CHAPTER 1

INTRODUCTION

"The Brain - is wider than the Sky – For - put them side by side –
The one the other will contain - With ease - and You - beside-."

Emily Dickinson (1999)

The answers to archaic questions have ebbed and flowed with the tides of changing thoughts and discoveries. The proverbial giant turtle once served as the pivot on which a flat world balanced, until a leap of faith and logic illuminated the void beneath which the giant turtle rested. Notions such as these have their parallels in the progressive history of neuroscience. Some great thinkers were wont to sharing untested and sensational theories whereby they paradoxically devolved to the brain great faculties of thought but judicious responsibility: it was Flourens who proposed that the brain secretes thought as the liver secretes bile (cited in Kandel, 2000). It has been a long path of discovery from the early cephalocentric theories of brain function to the current day notions of functional systems, and many metaphors derived from computer science, mechanics, philosophy, and cybernetics have served as heuristics for understanding functional systems.

Alzheimer's disease, named after Alois Alzheimer who discovered this insidious and progressive degeneration of the brain, by virtue of its neuropathological, cognitive and noncognitive manifestations encompasses the notion of dynamic interacting systems that underlie human thought, emotion, and behaviour. In terms of the neuropathological and cognitive substrates, this disease is imbued with a relative uniformity that expedites classification and diagnosis. The noncognitive manifestations, however, hint at an intricate network of psychological and biological antecedents and disease processes that may confound the occurrence of these manifestations. The latter conjecture is strengthened by illustration; studies have found that neuropathology alone cannot account for the

heterogeneous noncognitive profiles observed in Alzheimer's disease patients. By implication, it illuminates the need to understand the ontology of the antecedents that may colour the neuropsychological profile of an Alzheimer's patient.

In this brief chapter, the problem statement, research questions, aims, and hypotheses are described. Thereafter a chapter-by-chapter synopsis is provided.

1.1 Problem statement

As mentioned above, noncognitive features that accompany Alzheimer's disease are not directly attributable to underlying neural pathology nor are they sufficiently explained as by-products of cognitive impairment. One of the reasons for the limited research interest in noncognitive features pertains to the methodological challenges that face researchers. Firstly, standardised rating instruments for the noncognitive manifestations have only recently been developed, but even these instruments often do not address the gamut of noncognitive features. Secondly, unlike the strong theoretical and experimental paradigms underlying cognitive research, the area of noncognitive Alzheimer's disease symptoms has no comparable epistemology. The consequence of this has been a proliferation of terms that muddy the conceptual waters and discourage comparisons among studies. Moreover, different terms and descriptions of disease symptoms have contributed to the equivocal findings reported by researchers. Thirdly, caregivers serve as collateral sources of information because of the incapability of Alzheimer's patients to provide information. This creates a methodological dilemma that concerns the issue of retrospective bias and caregiver issues influencing the rating of challenging behaviours. Finally, most studies are cross-sectional because of the high attrition rate in the target population and the influence of age-related co-morbid conditions. Cross-sectional studies cannot address the issue of

symptom change in the disease course and is limited to providing insights on symptom manifestation in different age, gender or neurologically impaired groups. The current proliferation of studies, however, attests to the importance of noncognitive symptoms to caregivers and the acceptance of these in the clinical presentation. Caregiver psychological mortality and decisions to institutionalise their wards is usually precipitated by the onset and progression of noncognitive challenging behaviours.

Taken together, the fact that noncognitive symptoms may not entirely be by-products of cognitive decline and they reflect underlying functional and structural mutations, the deliberations provide a motivation for investigating the probable correlates of noncognitive features. One of the dimensions or antecedents of noncognitive manifestations have been identified as premorbid temperament disposition. This possible association arises from: a) the involvement of temperament as a predictor of general psychopathological onset (Andrews, 1996) and, b) the findings that temperament may act as salutogenic factors that protect against psychopathological onset (Cederblad, Dahlin, Hagnell, & Hansson, 1995.). The association between temperament and noncognitive manifestations in Alzheimer's disease is likely on two levels. On a psychological level, the hypothesis states that adaptive responses to the environment are mediated by certain dispositional traits and Alzheimer's disease creates stimuli-response conditions that may cause usually normative adaptation to present as maladaptive, depending on the premorbid disposition of a person. On a neural level, the hypothesis states that the disease alters specific neurochemical and morphological connections and the latter have inherent thresholds and connectivity patterns that are differentially optimal for people with different dispositions. By inference, it would seem that an alteration will influence outcome differentially depending on the inherent threshold levels and functioning of connected systems.

This thesis therefore, investigates the viability and variability of noncognitive symptoms and addresses the relationship between these neuropsychological correlates and premorbid temperament in a cohort with Alzheimer's disease.

