

Cognitive functioning in chronic fatigue syndrome

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Thesis submitted for the degree of Doctor of Philosophy

October 2015

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Abstract

Chronic fatigue syndrome (CFS) involves long-standing and disabling fatigue of unknown aetiology that has a profound effect on a persons' ability to function in daily life. However, little is understood of the condition and many of the research findings are conflicting, making the treatment and identification of causes problematic. Aside from fatigue, problems with memory and concentration are reported to be amongst the most disabling symptoms; however cognitive testing has revealed ambiguous results, with numerous studies finding deficits and others not. Few studies have investigated how these problems impact on daily functioning. In the absence of a recognised cause for CFS, cognitive problems have been attributed to a range of factors - including psychiatric problems, reduced effort, fatigue and poor sleep - but the contribution of each of these variables to cognitive impairment is unknown.

This thesis was designed to clarify the type and magnitude of cognitive problems in CFS by undertaking a meta-analysis to examine the literature on cognitive testing (Chapter 3), which has previously only been summarised in narrative reviews. This was used to select the cognitive tests for a subsequent empirical study that investigated cognitive functioning in CFS, and explored factors that may influence impaired cognitive performance, specifically test effort (Chapter 4); motor slowing, psychological problems, fatigue and poor sleep, and also investigated factors that may be impacted by cognitive dysfunction, including everyday functioning, employment and mental fatigue (Chapter 5). Self-reported memory and attention problems form part of the CFS diagnostic criteria, consequently their relationship with memory and attention test results were also studied (Chapter 6). The results of these investigations have been published in four journal articles (Cockshell & Mathias, 2010, 2012, 2013, 2014).

The meta-analysis analysed data from fifty studies that had assessed cognitive performance in adults who had been diagnosed with CFS (using published criteria) and in healthy controls (Chapter 3; Cockshell & Mathias, 2010). Compared to their healthy peers, persons with CFS showed large deficits on tests of reaction time and moderate deficits on tests of attention, memory and motor functioning. Smaller deficits were found on tests of visuospatial ability, cognitive reasoning and flexibility, indicating subtle problems in these areas. Global functioning and verbal abilities were unaffected. These findings indicated that people with CFS have moderate to large impairments in simple and complex information processing speed, and on tasks that required the sustained use of working memory. Tests that assessed these impairments were then selected for use in an empirical study, as were tests on which the CFS group was not impaired, to enable the differentiation of specific impairments from global deficits due to fatigue and/or lack of effort.

The empirical study assessed 54 people with CFS and 54 age-, gender- and education- matched healthy controls on tests of reaction time, attention, memory, motor functioning, verbal and visuospatial abilities. All participants were additionally assessed for factors that may be related to cognitive impairment, which included a test of effort, a psychiatric interview (to screen for drug and alcohol abuse, and diagnose depressive and anxiety disorders), and questionnaire measures of psychological status (levels of depression and anxiety), CFS symptom severity, fatigue (prior, during and after the testing session), sleep quality, everyday functioning and self-reported problems with attention and memory.

The initial analysis focussed on test effort which was assessed using the Validity Indicator Profile (VIP), to determine the extent to which people with CFS were performing to the best of their ability to ensure that their cognitive test results could

be validly interpreted (Chapter 4; Cockshell & Mathias, 2012). The VIP identifies effort (high or low) and intention to perform well (or not) by analysing the pattern of responses, providing potential causes of poor performance. Four people in each group demonstrated an intention to perform well, but with reduced effort, possibly due to fatigue. Fifty people in each group demonstrated good effort, and only the results of this group were further analysed.

The cognitive performance of the CFS and controls was then examined, and those measures on which the CFS group performed poorly were correlated with psychological status, CFS symptomatology and everyday functioning (Chapter 5; Cockshell & Mathias, 2013). People with CFS were found to be impaired on tests of simple and choice reaction time. Further analyses revealed that slowed choice reaction time was primarily the consequence of slower simple reaction times, and that neither were the consequence of impaired motor speed. The deficits in reaction time were not related to psychiatric status or severity of CFS symptoms. Similarly, the cognitive deficits were not related to everyday functioning, indicating that level of impairment could not be used to directly predict functional ability.

Lastly, self-reported attention and memory problems were compared to attention and memory test results, and the impact of the testing session on fatigue was examined (Chapter 6; Cockshell & Mathias, 2014). Subjective and objective measures of attention and memory were not related in people with CFS or healthy controls, suggesting they may be measuring different constructs. However, people with CFS reported greater fatigue following cognitive testing and took several days longer than their peers to return to pre-testing fatigue levels.

Overall, the findings from this thesis suggest that people with CFS are impaired in a number of cognitive domains, including memory and attention; consistent with the

problems they frequently report. Many deficits are only minor and very specific, such as sustained working memory. The greatest impairment for people with CFS, however, was information processing speed; which was not explained by poor test effort, psychological problems or the severity of CFS symptoms (fatigue or poor sleep). People with CFS report experiencing cognitive problems and, although they are not directly related to their performance on cognitive tests, this research suggests that cognitive exertion can cause disabling fatigue for many days afterwards.

