectivity between the regions by contrariety the connection between SPL to IOG, DLPFC and Insular
- iv. Constructing the effective connectivity model for each case, which can explain how the ROIs interact with one another during computation of mental arithmetic tasks

1.5 Research Scope

The scope or boundaries of this research study comprise of a few aspects which include the modality used as well as the image format. Besides, it also explains the boundaries of subjects selected in this research study. For the modality, the present

study only uses functional Magnetic Resonance Imaging (fMRI) as one of the neuroimaging modalities. Other modalities will not be used in this study. Therefore, the image used in this study will be a set of fMRI time-series, which results from the brain scanning during mental calculation tasks given during the experimental session.

Subjects or participants selected for this research study were Diploma students from the University Teknologi Malaysia (Kuala Lumpur Campus) with 11 years of education background. Although the nature and origin of gender differences in mathematics remains unclear, variability in performance tends to be higher in males (Feingold, 1992; Geary, 1998). Consequently, to reduce variability in the present study, only male students are involved in this study. The whole analyses conducted in this study were based on Statistical Parametric Mapping (SPM8) and Dynamic Causal Modelling (DCM). This research study also focuses only on mental calculation involving four basic arithmetic operations, which is one of the basic cognitive functions.

1.6 Significance of Study

Compared to the developed countries in the world, research on brain activities using non-invasive, radiation – free technology of fMRI is still new and growing in the developing countries, especially in Malaysia. This functional Magnetic Resonance Imaging (fMRI) is utilized to assess how the brain's blood flow and oxygen change, in the specific areas, react to certain stimuli. It can outline how language and speech are acquired, how pain and other emotions are handled, how numbers are prepared and accumulated and a bunch of other brain functions.

From this study, we will be able to give new and important information on various types of mental arithmetic problems and how the regions of interest interact

with one another during mathematics computation tasks, which is unable to be obtained simply through behavioural analysis or clinical tasks. In addition, the understanding on how mental arithmetic computes under different cases can be done in this study in terms of functional specialization and integration aspects.

Robust studies have been conducted on simple addition and multiplication tasks involving single-digits and the brain regions that specialize in number processing have been identified. However, not much research has been done to tackle the double-digit problems and effects of math computation of more than one operator. Therefore, this study was conducted in order to give new insight of math computation via fMRI data analysis. Moreover, from this study, it is hoped that the construction of effective connectivity model for each case will give some basic understanding of the connectivity patterns between SPL and the fronto-parietal system, including insular, DLPFC and IOG.

Besides, analysis of mental arithmetic using fMRI can give additional info to the current psychological analysis in terms of brain neurophysiology mechanism as well as functional specialization and integration. By comparing with previous findings, this study contributes in the use of dynamic causal modelling (DCM), together with Bayesian Model Selection (BMS) and Bayesian Model Averaging (BMA) to scrutinize brain connectivity between regions during mental arithmetic tasks. In addition, this is the first study that investigates the intrinsic connectivity constructed between regions that is modulated by problem-size effects as well as the arithmetic operators (the mathematic computation and fact retrieval).

1.7 Thesis Organization

This thesis is organized into six chapters.

Chapter 1 provides the introduction of the project, which contains a brief executive summary information where the scope of the project is also discussed. It also presents the motivation and objectives of the research done. Several facts about the previous work by other researchers are also touched.

Chapter 2 contains literature review and details about the information and scope of the research. It also illustrates prior knowledge concerning the brain and its cognitive functions as well as modern neuroimaging technologies used to examine and discover the neural network underlying these functions.

Chapter 3 discusses briefly on the methodology for the project in every research stages. These include the five main phases which is data collection, data pre-processing, model specification, inference on the brain activation and the intrinsic connectivity analysis.

Chapter 4 presents the results obtained from Statistical Parametric Mapping (SPM8) and Dynamic Causal Modelling (DCM10) analysis during the problem size tasks. These include Fixed Effect Analysis (FFX), Random Effect Analysis (RFX), Region of Interest (ROIs) and Effective Connectivity (EC) analysis. Discussion will be made based on i) FFX and RFX analysis as well as ROI analysis involving functional specialization of activated brain regions and ii) effective connectivity analysis demonstrating the interaction between regions of interest (ROIs) during single- and double-digit.

Chapter 5 presents the results obtained from SPM8 and DCM10 analysis carried out to discover the effect of Arithmetic Component. Discussion will be made based on both functional specialization of activated brain regions as well as the effective connectivity analysis demonstrating the interaction between ROIs during math computation and fact retrieval.

Chapter 6 concludes the thesis with a review of the objectives and their fulfilment, a summary of the work that has been accomplished, and recommended future work.

