BEHAVIOURAL MANIFESTATIONS IN PATIENTS WITH ALZHEIMER'S DISEASE - A CROSS SECTIONAL STUDY

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CERTIFICATE

This is to certify that the dissertation titled **"BEHAVIOURAL MANIFESTATIONS IN PATIENTS WITH ALZHEIMER'S DISEASE - A CROSS SECTIONAL STUDY"** is the bonafide original work of DR. KARPAGAM .V in partial fulfillment of the requirements for M.D. Branch – XVIII (Psychiatry) Examination of the Tamilnadu DR. M.G.R Medical University to be held in March 2007. The Period of study was from August 2005 to August 2006.

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DECLARATION

I, DR**. KARPAGAM .V,** solemnly declare that dissertation titled **"BEHAVIOURAL MANIFESTATIONS IN PATIENTS WITH ALZHEIMER'S DISEASE - A CROSS SECTIONAL STUDY"** is a bonafide work done by me at The Institute Of Mental Health, Chennai during August 2005- August 2006 under the guidance and supervision of Prof. M. Murugappan, M.D., D.P.M., Professor of Psychiatry, Madras Medical College.

This dissertation is submitted to Tamilnadu DR. M.G.R Medical University towards part fulfillment of requirements for the award of **M.D. Degree (Branch – XVIII) in Psychiatry.**

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INTRODUCTION

WHO defines dementia as a “syndrome due to disease of brain, usually of a chronic progressive nature, in which there is disturbance of multiple cortical functions, calculations, learning capacity, language and judgement. Consciousness is not clouded. Impairments in cognitive functions are commonly accompanied, and occasionally preceded by emotional control, social behaviour and motivation”.

Dementia is defined as “ the development of multiple cognitive deficits that include memory impairment and at least one of the following: aphasia, apraxia, agnosia, or a disturbance in executive functioning, where executive functioning involves selection of key information and behaviours for problem solving and the inhibition of inappropriate responses”(DSM IV, TR).

The most common causes of dementia in individuals older than 65 years of age are: Alzheimer’s disease, vascular dementia and mixed vascular and Alzheimer’ s disease, of

which Alzheimer's disease accounts for approximately 60% of all dementias. The prevalence of Alzheimer's disease is 3 to 5% of people older than 65 years of age and as much as 50% of people older than 85 years of age. The female to male ratio is approximately 2:1.

Patients with Alzheimer's disease display characteristic cognitive and non-cognitive symptoms over the course of the illness. Neuropsychiatric symptoms may be prominent at presentation or emerge later in the course. Almost all patients are affected at some point in their disease.

Neuropsychiatric symptoms in Alzheimer's disease have significant consequences. Disorders such as depression, anxiety, and psychosis clearly affect the quality of life of the patient. Besides being a source of considerable stress, caregiver burden and potential injury, such disturbances are associated with increased use of psychotropic medications, patient and caregiver abuse. Non-cognitive symptoms are associated with an

increased risk for institutionalization, which carries with it financial consequences for the individual and for society.

Characteristics of Neuropsychiatric symptoms in Alzheimer's disease include the following:

- They may be the sentinel event heralding the onset of Alzheimer's disease.
- Several types of symptoms may occur simultaneously, fluctuate and recur over the course of illness.
- They tend to become more frequent as the disease progresses.
- They are associated with rapid cognitive decline and worsen function.
- They may lead to institutionalization.
- Importantly, these Neuropsychiatric symptoms may improve with cholinergic therapy, disease modifying therapy and psychotropic agents.

The Neuropsychiatric symptoms play an important role in the diagnosis and management of Alzheimer's disease. Early identification and treatment of these symptoms reduces patient's suffering, caregiver burden and delay institutionalization.

REVIEW OF LITERATURE

Approximately 5% of community dwelling elderly individuals have dementia and the prevalence of dementia will quadruple by the year 2050 (Judith *et al*). Stevens *et al*, in his study in 2002 found that Alzheimer‘s dementia, vascular dementia, mixed dementia and diffuse Lewy body dementia account for the majority of dementia cases

Alzheimer‘s dementia, the most common cause of dementia in most countries is a slowly progressive dementia in which memory disorder is the usual presenting symptom. The earliest sign of a memory problem is usually a defect in the delayed verbal recall. As disease progresses, memory impairment is manifested by difficulty in learning new information. Language disturbances, difficulty in performing coordinated motor tasks, failure to recognize sensory stimuli in the absence of sensory deficits and deficits in executive functioning evolve during the course of illness. As the disease advances, non-cognitive symptoms become evident.