1.2 Research questions

The following research questions arise from the above discussion:

- What is the nature and frequency of neuropsychiatric and neurobehavioural (noncognitive) symptom occurrence in Alzheimer's disease?
- What is the relationship between noncognitive symptom occurrence and patient characteristics such as age, gender, education level, and cognitive status?
- How does retrospective bias colour the impressions of caregiver descriptions of premorbid temperament and current ratings of noncognitive disturbances?
- What is the relationship between premorbid temperament and noncognitive symptom profile?
- On what premorbid trait dimensions can one predict the occurrence of specific noncognitive disturbances?

1.3 Research aims

The aims are divided into a primary aim and a secondary aim.

1.3.1 Primary aim

The aim of this study is to elucidate the relationship between noncognitive symptoms and premorbid temperament in a group of people with Alzheimer's disease.

1.3.2 Secondary aim

Measures of temperament and noncognitive manifestations can be utilised as important components for understanding symptom susceptibility and risk, caregiver burdens, as well as providing insights into the neuroanatomical substrates of temperament and noncognitive behaviour.

1.4 Basic hypotheses

a. There is a significant relationship between primary and secondary informants' ratings of premorbid temperament.
b. There is a significant relationship between the occurrence of noncognitive symptoms and premorbid temperament disposition in persons with Alzheimer's disease.

1.5 Chapter synopsis

Chapter 2 is an exploration of the neurobiological concomitants of Alzheimer's disease. It delves into the identity of Alzheimer's disease and provides evidence for a disease process separate from normal aging, and utilises principles of dynamic systems to juxtapose deterioration observed in Alzheimer's disease with degeneration observed in

normal aging. The chapter also addresses the aetiology and neuropathology of Alzheimer's disease.

In Chapter 3, the theoretical information and literature review of the neuropsychology of Alzheimer's disease is separated into two parts. Part I of Chapter 3 engages debate on the cognitive bias that accompanies research on brain diseases such as Alzheimer's and the methodological issues that challenge research in the noncognitive domain. Finally, utilising the neurobiological information addressed in the preceding chapter, a case is presented for the amalgamation of noncognitive and cognitive symptoms based on the reciprocal workings of the neural substrates that produce such behaviours. Of note, the term neuropsychology in this thesis refers to both cognitive and noncognitive features, following the idea of reciprocity of function as endorsed by Taylor and Saint-Cyr (1995). The term noncognitive is used to describe specific features, and for descriptive purposes to distinguish them from 'cognitive' aspects. Furthermore, noncognitive alludes to both neuropsychiatric and neurobehavioural symptoms that accompany the disease.

Part II of Chapter 3 provides an extensive literature review on the noncognitive symptoms observed in the disease, and utilises the triadic categorisation of Burns, Jacoby, and Levy (1990a, 1990b, 1990c, 1990d) to illustrate the prevalence, co-morbidity, and phenomenology of various disorders of thought and perception, disturbances of mood, and behavioural dysregulation. The latter symptoms include neurovegetative features, and the disorders of thought and perception and mood that account for the neuropsychiatric symptoms. Chapter 3-I shows that noncognitive symptoms may be related to cognitive impairment not in a causal manner but rather reciprocally if one considers neurobiologic deterioration as malfunctioning of dynamic systems. The reviews in chapter 3-II suggest that although the results of many studies are equivocal, there is consensus among

researchers that noncognitive disturbances do occur and confound the caregiving process. If one accepts the contention that noncognitive symptoms may not be merely by-products of cognitive impairment then by inference one is motivated to better understand the factors or dimensions that may be associated with noncognitive manifestations.

One such factor that is implicated as an antecedent for symptom manifestation is premorbid temperament disposition. Chapter 4 focuses on the biological premise of temperament and elaborates on the various theoretical accounts of temperament as a prelude to interpreting and discussing the relationship between premorbid disposition and noncognitive symptoms.

The above discussions contain the investigative parameters of this thesis and provide the motivation for the operationalisation of noncognitive symptoms and premorbid disposition as the primary variables in this study. Chapter 5 outlines the processes that were followed in the course of the empirical investigation. This includes the procedure followed in obtaining the sample, the design of the study, the instruments used and their relevance to the study, and finally the statistical analyses that were conducted.

The results of the empirical study are presented in Chapter 6 with the aid of figures and tables. The results pertain to the frequency of symptoms that occur, the association between primary and secondary caregiver ratings of premorbid temperament, and finally to the association between noncognitive symptoms and premorbid temperament.

Chapter 7 attempts to interpret and discuss the results with reference to the biological theories of temperament outlined in chapter 4, and the neurobiological theories of

Alzheimer's disease espoused in chapter 2. Finally, the limitations of the study and recommendations for future investigations are provided.

From the preceding synopsis, the chapters are organised in the following manner to enhance the logistical flow:

- Neurobiology of Alzheimer's Disease
- The Neuropsychology of Alzheimer's Disease: Part I & Part II
- Theoretical Foundations of Temperament
- Empirical Investigation
- Results
- Discussion