REFERENCES

- Abd Hamid, A. I., Yusoff, A. N., Mukari, S. Z.-M. S., & Mohamad, M. (2011). Brain Activation during Addition and Subtraction Tasks In-Noise and In-Quiet. *The Malaysian Journal of Medical Sciences : MJMS*, *18*(2), 3–15.
- Amaro, E., & Barker, G. J. (2006). Study design in fMRI: basic principles. *Brain and Cognition*, *60*(3), 220–232.
- Ambady, N., & Bharucha, J. (2009). Culture and the Brain. *Current Directions in Psychological Science*, *18*(6), 342–345.
- Anderson, J. R., Betts, S., Ferris, J. L., & Fincham, J. M. (2011). Cognitive and metacognitive activity in mathematical problem solving: prefrontal and parietal patterns. *Cognitive, Affective & Behavioral Neuroscience*, *11*(1), 52–67.
- Ansari, D., & Dhital, B. (2006). Age-related changes in the activation of the intraparietal sulcus during nonsymbolic magnitude processing: an event-related functional magnetic resonance imaging study. *Journal of Cognitive Neuroscience*, *18*(2004), 1820–1828.
- Ansari, D., Fugelsang, J. a, Dhital, B., & Venkatraman, V. (2006). Dissociating response conflict from numerical magnitude processing in the brain: an event-related fMRI study. *NeuroImage*, *32*(2), 799–805.
- Ansari, D., Garcia, N., Lucas, E., Hamon, K., & Dhital, B. (2005). Neural correlates of symbolic number processing in children and adults. *Neuroreport*, *16*(16), 1769–1773.
- Arsalidou, M., & Taylor, M. J. (2011). Is $2+2=4$? Meta-analyses of brain areas needed for numbers and calculations. *NeuroImage*, *54*(3), 2382–2393.
- Ashcraft, M. H. (1992). Cognitive arithmetic: a review of data and theory. *Cognition*.
- Babajani, A., Soltanian-zadeh, H., & Member, S. (2006). Integrated MEG / EEG and fMRI Model Based on Neural Masses, *53*(7), 1794–1801.
- Barrouillet, P., Mignon, M., & Thevenot, C. (2008). Strategies in subtraction problem solving in children. *Journal of Experimental Child Psychology*, *99*(4), 233–251.

- Bartolomeo, P., Thiebaut de Schotten, M., & Chica, A. B. (2012). Brain networks of visuospatial attention and their disruption in visual neglect. *Frontiers in Human Neuroscience*, 6(May), 1–10.
- Bongard, S., & Nieder, A. (2010). Basic mathematical rules are encoded by primate prefrontal cortex neurons. *Proceedings of the National Academy of Sciences of the United States of America*, 107(5), 2277–2282.
- Büchel, C., & Friston, K. J. (1991). Effective connectivity and neuroimaging, 1–18.
- Buckner, R. L. (1998). Event-related fMRI and the hemodynamic response. *Human Brain Mapping*, 6(5-6), 373–377.
- Burbaud, P., Camus, O., Guehl, D., Bioulac, B., Caillé, J., & Allard, M. (2000). Influence of cognitive strategies on the pattern of cortical activation during mental subtraction. A functional imaging study in human subjects. *Neuroscience Letters*, 287(1), 76–80.
- Burbaud, P., Camus, O., Guehl, D., Bioulac, B., Caillé, J. M., & Allard, M. (1999). A functional magnetic resonance imaging study of mental subtraction in human subjects. *Neuroscience Letters*, 273(3), 195–199.
- Burbaud, P., Müller, E., Guehl, D., Franconi, J. M., Degr, P., Lafon, P., ... Allard, M. (1995). Differential Prefrontal and Parietal Activation in Numeric Working Memory and Calculation Procedures : a Functional Magnetic Resonance Imaging Study . *Magnetic Resonance Imaging*, 74(5), 2200.
- Butterworth, B., Reeve, R., Reynolds, F., & Lloyd, D. (2008). Numerical thought with and without words: Evidence from indigenous Australian children. *Proceedings of the National Academy of Sciences of the United States of America*, 105(35), 13179–13184.
- Buxton, R. B., Wong, E. C., & Frank, L. R. (1998). Dynamics of Blood Flow and Oxygenation Changes During Brain Activation : The Balloon Model, (17), 855–864.
- Campbell, J. I., & Xue, Q. (2001). Cognitive arithmetic across cultures. *Journal of Experimental Psychology. General*, 130(2), 299–315.
- Cantlon, J. F., Libertus, M. E., Pinel, P., Dehaene, S., Brannon, E. M., & Pelphrey, K. a. (2009). The neural development of an abstract concept of number. *Journal of Cognitive Neuroscience*, 21, 2217–2229.
- Cappelletti, M., Muggleton, N., & Walsh, V. (2009). Quantity without numbers and