The neuropsychological and functional deficits in dementia are often accompanied by neuropsychiatric symptoms. Eisdorfer *et al*, described two syndromes that Alzheimer ‘s dementia a cognitive syndrome and a behavioural syndrome, which overlap between the courses of the disease.

These neuropsychiatric symptoms may be the presenting complaint or may emerge in the course of the disease. In 1996, the International Psycho geriatric association (IPA) arrived at a consensus on the use of more appropriate and descriptive term regarding behavioural symptoms that would facilitate communication among researchers and therefore foster further development of the Dementia. Behavioural and psychological symptoms of Dementia (BPSD), was introduced and defined as " signs and symptoms ofdisturbed perception, thought content, mood or behaviour that frequently occur in patients with dementia". BPSD includes Sub syndromes like psychosis, circadian rhythm disturbance, depression, anxiety, agitation and other less well defined syndromes (Finkel *et al*).

Most patients with Alzheimer's dementia exhibit non-cognitive symptoms at some point during the course of their illness. Some symptoms, such as agitation and psychosis are more likely to result in medical evaluation of others. Assessment instruments that probe for behaviours occurring with in a defined time period may miss other symptoms, such as intermittent physical aggression. These disturbances may adversely affect the functional status of patients with Alzheimer's dementia resulting in significant disability.

FACTORS CONTRIBUTING TO THE ETIOLOGY OF BEHAVIORAL

PROBLEMS IN ALZHEIMER ‘S DEMENTIA

Regarding the genesis of noncognitive psychiatric symptoms of Alzheimer ‘ s dementia, several factors have been implicated, important being the structural involvement, environmental factors, iatrogenic causes and somatic illnesses. Farber *et al* suggested an interaction between mechanisms in the brain that regulate psychosis and disease mechanisms specific to Alzheimer ‘s dementia.

This disease is also known to affect brainstem nuclei that manufacture the neurotransmitters that are commonly implicated in psychiatric illness, and adrenergic and serotoninergic systems as well as cholinergic are involved in Alzheimer ‘s dementia. This concept is supported by the observation by Levy *et al***,** Alzheimer ‘s dementia is often treatable by psychotropic agents that have little effect on cognition or the underlying degenerative process of the disease In patients with Alzheimer’s disease, degeneration of brainstem nuclei may produce a deficit in norepinephrine that relates to alteration in the mood. Zubenko and colleagues noted that the brain of patients with dementia and major depression had neurochemical disturbances, including decreased levels of norepinephrine. Other studies have found that depressed AD patients have greater reductions in cell numbers in the substantia nigra when compared with non-depressed patients.

The apolipoprotein E4 allele is the most consistently identified genetic risk factor for Alzheimer ‘s dementia. However, this allele has not been consistently associated with any of the neuropsychiatric manifestations of Alzheimer ‘s dementia. With regard to delusions and hallucinations, three studies have found an association between psychosis and apolipoprotein E4 allele (Ramachandran *et al*). Zubenko and colleagues examined brain tissue from 27 patients with AD and found that psychosis was associated with increased senile plaques in prosubiculum, increased neuro fibrillary tangles in middle frontal cortex, the relative preservation of nor epinephrine in substantia nigra, and a reduction of serotonin in the prosubiculum. In the Cache county study by Steinberg *et al*, gender, age, dementia, apolipoprotein E4 allele, type of dementia and general medical health were reported to influence the occurrence of individual neuro psychiatric symptoms.

Alan Jacques and Graham in their study reported that environmental factors such as large group living, lack of activities, locked doors, loneliness, inappropriate noises may contribute to the development of behavioural and psychiatric symptoms in dementia. Cohen-Mansfield *et al*, have studied relationship between patients needs, the environment and

agitation. Cohen-Mansfield *et al* have defined agitation as “inappropriate verbal, vocal end motor activity that is not judged by an outside observer to result directly from the needs or confusion of the agitated individual”. They found that a large number of patients with verbal aggression had undiagnosed hip fracture and suggested that presence of unmet medical needs is an important contributor of all behavioural and psychiatric symptoms in dementia. Further more, an evaluation of the correlation between behaviours such as verbal aggression and environmental factors shows that the quality of the patient’s social environment is inversely proportional to the presence of verbal aggression.

