

Copyright is owned by the Author of the thesis. Permission is given for a copy to be downloaded by an individual for the purpose of research and private study only. The thesis may not be reproduced elsewhere without the permission of the Author.

**The Blue Brain: Hemispheric Asymmetry in Depression as
an Explanation for Working Memory Impairment**

A thesis presented in partial fulfilment of the requirements for the degree of

Doctor of Philosophy

In Psychology

At Massey University, Manawatu,

New Zealand

Kathryn Campbell

2015

*"If you immediately know the candlelight is fire, then the meal was cooked a long time ago."
– Oma Desala*

To Colin, my rock, for always helping me to see the big picture.

Abstract

Due to substantial variability in past research regarding the cognitive and neurobiological correlates of depression, the current study investigated whether taking the possible relationship between asymmetric brain activity and cognitive impairment into account would help to clarify the matter. A total of 78 participants including 36 currently depressed, 11 previously depressed, and 31 never depressed participants, completed three mood questionnaires (Beck Depression Inventory, Hamilton Depression Inventory Short-Form, and the State-Trait Anxiety Inventory), and four working memory tasks (a spatial and verbal variant of both the N-back and complex span task). All participants had their resting brain activity recorded using an electroencephalogram. It was hypothesised that depressed participants would show relatively reduced left frontal activity, since left frontal activity is linked to positive affect and approach motivation, and that participants with depression but low levels of anxiety would show reduced right parietal activity while those with high anxiety would show increased right parietal activity due to the role of the right parietal area in arousal. These hypotheses were not supported as there were no differences in asymmetry scores between the currently depressed and the never depressed groups. However, investigation of this hypothesis was hindered by the high comorbidity of anxiety and depression making it impossible to disentangle the effects of depression and anxiety on parietal activity. It was also hypothesised that participants with depression would show impaired working memory with disproportionate impairment in the verbal working memory tasks that are thought to utilise left frontal brain activity. There was no clear support for this hypothesis. In fact, there was a trend toward improved performance possibly related to increased attention to detail due to activation of stress systems signalling a potential threat in the environment. A final hypothesis was that there would be an association between different patterns of brain activity and WM impairment but no association was found. These results highlight problems with research in this field including the conceptualisation and measurement of depression and cognitive performance as well as problems distinguishing between anxiety and depression. Future research needs to address these issues.

Acknowledgements

I would like to express my heartfelt gratitude to everyone who has helped me along this journey.

First and foremost, I would like to extend a sincere thanks to my supervisors Dr Stephen Hill and Associate Professor John Podd. Their continued support, patience, and generosity in sharing their knowledge throughout this research has been invaluable.

Secondly, I would like to acknowledge the ongoing assistance of Malcolm Loudon who was instrumental in setting up the EEG systems and programming of the cognitive tasks. Thanks to Hung Ton for assisting me in obtaining access to the inventories.

A special thanks also goes to Dr Annette Henricksen for her assistance in data collection and her continued moral support.

The support from the graduate assistant and alumni group has been fantastic in providing encouragement, reminding me to maintain a balanced lifestyle during this process, and for volunteering to act as guinea-pigs during EEG pilot testing. Thanks Ann, Annette, Maria, Geneva, Steph, Mel, Ross, and Sarah.

Thanks to the Health and Disability Ethics Committee (HDEC) for providing ethical approval for this research (Reference: CEN/11/EXP/002)

Finally, without the continued support and strength of my family, friends, and my partner Colin, this thesis would never have reached completion.