- numbers without quantity in the parietal cortex. *NeuroImage*, 46(2), 522–9.
- Castelli, F., Glaser, D. E., & Butterworth, B. (2006). Discrete and analogue quantity processing in the parietal lobe: a functional MRI study. *Proceedings of the National Academy of Sciences of the United States of America*, 103(12), 4693–8.
- Chee, M. W., Tan, E. W., & Thiel, T. (1999). Mandarin and English single word processing studied with functional magnetic resonance imaging. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, 19(8), 3050–6.
- Chen, C. L., Wu, T. H., Cheng, M. C., Huang, Y. H., Sheu, C. Y., Hsieh, J. C., & Lee, J. S. (2006). Prospective demonstration of brain plasticity after intensive abacus-based mental calculation training: An fMRI study. *Nuclear Instruments and Methods in Physics Research Section A: Accelerators, Spectrometers, Detectors and Associated Equipment*, 569(2), 567–571.
- Chen, F., Hu, Z., Zhao, X., Wang, R., Yang, Z., Wang, X., & Tang, X. (2006). Neural correlates of serial abacus mental calculation in children: a functional MRI study. *Neuroscience Letters*, 403(1-2), 46–51.
- Chen, H., Yao, D., & Chen, L. (2002). A new method for detecting brain activities from fMRI dataset. *Science And Technology*, 48, 1047–1052.
- Chochon, F., Cohen, L., van de Moortele, P. F., & Dehaene, S. (1999). Differential contributions of the left and right inferior parietal lobules to number processing. *Journal of Cognitive Neuroscience*, 11(6), 617–630.
- Cohen Kadosh, R., Henik, A., Rubinsten, O., Mohr, H., Dori, H., van de Ven, V., and Linden, D. E. J. (2005). Are numbers special? The comparison systems of the human brain investigated by fMRI. *Neuropsychologia*, 43(9), 1238–1248.
- Cowell, S. F., Egan, G. F., Code, C., Harasty, J., & Watson, J. D. (2000). The functional neuroanatomy of simple calculation and number repetition: A parametric PET activation study. *NeuroImage*, 12(5), 565–573.
- Crollen, V., Seron, X., & Noël, M.-P. (2011). Is Finger-counting Necessary for the Development of Arithmetic Abilities? *Frontiers in Psychology*, 2(September), 242.
- Dagenbach, D. and McCloskey, M. (1992). The organization of arithmetic facts in memory: evidence from a brain-damaged patient. *Brain and Cognition*, 20(2), 345–66.

- Dehaene, S. (1999). Sources of Mathematical Thinking: Behavioral and Brain-Imaging Evidence. *Science*, 284(5416), 970–974.
- Dehaene, S., Molko, N., Cohen, L. and Wilson, A. J. (2004). Arithmetic and the brain. *Current Opinion in Neurobiology*, 14(2), 218–24.
- Dehaene, S., Piazza, M., Pinel, P. and Cohen, L. (2003a). Three parietal circuits for number processing. *Cognitive Neuropsychology*, 20(3), 487–506.
- Dehaene, S., Tzourio, N., Frak, V., Raynaud, L., Cohen, L., Mehler, J. and Mazoyer, B. (1996). Cerebral activations during number multiplication and comparison: a PET study. *Neuropsychologia*, 34(11), 1097–1106.
- Delazer, M., Ischebeck, a, Domahs, F., Zamarian, L., Koppelstaetter, F., Siedentopf, C. M. and Felber, S. (2005). Learning by strategies and learning by drill--evidence from an fMRI study. *NeuroImage*, 25(3), 838-849.
- Deshpande, G., Hu, X., Stilla, R. and Sathian, K. (2008). Effective connectivity during haptic perception: a study using Granger causality analysis of functional magnetic resonance imaging data. *NeuroImage*, 40(4), 1807–14.
- DeYoe, E. a., Bandettini, P., Neitz, J., Miller, D. and Winans, P. (1994). Functional magnetic resonance imaging (fMRI) of the human brain. *Journal of Neuroscience Methods*, 54, 171–187.
- Eickhoff, S. B., Heim, S., Zilles, K., & Amunts, K. (2009). A systems perspective on the effective connectivity of overt speech production. *Philosophical Transactions. Series A, Mathematical, Physical, and Engineering Sciences*, 367(1896), 2399–421.
- Emerson, R. W. and Cantlon, J. F. (2012). Early math achievement and functional connectivity in the fronto-parietal network. *Developmental Cognitive Neuroscience*, 2 Suppl 1, S139–51.
- Enno, K. and Roebroeck, A. (2012). NeuroImage A short history of causal modeling of fMRI data. *NeuroImage*.
- Fehr, T., Code, C. and Herrmann, M. (2007). Common brain regions underlying different arithmetic operations as revealed by conjunct fMRI-BOLD activation. *Brain Research*, 1172, 93–102.
- F.Krueger, M.V.Spampinato and J.Grafman. (2009). Integral calculus problem solving : An fMRI investigation, 19(11), 1095–1099.
- Frackowiak, R. S. J. (1995). Statistical Parametric Maps in Functional Imaging : A

General Linear Approach.