Although the exact etiology of behavioural and psychiatric symptoms in dementia remains unknown, evidence suggests that a combination of behaviour specific biological and environmental factors may be responsible for the onset of symptoms. Understanding the various factors in the causation of behavioural and psychiatric symptoms in dementia would help us create a new and creative intervention in managing them.

NEED FOR ASSESSMENT OF BEHAVIOURAL SYMPTOMS IN DEMENTIA

Neuropsychiatric symptoms may be the presenting manifestations of dementing disorders, appearing before cognitive alterations and heralding the onset of brain disease (Rubin *et al*). Shaji and colleagues reported that these symptoms remain the major source of caregivers distress. They remain as an important contributor to the decision of instituitionalise Alzheimer's disease patients (Deutsch *et al*). Some of these symptoms like agitation and aberrant motor behaviour predict severe cognitive decline. As the disease progress, the symptomatology changes, requiring re evaluation and implementation of new interventions in the course of illness.

Thus neuropsychiatric features in dementia have important diagnostic, prognostic and management implications. Cynthia *et al*, found that early detection and assessment of these potentially treatable (non cognitive) behavioural and psychiatric symptoms might delay the process of institutionalization, caregiver burden and also would decrease the functional impairment. Further, behavioural assessment may help differentiating between different forms of dementia, further stressing the need for the development of new and more sensitive behavioural assessment scales (Engelborghs *et al*) Also, the loss of autonomy of activities of daily living is determined by the presence of behavioural symptoms and cognitive decline (Lechowski *et al*).

A number of standardized instruments have been developed for the assessment of non-cognitive symptoms in dementia. The validated and reliable multi dimensional tools that are most commonly used are the Alzheimer's disease–Non cognitive portion (ADAS-noncog), the Neuropsychiatric inventory (NPI) and the Behavioural Pathology In Alzheimer's disease Rating Scale (BEHAVE-AD). The ADAS-non cog covers a variety of symptoms like tearfulness, depression, loss of concentration, uncooperativeness, pacing, delusions, hallucinations, tremor and appetite changes. The NPI evaluates delusions, hallucinations, agitation, anxiety, dysphoria, euphoria, irritability, disinhibition, apathy and aberrant motor behaviour. The BEHAVE-AD focuses on paranoia, hallucinations, activity disturbances, aggressiveness, diurnal rhythm disturbances, anxiety and phobias.

SPECTRUM OF BEHAVIOURAL CHANGES IN ALZHEIMER'S DEMENTIA AND IT'S RELATION TO COGNITIVE DECLINE

Neuropsychiatric disorders have an impact on the course of cognitive decline in patients with Alzheimer's disease.The presence of psychosis, agitation and depression have been identified as being possible predictors of accelerated intellectual decline.

Patients with Alzheimer's dementia are commonly assumed to experience a linear decline in behavioural functioning that parallels cognitive decline. However, the behavioural manifestations may vary as the disease progresses.

Cross-sectional studies indicated curvilinear associations between dementia severity and certain behavioral problems (forgetful behaviors, and motional and impulsive behaviors). Longitudinal analyses by McCarty *et al*, further indicated trends for curvilinear rates of behavioral disturbance across time, with some problem areas showing improvement as AD progresses through the most severe stages. There exists controversy regarding the occurrence of behavioural disturbance in patients with varying severity of dementia although it is generally accepted that the prevalence of delusions and hallucinations increase as the disease progresses (Burns *et al*).

In a study done by Mega et al, symptoms like agitation, dysphoria, apathy and aberrant motor behaviour had significant

correlation with cognitive impairment .The frequency and clinical correlates of physically aggressive behaviour in patients with dementia have been assessed in several studies. Several other neuropsychiatric symptoms like delusions may predispose an individual with dementia to aggression (Morris *et al*).