Table of Contents

| | |
|--|------|
| <i>Dedication</i> | iii |
| <i>Abstract</i> | v |
| <i>Acknowledgements</i> | vii |
| <i>Table of Contents</i> | ix |
| <i>Appendix List</i> | xiii |
| <i>List of Tables</i> | xv |
| <i>List of Figures</i> | xvii |
| | |
| Introduction | 1 |
| Chapter 1- A Brief Review of Depression | 2 |
| Symptoms of Depression | 3 |
| Subtypes of Depression | 5 |
| Comorbidity of Anxiety and Depression | 10 |
| Prevalence of Depression | 12 |
| Genetics and Depression | 15 |
| Biomarkers of Depression | 17 |
| | |
| Chapter 2- Brain Activity in Depression | 19 |
| Models of Emotion | 19 |
| Right Hemisphere Model of Emotion | 19 |
| Valence Model of Emotion | 22 |

| | |
|---|-----------|
| Motivational Model of Emotion | 24 |
| Circumplex Model of Emotion | 25 |
| Asymmetrical Brain Activity in Depression | 26 |
| Frontal Asymmetry | 26 |
| Posterior Asymmetry | 35 |
| Persistence of Asymmetric Brain Activity | 37 |
| What does the Asymmetry Represent? | 40 |
| Subcortical Abnormalities in Depression | 41 |
| Usefulness of Asymmetric Metrics in Treating Depression | 42 |
| Chapter 3- Cognitive Impairment in Depression | 45 |
| Self-Reported Impairment | 45 |
| Objective Measurement of Cognitive Impairment | 46 |
| Theories of Cognitive Profiles in Depression | 46 |
| Specificity of Cognitive Impairment | 48 |
| Domains of Cognitive Impairment | 50 |
| Executive Function | 50 |
| Memory Impairment | 51 |
| Working Memory | 52 |
| Origin of Impairment | 55 |
| Persistence of Impairment Beyond Recovery | 58 |
| Cause of Inconsistencies | 60 |
| Chapter 4- The Missing Link: Abnormal Brain Activity in Depression as an | 65 |

Explanation for Cognitive Dysfunction

| | |
|---|----|
| The Relationship between Abnormal Brain Activity and Cognitive Impairment | 65 |
| Aims of the Current Study | 68 |
| Hypotheses of the Current Study | 70 |

Chapter 5- Method

| | |
|-------------------------|----|
| Participants | 73 |
| Materials and Procedure | 75 |
| Mood Questionnaires | 76 |
| BDI-II | 76 |
| HDI-SF | 77 |
| STAI | 77 |
| Working Memory Measures | 78 |
| N-back Tasks | 78 |
| Verbal Span Task | 80 |
| Spatial Span Task | 81 |
| CST Scoring | 82 |
| EEG Phase | 82 |
| EEG Recording | 82 |
| Debriefing | 85 |
| EEG Data Analysis | 86 |
| Storage of Data | 87 |
| Ethics | 87 |

Chapter 6- Results and Discussion

| | |
|--|-----|
| <i>Hypothesis 1: Participants With Depression Will Show Relatively Reduced</i> | 88 |
| Left Frontal Activity Compared With Control Participants | |
| <i>Hypothesis 2: Depressed Participants Without Comorbid Anxiety Will</i> | 101 |
| Show Reduced Parietal Activity | |
| <i>Hypothesis 3: Depressed Participants Will Perform Worse on Working</i> | 108 |
| Memory Tasks Than Control Participants With Disproportionate | |
| Impairment On Verbal Working Memory Tasks Due To Reduced Left | |
| Frontal Activity | |
| <i>Hypothesis 4: Working Memory Performance Will Be Related to Specific</i> | 117 |
| Patterns of Asymmetric Brain Activity. | |
| <i>Supplementary Results 1: A Comparison of Depression and Anxiety</i> | 126 |
| Inventories | |
| <i>Supplementary Results 2: Relationship between Working Memory Tasks</i> | 128 |
| | |
| Chapter 7- General Discussion | 131 |
| Summary of Key Findings | 131 |
| Measurement of Depression | 133 |
| Measurement of Working Memory | 141 |
| Measuring Brain Activity | 144 |
| Conclusions | 147 |
| | |
| References | 149 |

List of Appendices

| | |
|--|-----|
| Appendix A- Copy of Depression History Survey | 192 |
| Appendix B- Supplementary Descriptive Statistics | 193 |
| Appendix C- Data Distributions | 198 |
| Appendix D- A Comparison of Data Recorded on the Two EEG Systems | 203 |
| Appendix E- Epoch Analysis | 211 |
| Appendix F-Distribution of Depression and Anxiety Inventory Scores | 212 |