- Freeman, W. J., Ahlfors, S. P. and Menon, V. (2009). Combining fMRI with EEG and MEG in order to relate patterns of brain activity to cognition. *International Journal of Psychophysiology : Official Journal of the International Organization of Psychophysiology*, 73(1), 43–52.
- Friston, K. J. (1994). Functional and effective connectivity in neuroimaging: A synthesis. *Human Brain Mapping*, 2(1-2), 56–78.
- Friston, K. J., Harrison, L., & Penny, W. (2003). Dynamic causal modelling. *NeuroImage*, 19(4), 1273–1302.
- Friston, K. J., Holmes, a P., Price, C. J., Büchel, C. and Worsley, K. J. (1999). Multisubject fMRI studies and conjunction analyses. *NeuroImage*, 10(4), 385–396.
- Friston, K. J., Holmes, a P., Worsley, K. J., Poline, J.-P., Frith, C. D. and Frackowiak, R. S. J. (1995). Statistical parametric maps in functional imaging: A general linear approach. *Human Brain Mapping*, 2(4), 189–210.
- Friston, K. J., Zarahn, E., Josephs, O., Henson, R. N. and Dale, a M. (1999). Stochastic designs in event-related fMRI. *NeuroImage*, 10(5), 607–619.
- Gilmore, C. (2006). Profiles of understanding and profiles of development in early arithmetic. *Proceedings of the British Society Ino Learning Mathematics*, 26(November), 7–12.
- Gore, J. C. (2003). Principles and practice of functional MRI of the human brain. *The Journal of Clinical Investigation*, 112(1), 4–9.
- Grabner, R. H., Ansari, D., Koschutnig, K., Reishofer, G., Ebner, F. and Neuper, C. (2009). To retrieve or to calculate? Left angular gyrus mediates the retrieval of arithmetic facts during problem solving. *Neuropsychologia*, 47(2), 604–608.
- Grabner, R. H., Ansari, D., Reishofer, G., Stern, E., Ebner, F. and Neuper, C. (2007). Individual differences in mathematical competence predict parietal brain activation during mental calculation, 38, 346–356.
- Grefkes, C., Eickhoff, S. B., Nowak, D. a, Dafotakis, M. and Fink, G. R. (2008). Dynamic intra- and interhemispheric interactions during unilateral and bilateral hand movements assessed with fMRI and DCM. *NeuroImage*, 41(4), 1382–1394.
- Grünling, C., Ligges, M., Huonker, R., Klingert, M., Mentzel, H.-J., Rzanny, R., ... Blanz, B. (2004). Dyslexia: the possible benefit of multimodal integration of

- fMRI- and EEG-data. *Journal of Neural Transmission (Vienna, Austria : 1996)*, 111(7), 951–969.
- Gut, J., Heckmann, C., Meyer, C. S., Schmid, M. and Grob, A. (2012). Language skills, mathematical thinking, and achievement motivation in children with ADHD, disruptive behavior disorders, and normal controls. *Learning and Individual Differences*, 22(3), 375–379.
- Hanakawa, T., Honda, M., Okada, T., Fukuyama, H. and Shibasaki, H. (2003a). Differential activity in the premotor cortex subdivisions in humans during mental calculation and verbal rehearsal tasks: a functional magnetic resonance imaging study. *Neuroscience Letters*, 347(3), 199–201.
- Hanakawa, T., Honda, M., Okada, T., Fukuyama, H., and Shibasaki, H. (2003b). Neural correlates underlying mental calculation in abacus experts: a functional magnetic resonance imaging study. *NeuroImage*, 19(2), 296–307.
- Harrison, L., Penny, W. ., & Friston, K. (2003). Multivariate autoregressive modeling of fMRI time series. *NeuroImage*, 19(4), 1477–1491.
- Horwitz, B. (2003). The elusive concept of brain connectivity. *NeuroImage*, 19, 466–470.
- Hugdahl, K., Ph, D., Rund, B. R., Lund, A., Asbjørnsen, A., Egeland, J. and Thomsen, T. (2004). Brain Activation Measured With fMRI During a Mental Arithmetic Task in Schizophrenia and Major Depression, (February), 286–293.
- Ischebeck, A., Zamarian, L., Siedentopf, C., Koppelstätter, F., Benke, T., Felber, S., & Delazer, M. (2006). How specifically do we learn? Imaging the learning of multiplication and subtraction. *NeuroImage*, 30(4), 1365–1375.
- Izzetoglu, M., Izzetoglu, K., Bunce, S., Ayaz, H., Devaraj, A., Onaral, B., and Pourrezaei, K. (2005). Functional near-infrared neuroimaging. *IEEE Transactions on Neural Systems and Rehabilitation Engineering : A Publication of the IEEE Engineering in Medicine and Biology Society*, 13(2), 153–159.
- Janeiro, R. De, Zylberberg-landeira, R., & Charchat-fichman, H. (n.d.). Working Memory and Mathematical Thinking : A Cognitive and Affective Neuroscience Approach, 5(2), 65 - 88.
- Jeanette A. Mumford (2012), A power calculation guide for fMRI, *Scan*, 7, 738 - 742
- Jiao, Q., Lu, G., Zhang, Z., Zhong, Y., Wang, Z., Guo, Y., and Liu, Y. (2011). Granger causal influence predicts BOLD activity levels in the default mode network.