Both major and minor depression is common in Alzheimer's dementia produce considerable mood and nonmood morbidity affecting both patients and caregivers (Lykestos *et al*). Disturbances in mood and manifestations of agitation and psychotic symptoms are not closely related to one another and show little progressive worsening over time. Rather, they tend to be episodic such that increasing severity at one time is usually followed by improvement later. Concentration problems are a manifestation of cognitive dysfunction rather than behavioral disturbance in Alzheimer's dementia (Marin *et al*).

Ravetz RS in his study found that the first stage of Alzheimer's disease commonly is marked by anxiety and depression secondary to memory impairment, and delusions. In the second stage, delusions often become more bizarre. Impairment of visuospatial memory, improper advances, and obscene language begin to replace disinhibited behavior, often to the point of violence directed at others. Increasing agitation requires restraints. In the third and final stage, screaming, banging, and cursing are common features. Verbal and behavioral perseverations are very common.

One year longitudinal evaluation of neuropsychiatric symptoms in Alzheimer's disease in the REAL FR study by Benoit *et al*, reported that When compared to non institutionalized patients, the institutionalized group was characterized at base line by a lower MMSE score, a higher caregiver burden score, and a higher NPI agitation and disinhibition scores.

Delusions and hallucinations are among the most common noncognitive neuropsychiatric symptoms seen in patients with dementia and have been reported to occur in a large proportion of patients with Alzheimer's disease. Delusions and hallucinations strongly contribute to early institutionalization, reduce patients' well being, and increase the burden of the caregiver in managing the patient Furthermore, these disturbances are associated with more rapid progression of the dementia syndrome. . The prevalence of delusions in Alzheimer's disease patients ranged from 16% to 70% (median=36.5%) in the reviewed reports, and the prevalence of hallucinations ranged from 4% to 76% (median=23%). Delusions and hallucinations tended to persist over time, tended to recur often during the course of Alzheimer's disease (Bassiony *et al*).

Devanand *et al*, found that the delusions and hallucinations in Alzheimer 's disease flutuate with time but their over all prevalence increases slowly with dementia progression. Psychotic symptoms occur

commonly in Alzheimer's disease (AD), predict a more rapid rate of cognitive decline and increase the risk of aggressive behaviour (Gormley *et al*). Bassiony *et al* in his study found that hallucinations were associated with less education, African-American race, more severe dementia, longer duration of illness, falls and use of anxiolytics. Delusions were associated with older age, depression, aggression, poor general health and use of antihypertensives indicating that risk factors varies for different psychotic symptoms.

Delusional patients are more aggressive and exhibit more severe activity disturbances than nondelusional patients. Delusional patients are more severely cognitively impaired, but the neuropsychological differences between the two groups are not outstanding. Delusional patients are more behaviorally disturbed than those without delusions (Flynn *et al*).

Studies by Dag Aarsland *et al* ,explored the relationship between aggressive behaviour and other neuropsychiatric symptoms in patients with Alzheimer’s dementia. There exists a significant, but modest association between aggressive behaviour and severity of dementia. One-fourth of variance in aggression could be attributed to psychosis. Constantine *et al* reported that aggression is strongly linked with the presence of depressive symptoms and concluded that the identification of depression in dementia may be a means of preventing and managing physically aggressive behaviour.

Depression with dementia appeared to lower performance on cognitive tests. Following treatment, although cognitive impairment remained in the demented range, test performance improved (Greenwald *et al*). It has been suggested that a new diagnosis should exist, depression in Alzheimer's disease. In this diagnosis symptoms of irritability and social isolation or withdrawal would be included. An efficient strategy to diagnose depression in dementia amongst elderly patients is to administer the Single Question followed by, when necessary, the Cornell scale (Lam *et al*). High levels of depressive symptoms, when persistent in elderly are associated with cognitive decline (Sabrina *et al*).

2-year persistence of BPSD in AD was frequently observed in patients with agitation and with depressiveness, with less frequency in patients with anxiety and aggressiveness, but not in patients with delusions or hallucinations. 2-year persistent aggressiveness was associated with older age and more functional impairment. More functional impairment was also related to 2-year non-persistent hallucinations. Counseling AD patients and their families and tailoring therapeutic strategies should take into account the different modi of BPSD in AD occurring and persisting longitudinally and interacting with functional disturbances (Haupt *et al*).