Declaration

I certify that this work contains no material that has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide.

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Date

List of Publications

Publications are listed in order of appearance in this dissertation. All publications are presented in the body of the thesis in a common format (double spaced), with the published version appearing in the appendices when permitted.

Cockshell, S. J., & Mathias, J. L. (2010). Cognitive functioning in chronic fatigue syndrome: a meta-analysis. *Psychological Medicine, 40*(8), 1253-1267.

Cockshell, S. J., & Mathias, J. L. (2012). Test effort in persons with Chronic Fatigue Syndrome when assessed using the Validity Indicator Profile. *Journal of Clinical and Experimental Neuropsychology, 34*(7), 679-687.

Cockshell, S. J., & Mathias, J. L. (2013). Cognitive deficits in Chronic Fatigue Syndrome and their relationship to psychological status, symptomatology and everyday functioning. *Neuropsychology, 27*(2), 230-242.

Cockshell, S. J., & Mathias, J. L. (2014). Cognitive functioning in people with Chronic Fatigue Syndrome: A comparison between subjective and objective measures. *Neuropsychology, 28*(3), 394-405.

**Statement of the Contributions on Jointly Authored Papers and Permission for
use of Published Papers**

Title of Paper Cognitive functioning in chronic fatigue syndrome: a meta-analysis.

Publication Status Published ✓

Publication Details Cockshell, S. J., & Mathias, J. L. (2010). Cognitive functioning in chronic fatigue syndrome: a meta-analysis. *Psychological Medicine*, 40(8), 1253-1267.

Author Contributions

By signing the Statement of Authorship, each author certifies that their stated contribution to the publication is accurate and that permission is granted for their publication to be included in the candidate's thesis

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Contribution to the Paper Planned and conducted the study, undertook all data extraction and analysis, interpreted data, wrote manuscript and acted as corresponding author

Signature: _____

Date: 15 Oct 2015

Name of Co-Author Jane L. Mathias

Contribution to the Paper Supervised all aspects of the study design and analysis and participated in manuscript preparation

Signature: _____

Date: 15/10/15

Title of Paper Test effort in persons with Chronic Fatigue Syndrome when assessed using the Validity Indicator Profile.

Publication Status Published ✓

Publication Details Cockshell, S. J., & Mathias, J. L. (2012). Test effort in persons with Chronic Fatigue Syndrome when assessed using the Validity Indicator Profile. *Journal of Clinical and Experimental Neuropsychology*, 34(7), 679-687.

Author Contributions

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Name of Co-Author Jane L. Mathias

Contribution to the Paper Supervised all aspects of the study design and analysis and participated in manuscript preparation

Signature: _____

Date: 15/10/15

Title of Paper Cognitive deficits in Chronic Fatigue Syndrome and their relationship to psychological status, symptomatology and everyday functioning.

Publication Status Published ✓

Publication Details Cockshell, S. J., & Mathias, J. L. (2013). Cognitive deficits in Chronic Fatigue Syndrome and their relationship to psychological status, symptomatology and everyday functioning. *Neuropsychology*, 27(2), 230-242.

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Publication Status Published ✓

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Date: 15/10/15

Acknowledgements

I would like to thank my supervisor, Professor Jane Mathias, for her ongoing support and encouragement, and for the time and effort that she has committed to this endeavour. I am grateful to you for pushing me to achieve more and celebrating with me when I did. It has been a long journey with many interruptions, and I have appreciated your continuous support and enthusiasm for my research during this time. Thank you also to Dr Lynn Ward for her feedback on the final thesis draft.

I would like to thank my employer, the Defence Science and Technology Group, for providing me with time to work on this thesis. Particularly, my current supervisor, Mark Krieg, for his continuous support and seeing the value in this undertaking for both me and the organisation, my former managers, Shane Canney and Stuart Sutherland, for their support and assistance during my candidature, and my colleague, Kingsley Fletcher, for reading an early draft of my meta-analysis and test effort poster, and educating me on the use of spreadsheets.

For my husband, Tony O'Brien, I know this has consumed much time and caused much stress, but I am grateful for your understanding and support, and thank you for providing food, drinks and shoulder rubs when I became so focused on my studies that the outside world would disappear. Thank you to my daughter, Emma Cockshell, who loved to come and visit me when I was studying and was always fun to play with when I was finished for the day. For my parents, Joy and Malcom Cockshell, for encouraging me to study and instilling in me the value of hard work and persistence. I am also grateful to my family and friends for their interest in my research.

Lastly, and very importantly, I would like to thank the participants involved in the empirical study. I am aware that for many it was a considerable effort to travel and undertake the cognitive testing, with consequences unbeknownst to me at the commencement of the study that would impact your health for many days afterwards. Your involvement in this research was of great importance, and I hope that the sharing of these findings via publications and presentations has helped improve understanding of this condition and made it worthy of your contribution.