Human Brain Mapping, 32(1), 154–161.

- Jost, K., Khader, P. H., Burke, M., Bien, S., and Rösler, F. (2011). Frontal and parietal contributions to arithmetic fact retrieval: a parametric analysis of the problem-size effect. *Human Brain Mapping*, 32(1), 51–59.
- Kamal, N. F., Othman, M. F., and Zulkifli, N. A. (2013). Developing fMRI Protocol for Mathematics Working Memory Functions: Block Paradigm. *Procedia - Social and Behavioral Sciences*, 97, 561–565.
- Kaufmann, L., Vogel, S. E., Starke, M., Kremser, C., and Schocke, M. (2009). Numerical and non-numerical ordinality processing in children with and without developmental dyscalculia: Evidence from fMRI. *Cognitive Development*, 24(4), 486–494.
- Kawashima, R., Taira, M., Okita, K., Inoue, K., Tajima, N., Yoshida, H. and Fukuda, H. (2004). A functional MRI study of simple arithmetic—a comparison between children and adults. *Cognitive Brain Research*, 18(3), 227–233.
- Kim, S.-G., & Ugurbil, K. (1997). Functional magnetic resonance imaging of the human brain. *Journal of Neuroscience Methods*, 74, 229–243.
- Klein, E., Moeller, K., Glauche, V., Weiller, C., & Willmes, K. (2013). Processing pathways in mental arithmetic—evidence from probabilistic fiber tracking. *PLoS One*, 8(1), e55455.
- Kong, J., Wang, C., Kwong, K., Vangel, M., Chua, E., & Gollub, R. (2005). The neural substrate of arithmetic operations and procedure complexity. *Brain Research. Cognitive Brain Research*, 22(3), 397–405.
- Krueger, F., Landgraf, S., Meer, E. Van Der, Deshpande, G., Hu, X., Neuroscience, M., ... Vi, P. (2011). Effective Connectivity of the Multiplication Network : A Functional MRI and Multivariate Granger Causality Mapping Study, 1431(June 2010), 1419–1431.
- Kucian, K., Aster, M. Von, Dietrich, T., Martin, E., Red, G., & Hospitals, C. (2008). Developmental Neuropsychology Development of Neural Networks for Exact and Approximate Calculation : A fMRI Study. *Children*, (February 2012), 447–473.
- LeFevre, J.-A., Smith-Chant, B. L., Fast, L., et al. (2006). What counts as knowing? The development of conceptual and procedural knowledge of counting from kindergarten through grade 2. *Journal of Experimental Child Psychology*, 93, 285