Currently, there is little that can be done to treat the cognitive components of AD. Consequently, our most successful and beneficial interventions may focus on the remediable behavioral manifestations of the disease. The most valuable treatment approach for patients with AD and their caregivers interweaves medications, psychosocial services, environmental strategies, and caregiver education.

Although Alzheimer's disease has long been considered mainly a cognitive disorder, behavioral and psychological symptoms are present from its onset and at all the stages of the disease in most patients. They must be identified from the beginning because they orient the diagnosis. They include affective and emotional disorders, delusions and hallucinations, disorders of instinctual behavior and behavioral problems. The best tool for assessing them is the Neuropsychiatric Inventory (NPI). They are generally related to neurobiological aspects of the disease but may, especially when acute, have multiple etiologies: somatic, iatrogenic, psychological and environmental. They condition the course of the disease. As a source of suffering and reduced quality of the life and as the primary cause of distress for the caregivers and hence of hospitalization and institutionalization, they increase the costs of care. The challenge today is to learn more about them and thus improves their treatment and especially their prevention.

AIM OF THE STUDY

1. To assess the following behavioural and psychiatric problems in patients with Alzheimer ‘s disease
    - Delusions
    - Hallucinations
    - Agitation
    - Dysphoria
    - Anxiety
    - Apathy
    - Elation
    - Disinhibition
    - Irritability
    - Aberrant motor behaviour.
2. To determine the pattern of behavioural symptoms across the three stages of illness in patients with Alzheimer ‘s disease.
3. To analyse the association between the various behavioural domains in patients with Alzheimer ‘s disease.

HYPOTHESIS OF THE STUDY

1. There is no significant relationship between advancing age and extent of cognitive decline in Alzheimer's disease.
2. There exists no difference in the severity of cognitive decline between males and females with Alzheimer's disease.
3. Low educational status in Alzheimer's disease is not associated with worsening of cognitive decline.
4. There is no significant relationship between duration of illness and cognitive decline in Alzheimer's disease.
5. There exists no difference in the pattern of behavioural manifestations in the three stages of Alzheimer's disease.
6. The frequency of occurrence of behavioural problems does not decrease with increase in severity of illness in Alzheimer's disease.
7. There is no significant correlation between behavioural problems and worsening cognitive function in patients with Alzheimer's disease.
8. There is no significant correlation among the 10 behavioural domains

MATERIALS AND METHODS

STUDY DESIGN- Cross sectional study

SETTING

The study was conducted at the Outpatient department of Institute Of Mental Health, Chennai –10 and Outpatient department, Department Of Psychiatry, Government General Hospital, Chennai. The study was conducted from August 2005-August 2006.

SAMPLE

50 elderly patients suffering from Alzheimer ` s dementia (cases) along with their caregivers were recruited from Outpatient department, Institute Of Mental Health and Government General Hospital, Chennai.

INCLUSION CRITERIA

1. Diagnosis satisfying ICD 10 criteria for Alzheimer's dementia .

2. Duration of illness for a minimum period of 6 months

3. Age group above 65 years

EXCLUSION CRITERIA

1. Patients with delirium
2. H/O psychiatric disorder preceding the onset of memory loss
3. H/O head injury with loss of consciousness
4. H/O alcohol & other substance abuse
5. H/O systemic diseases like hypertension & diabetes.

INSTRUMENTS

1. Socio demographic data- semi structured interview
2. Clinical Dementia Rating Scale (CDRS)
3. Neuropsychiatric Inventory (NPI)

CLINICAL DEMENTIA RATING SCALE

The clinical dementia rating scale was created by Hughes and colleagues at Washington University during the early 1980 s and has now become the gold standards in global staging of Alzheimer' s

disease. It can be used to assess patients with a broad range of dementia, from ‘no impairment’ to ‘ severely impaired’.

It was originally assessed in 58 healthy control subjects and 59 people in a community setting suffering from probable or mild dementia. Each patient was assessed using the Initial Subject Protocol (IPS), a semi structured interview, incorporating the BDRS and the Short Portable Mental Status Questionnaire (SPMSQ). Collateral history was also collected from an informant. This information was then collated to give final scores.

A clinician who knows the patient well usually carries out the CDR.the CDR scale includes six domains.