List of Tables

| | |
|--|-----|
| Table 1 <i>Pearson's Correlation Coefficients and Significance Levels for Correlations Between Depression Inventories and Medial and Lateral Frontal Asymmetry Scores</i> | 96 |
| Table 2 <i>Pearson's Correlations between Parietal Asymmetry Score and Depression/Anxiety Inventory Scores</i> | 102 |
| Table 3 <i>Partial Correlation between Depression Inventory Scores (BDI-II, HDI-SF) and Parietal Asymmetry Scores</i> | 103 |
| Table 4 <i>Pearson's Correlations between Depression Measures (BDI-II, HDI-SF) and Trait/State Anxiety Subscales of STAI</i> | 103 |
| Table 5 <i>Pearson's Correlations between z-Scores of Working Memory Task Performance and Depression and Anxiety Inventories</i> | 113 |
| Table 6 <i>ANOVA Results and Effect Sizes (f) for Comparison of Working Memory Test Scores between Currently, Never, and Previously Depressed Groups</i> | 114 |
| Table 7 <i>Pearson's Correlations between Lateral Frontal, Medial Frontal, and Parietal Asymmetry Scores, and z-Scores of Working Memory Task Performance</i> | 118 |
| Table 8 <i>Pearson's Correlation between Lateral Frontal, Medial Frontal, and Parietal Asymmetry Scores and Sensitivity (d') and Bias (c) for N-back Task Performance</i> | 119 |
| Table 9 <i>One-Way ANOVA Results Comparing Depressed and Control Right and Left Dominant Groups Mean z-Score Performance on Working Memory Measures</i> | 124 |
| Table 10 <i>Descriptive Statistics for Depression (BDI-II, HDI-SF) and Anxiety (State and Trait Subscales of STAI)</i> | 128 |
| Table 11 <i>Pearson's Correlations between Depression (BDI-II, HDI-SF) and Anxiety (State and Trait Subscales of STAI)</i> | 128 |
| Table 12 <i>Pearson's Correlations between Complex Span and N-back Measures</i> | 130 |

| | |
|--|-----|
| Table B-1 | 193 |
| <i>Descriptive Statistics for Asymmetry Metrics for Lateral and Medial Frontal Sites, and Parietal Site for Never, Currently, and Previously Depressed Groups</i> | |
| Table B-2 | 194 |
| <i>Descriptive Statistics for Never, Currently, and Previously Depressed Groups Split by EEG System for Both Medial And Lateral Frontal Asymmetry Scores</i> | |
| Table B-3 | 194 |
| <i>Descriptive Statistics for High and Low Anxiety Depressed Groups and Non-Depressed Group's Parietal Asymmetry Scores When Grouped Using State or Trait Anxiety Scores</i> | |
| Table B-4 | 195 |
| <i>Descriptive Statistics for Working Memory Task Performance (z-Scores) in Currently, Never, and Previously Depressed Groups</i> | |
| Table B-5 | 196 |
| <i>z-Score Working Memory Task Descriptive Statistics for Depressed and Control Groups Subtyped by Medial Frontal Asymmetry Scores</i> | |
| Table B-6 | 196 |
| <i>z-Score Working Memory Task Descriptive Statistics for Depressed and Control Groups Subtyped by Lateral Frontal Asymmetry Scores</i> | |
| Table B-7 | 197 |
| <i>z-Score Working Memory Task Descriptive Statistics for Depressed and Control Groups Subtyped by Parietal Asymmetry Scores</i> | |
| Table B-8 | 197 |
| <i>Descriptive Statistics for Depression and Anxiety Inventories in the Never, Currently, and Previously Depressed Groups</i> | |
| Table D-1 | 203 |
| <i>Descriptive Statistics for Comparison of Neuroscan and ADI EEG Recording Systems</i> | |
| Table D-2 | 207 |
| <i>Descriptive Statistics for Comparison of Neuroscan and ADI EEG Recording Systems With Extreme Scores Removed</i> | |
| Table D-3 | 208 |
| <i>Comparison of Left and Right Dominant Asymmetry Scores for Neuroscan and ADI Recording Systems for Medial, Lateral, and Parietal Recording Sites</i> | |