- 303. doi: 10.1016/j.jecp.2005.11.002

- Lin, J.-F. L., Imada, T., & Kuhl, P. K. (2012). Mental addition in bilinguals: an fMRI study of task-related and performance-related activation. *Cerebral Cortex (New York, N.Y. : 1991)*, 22(8), 1851–1861.
- Lindquist, M. a. (2008). The Statistical Analysis of fMRI Data. *Statistical Science*, 23(4), 439–464.
- Liu, Z., Bai, L., Dai, R., Zhong, C., Wang, H., You, Y., ... Tian, J. (2012). Exploring the effective connectivity of resting state networks in Mild Cognitive Impairment: An fMRI study combining ICA and multivariate Granger causality analysis. *2012 Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 5454–5457.
- Logothetis, N. K. (2002). The neural basis of the blood-oxygen-level-dependent functional magnetic resonance imaging signal. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, 357(1424), 1003–1037.
- Logothetis, N. K., Pauls, J., Augath, M., Trinath, T., & Oeltermann, a. (2001). Neurophysiological investigation of the basis of the fMRI signal. *Nature*, 412(6843), 150–157.
- Long, C. (2011). Maths concepts in teaching: Procedural and conceptual knowledge. *Pythagoras*, 0(62), 59–65.
- Trans Cranial Technology. (2012). Cortical Functions, *Reference*, 1-66.
- Mann, A. R., & Mann, A. (2013). The Experiences of Mothers of Children with Autism in Jamaica : An Exploratory Study of Their Journey by, (January).
- Marco, G. De, Devauchelle, B., & Berquin, P. (2009). Brain functional modeling , what do we measure with fMRI data ?, *64*, 12–19.
- Marco, G. De, Picardie, U. De, & Verne, J. (2009). Effective Connectivity and Brain Modeling by fMRI. *Advanced Studies in Biology*, 1(3), 139–144.
- McCloskey, M., Caramazza, a, & Basili, a. (1985). Cognitive mechanisms in number processing and calculation: evidence from dyscalculia. *Brain and Cognition*, 4(2), 171–196.
- McIntosh, a R. (2000). Towards a network theory of cognition. *Neural Networks : The Official Journal of the International Neural Network Society*, 13(8-9), 861–870.
- McLeod, S.A (2014), Sampling Methods.

<http://www.simplypsychology.org/sampling.html>

- Menon, V., Mackenzie, K., Rivera, S. M., & Reiss, A. L. (2002). Prefrontal Cortex Involvement in Processing Incorrect Arithmetic Equations: Evidence From Event-Related fMRI, *130*(January), 119–130.
- Menon, V., Rivera, S. M., White, C. D., Glover, G. H., & Reiss, a L. (2000). Dissociating prefrontal and parietal cortex activation during arithmetic processing. *NeuroImage*, *12*(4), 357–365.
- MOHAMAD, M. (2012). KAJIAN FMRI KE ATAS PENGKHUSUSAN KEFUNGSIAN DAN KEHUBUNGAN EFEKTIK OTAK DI KALANGAN SUBJEK HILANG PENDENGARAN UNILATERAL. *Thesis Dissertation*.
- Molko, N., Cachia, a, Riviere, D., Mangin, J. F., Bruandet, M., LeBihan, D., ... Dehaene, S. (2004). Brain anatomy in Turner syndrome: evidence for impaired social and spatial-numerical networks. *Cerebral Cortex (New York, N.Y. : 1991)*, *14*(8), 840–850.
- Ngan Ng, S. S., & Rao, N. (2010). Chinese Number Words, Culture, and Mathematics Learning. *Review of Educational Research*, *80*(2), 180–206.
- Nieder, A. (2009). Prefrontal cortex and the evolution of symbolic reference. *Current Opinion in Neurobiology*, *19*, 99–108.
- Nieder, A., & Dehaene, S. (2009). Representation of Number in the Brain.
- Park, J., Park, D. C., & Polk, T. a. (2012). Parietal Functional Connectivity in Numerical Cognition. *Cerebral Cortex (New York, N.Y. : 1991)*, 1–9. doi:10.1093/cercor/bhs193
- Park, J., Park, D. C., & Polk, T. a. (2013). Parietal functional connectivity in numerical cognition. *Cerebral Cortex*, *23*(September), 2127–2135.
- Passolunghi, M. C., & Pazzaglia, F. (2004). Individual differences in memory updating in relation to arithmetic problem solving. *Learning and Individual Differences*, *14*(4), 219–230.
- Penny, W. D., Stephan, K. E., Daunizeau, J., Rosa, M. J., Friston, K. J., Schofield, T. M., & Leff, A. P. (2010). Comparing families of dynamic causal models. *PLoS Computational Biology*, *6*(3).
- Penny, W. D., Stephan, K. E., Mechelli, a, & Friston, K. J. (2004). Modelling functional integration: a comparison of structural equation and dynamic causal models. *NeuroImage*, *23 Suppl 1*, S264–274.