The primary domain assessed is Memory.

The five secondary domains are

1. Orientation
2. Judgement and problem solving
3. Community affairs
4. Home and hobbies
5. Personal care.

Scoring in CDR scale.

The global CDR score is derived from the scores in each of the six domains. Scoring of primary domain, memory (M) is first carried out. If atleast three secondary domains have the same score as the primary domain the CDR score is equal to the score of the primary domain (M). Whenever three or more secondary domains are given a score greater or less than the primary domain score (M) the majority of scores of the secondary domains that are on whichever side of the primary domain, is taken as the CDR score. If there are ties in the scores of the secondary domains, the CDR score closest to M is chosen.

A modified likert scale is used to rate each domain.

- 0 - healthy people
- 0.5 -questionable dementia
- 1- mild dementia
- 2- moderate dementia
- 3- severe dementia

Hughes et al also assessed the validity and reliability of the CDR, and found an inter- rater reliability of 0.89(excellent). The reliability has been further supported by Burke et al .The CDR is also acknowledged to have excellent face validity. Furthermore, the results of multicentre trials have shown the CDR to remain reliable (Morris JC)

As the CDR has been in clinical use for several years, it has been modified a number of times. The version used in the study is the most recent version given by Morris JC' which explains the ratings more accurately.

NEUROPSYCHIATRIC INVENTORY

The Neuropsychiatric inventory (NPI) is a multi dimensional instrument that assesses 10 behavioural disturbances in people with dementia (Cummings et al). Published in 1994, it drew on scales already developed in the field of dementia (BEHAVE-AD, the CSDD and the other scales such as the neurobehavioural rating scale used to assess the behavioural disturbances following head injury).

The ten domains (chosen from appropriate literature and from UK and US studies examining behavioural disturbances in patients with Alzheimer' s disease, vascular dementia and fronto temporal dementia) are as follows:

1. Delusions
2. Hallucinations
3. Agitation
4. Dysphoria
5. Anxiety
6. Elation
7. Apathy
8. Disinhibition
9. Irritability
10. Aberrant motor behaviour

Many of the subscales in NPI require comment. Many scales used in dementia research do not include alterations in personality, such as apathy and irritability. However, recent studies suggest that these are the most common behavioural disturbances that occur in dementia patients (Petry et al). The NPI includes these items to

encompass common behaviours in dementia. Investigation of the relationship between apathy and regional cerebral blood flow measured by SPECT revealed that changes in prefrontal and anterior temporal perfusion are most highly correlated with
apathy scores (Craig et al).

Aberrant motor behaviour refers to the spontaneous activities engaged in by many dementia patients. Included are the purposeless activities common in AD patients such as pacing and rummaging (Reisberg et al). The NPI helps to distinguish among different dementias and includes symptoms known to be rare in AD, but common in other types of dementia. Euphoria and disinhibition are uncommon in AD, but are features of fronto temporal dementia (Miller et al). These two features are included in NPI to increase its differential diagnostic utility.

One goal of NPI is to establish characteristic neuropsychiatric profiles of different neurological disorders. A variety of conditions have been studied, including AD, fronto temporal dementia (Levy et al) and progressive supra nuclear palsy (Litvan et al).

Whenever possible, terminology used in the sub questions was derived from standardised diagnostic criteria such as the Diagnostic and Statistical Manual Of Mental Disorders, Fourth edition.

Content validity was rated by an expert Delphi panel and was high for the first nine domains; as a result the tenth was changed to ‘ Aberrant motor behaviour’. Concurrentvalidity determined by correlation with the BEHAVE-AD and the Hamilton Depression Rating Scale (HDRS) was good (p.0.01 for nine domains, and p.0.05 for one domain). Further analyses showed the NPI to have good inter- rater, test-retest and item consistency reliability (Cummings).

In terms of administration, caregivers, who must have daily contact with the patient, provide the information to the clinician. The caregiver is asked to rate the severity and frequency of each of the 10 behavioural domains.

- Severity (1= mild, 2= moderate, 3= severe)
- Frequency (1= occasionally= often/once per week, 3= frequently / several times per week, 4= very frequently or daily).
- Composite score is calculated as frequency x severity.