List of Figures

| | |
|---|-----|
| Figure 1 <i>Verbal N-back Task</i> | 79 |
| Figure 2 <i>Spatial Span Task</i> | 81 |
| Figure 3 <i>Differences in Mean Lateral Frontal Asymmetry Scores for Never, Currently, and Previously Depressed Groups with Cohen's d Effect Sizes from Tukey Test Comparisons Indicated. Error Bars Indicate ± 1 SD.</i> | 89 |
| Figure 4 <i>Differences in Mean Medial Frontal Asymmetry Scores for Never, Currently, and Previously Depressed Groups with Cohen's d Effect Sizes from Tukey Test Comparisons Indicated. Error Bars Indicate ± 1 SD.</i> | 90 |
| Figure 5. <i>Differences in Mean Parietal Asymmetry Scores for High State Anxiety, Low State Anxiety, and Never Depressed Groups with Cohen's d Effect Sizes from Tukey Test Comparisons Indicated. Error Bars Indicate ± 1 SD.</i> | 104 |
| Figure 6. <i>Differences in Mean Parietal Asymmetry Scores for High Trait Anxiety, Low Trait Anxiety, and Never Depressed Groups with Cohen's d Effect Sizes from Tukey Test Comparisons Indicated. Error Bars Indicate ± 1 SD.</i> | 105 |
| Figure 7. <i>Mean z-Scores for Never, Previously, and Currently Depressed Groups on Working Memory Tasks (Labelled Task 1-10).</i> | 111 |
| Figure 8. <i>z-Score Mean z-Scores for Left and Right Dominant Subgroups Based on Medial Frontal Asymmetry Scores for Working Memory Tasks (Labelled Task 1-10).</i> | 121 |
| Figure 9. <i>z-Score Mean z-Scores for Left and Right Dominant Subgroups Based on Lateral Frontal Asymmetry Scores for Working Memory Tasks (Labelled Task 1-10).</i> | 122 |
| Figure 10. <i>z-Score Mean z-Scores for Left and Right Dominant Subgroups Based on Parietal Asymmetry Scores for Working Memory Tasks (Labelled Task 1-10).</i> | 123 |
| Figure C-1 <i>Distribution of Medial Frontal Asymmetry Scores in the Never, Currently, and Previously Depressed Groups</i> | 198 |
| Figure C-2 <i>Distribution of Lateral Frontal Asymmetry Scores in the Never, Currently, and Previously Depressed Groups</i> | 199 |

| | |
|---|-----|
| Figure C-3 | 200 |
| <i>Distribution of Parietal Asymmetry Scores in the Never, Currently, and Previously Depressed Groups</i> | |
| Figure C-4 | 201 |
| <i>Distribution of Lateral Asymmetry Scores in the Low and High Depression Groups</i> | |
| Figure C-5 | 202 |
| <i>Distribution of Medial Asymmetry Scores in the Low and High Depression Groups</i> | |
| Figure D-1 | 204 |
| <i>A Comparison of the Distribution of Parietal Asymmetry Scores Recorded on the Neuroscan and ADI EEG Recording Systems</i> | |
| Figure D-2 | 206 |
| <i>A Comparison of the Distribution of Lateral Frontal Asymmetry Scores Recorded on the Neuroscan and ADI EEG Recording Systems</i> | |
| Figure D-3 | 207 |
| <i>A Comparison of the Distribution of Medial Frontal Asymmetry Scores Recorded on the Neuroscan and ADI EEG Recording Systems.</i> | |
| Figure D-4. | 208 |
| <i>A Comparison of Season of Collection for the Neuroscan and ADI EEG Systems.</i> | |
| Figure E-1 | 202 |
| <i>Frequency Distribution of Average Percentage of Epochs Retained for EEG Data</i> | |