- Penny, W., & Holmes, a. (2003). Random-Effects Analysis. *Human Brain Function: Second Edition*, 843–850.
- Pinel, P., & Dehaene, S. (2013). Genetic and environmental contributions to brain activation during calculation. *NeuroImage*, *81*, 306–316.
- Plis, S. M., Weisend, M. P., Damaraju, E., Eichele, T., Mayer, A., Clark, V. P., ... Calhoun, V. D. (2011). Effective connectivity analysis of fMRI and MEG data collected under identical paradigms. *Computers in Biology and Medicine*, *41*(12), 1156–1165.
- Poldrack, R. a. (2007). Region of interest analysis for fMRI. *Social Cognitive and Affective Neuroscience*, *2*(1), 67–70.
- Prabhakaran, V., Smith, J. A. L., Desmond, J. E., Glover, G. H., & Gabrieli, J. D. E. (1997). Neural Substrates of Fluid Reasoning : An fMRI Study of Neocortical Activation during Performance of the Raven ' s Progressive Matrices Test, *63*, 43–63.
- Price, G. R., Mazzocco, M. M. M., & Ansari, D. (2013). Why mental arithmetic counts: brain activation during single digit arithmetic predicts high school math scores. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience*, *33*(1), 156–163.
- Ramnani, N., Behrens, T. E. J., Penny, W., & Matthews, P. M. (2004). New approaches for exploring anatomical and functional connectivity in the human brain. *Biological Psychiatry*, *56*(9), 613–619.
- Rasmussen, C., & Bisanz, J. (2005). Representation and working memory in early arithmetic. *Journal of Experimental Child Psychology*, *91*(2), 137–157.
- Rickard, T. C., Romero, S. G., Basso, G., Wharton, C., Flitman, S., & Grafman, J. (2000). The calculating brain: an fMRI study. *Neuropsychologia*, *38*(3), 325–335.
- Rivera, S. M., Menon, V., White, C. D., Glaser, B., & Reiss, A. L. (2002). Functional brain activation during arithmetic processing in females with fragile X Syndrome is related to FMR1 protein expression. *Human Brain Mapping*, *16*(4), 206–218.
- Rivera, S. M., Reiss, a L., Eckert, M. a, & Menon, V. (2005). Developmental changes in mental arithmetic: evidence for increased functional specialization in the left inferior parietal cortex. *Cerebral Cortex (New York, N.Y. : 1991)*, *15*(11), 1779–1790.
- Rocha, F. T., Rocha, a F., Massad, E., & Menezes, R. (2005). Brain mappings of the

- arithmetic processing in children and adults. *Brain Research. Cognitive Brain Research*, 22(3), 359–372.
- Roland, P. E., & Friberg, L. (1985). Localization of cortical areas activated by thinking. *Journal of Neurophysiology*, 53(5), 1219–1243.
- Rosenberg-Lee, M., Barth, M., & Menon, V. (2011). What difference does a year of schooling make? Maturation of brain response and connectivity between 2nd and 3rd grades during arithmetic problem solving. *NeuroImage*, 57(3), 796–808.
- Rypma, B., & D'Esposito, M. (1999). The roles of prefrontal brain regions in components of working memory: Effects of memory load and individual differences. *Proceedings of the National Academy of Sciences of the United States of America*, 96(May), 6558–6563.
- Rönnqvist, L., & Rösblad, B. (2007). Kinematic analysis of unimanual reaching and grasping movements in children with hemiplegic cerebral palsy. *Clinical Biomechanics*, 22(2), 165–175.
- Savoy, R. L., & Ph, D. (n.d.). Functional Magnetic Resonance Imaging (fMRI) resonance imaging (MRI) to detect the localized changes in blood flow and blood oxygenation that, 1–21.
- Schmithorst, V. J., & Brown, R. D. (2004). Empirical validation of the triple-code model of numerical processing for complex math operations using functional MRI and group Independent Component Analysis of the mental addition and subtraction of fractions. *NeuroImage*, 22(3), 1414–1420.
- Singh, M., Kim, S., & Kim, T.-S. (2003). Correlation between BOLD-fMRI and EEG signal changes in response to visual stimulus frequency in humans. *Magnetic Resonance in Medicine : Official Journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*, 49(1), 108–114.
- Smith, S. M. (2004). Overview of fMRI analysis. *British Journal of Radiology*, 77(suppl_2), S167–S175.
- Smith, S. M. (2012). The future of FMRI connectivity. *NeuroImage*, 62(2), 1257–66.
- Springer, J. a., Binder, J. R., Hammeke, T. a., Swanson, S. J., Frost, J. a., Bellgowan, P. S. F., ... Mueller, W. M. (1999). Language dominance in neurologically normal and epilepsy subjects. A functional MRI study. *Brain*, 122(11), 2033–2045.
- Stanescu-Cosson, R., Pinel, P., van De Moortele, P. F., Le Bihan, D., Cohen, L., &

- Dehaene, S. (2000). Understanding dissociations in dyscalculia: a brain imaging study of the impact of number size on the cerebral networks for exact and approximate calculation. *Brain : A Journal of Neurology*, *123* (Pt 1, 2240–2255.
- Stephan, K. E., Penny, W. D., Daunizeau, J., Moran, R. J., & Friston, K. J. (2009). Bayesian model selection for group studies. *NeuroImage*, *46*(4), 1004–1017.
- Stephan, K. E., Penny, W. D., Moran, R. J., den Ouden, H. E. M., Daunizeau, J., & Friston, K. J. (2010). Ten simple rules for dynamic causal modeling. *NeuroImage*, *49*(4), 3099–3109.
- Stevens, M. C. (2009). The developmental cognitive neuroscience of functional connectivity. *Brain and Cognition*, *70*(1), 1–12.
- Sumiyoshi, A., Riera, J. J., Ogawa, T., & Kawashima, R. (2011). A mini-cap for simultaneous EEG and fMRI recording in rodents. *NeuroImage*, *54*(3), 1951–1965.
- Tang, Y., Zhang, W., Chen, K., Feng, S., Ji, Y., Shen, J., ... Liu, Y. (2006). Arithmetic processing in the brain shaped by cultures. *Proceedings of the National Academy of Sciences of the United States of America*, *103*(28), 10775–10780.
- Tsang, J. M., Dougherty, R. F., Deutsch, G. K., Wandell, B. a, & Ben-Shachar, M. (2009). Frontoparietal white matter diffusion properties predict mental arithmetic skills in children. *Proceedings of the National Academy of Sciences of the United States of America*, *106*(52), 22546–22551.
- Tschentscher, N., & Hauk, O. (2014). How are things adding up? Neural differences between arithmetic operations are due to general problem solving strategies. *NeuroImage*, *92*, 369–380.
- Tschentscher, N., Hauk, O., Fischer, M. H., & Pulvermüller, F. (2012). You can count on the motor cortex: Finger counting habits modulate motor cortex activation evoked by numbers. *NeuroImage*, *59*(4), 3139–3148.
- Veroude, K., Norris, D. G., Shumskaya, E., Gullberg, M., & Indefrey, P. (2010). Functional connectivity between brain regions involved in learning words of a new language. *Brain and Language*, *113*(1), 21–27.
- Vukovic, R. K., & Lesaux, N. K. (2013). The relationship between linguistic skills and arithmetic knowledge. *Learning and Individual Differences*, *23*, 87–91.
- Wei, W., Lu, H., Zhao, H., Chen, C., Dong, Q., & Zhou, X. (2012). Gender differences in children's arithmetic performance are accounted for by gender differences in

- language abilities. *Psychological Science*, 23(3), 320–330.
- William D. Penny, Karl J. Friston, John T. Ashburner, Stefan J. Kiebel and Thomas E. Nichols (2007), *Statistical Parametric Mapping: The Analysis of Functional Brain Images* (1st Edition), Elsevier Ltd
- Yoo, J. J., Hinds, O., Ofen, N., Thompson, T. W., Whitfield-Gabrieli, S., Triantafyllou, C., & Gabrieli, J. D. E. (2012). When the brain is prepared to learn: enhancing human learning using real-time fMRI. *NeuroImage*, 59(1), 846–852.
- Yu, J., Pan, Y., Ang, K. K., Guan, C., & Leamy, D. J. (2012). Prefrontal cortical activation during arithmetic processing differentiated by cultures: a preliminary fNIRS study. *Conference Proceedings: ... Annual International Conference of the IEEE Engineering in Medicine and Biology Society. IEEE Engineering in Medicine and Biology Society. Annual Conference, 2012*, 4716–4719.
- Zago, L., Pesenti, M., Mellet, E., Crivello, F., Mazoyer, B., & Tzourio-Mazoyer, N. (2001). Neural correlates of simple and complex mental calculation. *NeuroImage*, 13(2), 314–327.
- Zago, L., Petit, L., Turbelin, M.-R., Andersson, F., Vigneau, M., & Tzourio-Mazoyer, N. (2008). How verbal and spatial manipulation networks contribute to calculation: an fMRI study. *Neuropsychologia*, 46(9), 2403–2414.
- Zamarian, L., Ischebeck, a, & Delazer, M. (2009). Neuroscience of learning arithmetic--evidence from brain imaging studies. *Neuroscience and Biobehavioral Reviews*, 33(6), 909–925.
- Zilles, K., & Amunts, K. (2010). Centenary of Brodmann's map - conception and fate. *Nature Reviews. Neuroscience*, 11(3), 139 – 145.
- Zbrodoff, N. J., and Logan, G. D. 1990. On the relation between production and verification tasks in the psychology of simple arithmetic. *J. Exp. Psychol. Learn. Mem. Cogn.* 16: 97-105