METHODOLOGY

A group of 50 patients who fulfilled the inclusion criteria and exclusion criteria for cases were selected from the Outpatient department of Institute Of Mental Health and Government General Hospital Psychiatric unit. The caregivers who accompanied the patients were also included in the study. All patients were above 65 years of age and satisfied the ICD 10 criteria for Alzheimer's dementia.

Clinical Dementia Rating Scale was administered to assess the severity of dementia. Based on CDR scores we identified three stages of dementia.

- Mild dementia (CDR= 1)
- Moderate dementia (CDR= 2)
- Severe dementia (CDR= 3)

The Neuropsychiatric Inventory (NPI) was used to assess the behavioural disturbances. The caregivers of all the 50 patients, who have daily contact with the patient, were administered Neuropsychiatric Inventory (NPI) questionnaire. Questions were asked

as per NPI protocol. Caregivers were asked to rate the frequency and severity of the ten behavioural domains-

Delusions, Hallucinations, Agitation, Dysphoria, Anxiety, Elation, Apathy, Disinhibition, Irritability, Aberrant motor behaviour.

As per NPI scoring frequency of the behavioural domain is given a score between 1 to 4 and severity of the behavioural domain is given a score between 1 to 3.The score 0 is used when a particular behavioural domain is absent.

Composite score is then calculated for each behavioural domain.

Composite score = frequency score (1 to 4) X severity score (1 to 3)

The Composite score lies between 1 and 12.

Statistical analysis was then carried out to assess the pattern of ten behavioural domains in the three groups of patients with Alzheimer's dementia.

The ethics committee and the research panel of the Institute Of Mental Health, Chennai after presentation, approved the objectives and the methodology of the dissertation.

STATISTICAL ANALYSIS

Statistical analysis was carried out for the 50 subjects after categorizing each variable. Base line data of the patients were collected from the caregivers. Based on CDR scores we identified three stages. Mild dementia (CDR= 1), Moderate dementia (CDR= 2) and Severe dementia (CDR= 3). Age, sex, educational status, relationship of the caregiver to the patient and the duration of illness were analysed. Chi-square test is used to assess the significance of association between the age, gender, and duration of illness of the sample in the three stages of illness. The number of patients manifesting each of the 10 behavioural domains in the three stages of illness is determined. Composite scores for each behavioural domain is calculated in all patients. The mean of the composite scores for each behavioural domain with in the three stages is calculated. The analysis of variance (ANOVA) is used to compare the mean values of the composite scores across the three stages. Pearson Correlation test is used to determine the correlation between the ten behavioural domains and to explore the relationship among behaviours.

RESULTS

Table 1

AGE AND GENDER DISTRIBUTION OF THE SAMPLE

Variable		N (%)
Age	66-70 yrs	33 (66)
	71-76 yrs	17 (34)
Sex	Male	30 (60)
	Female	20 (40)

The age of patients with Alzheimer's disease ranged from 66 to 76 years. . The mean age was 69.6(SD 2.63). Of the total sample of 50 patients, 30were males and 20 were females

Table 2

EDUCATIONAL STATUS OF THE SAMPLE POPULATION

Educational Status	N (%)
None	8(16)
Minimal	12(24)
Primary	13(26)
Secondary	12(24)
Tertiary	5(10)

8(16%) of them were not educated and 10 (24%) had completed tertiary education.12 (24%) patients had minimal education, 13(26%) with primary education, 12(24%) had completed secondary education.

Table 3

DURATION OF ALZHEIMER'S DEMENTIA IN YEARS

Duration (years)	N (%)
0.5	20(40)
1	19(38)
1.5	7(14)
2	3(6)
3	1(2)

The mean duration of illness in the sample population was 0.97 years. 20 (40%) of the sample group had 6 months duration of illness, 19 (38%) had 1 year of illness, 7(14%) had 1.5 years, 3(6%) had 2 years of illness. Only one patient in the sample had illness for 3 years.

Table 4

RELATIONSHIP OF CAREGIVERS TO PATIENTS WITH ALZHEIMER'S DEMENTIA

Caregiver relationship	N (%)
Spouse	15(30)
Son	16(32)
Daughter	11(22)
Daughter in law	3(6)
Others	5(10)

16(32%) 0f the caregivers were the sons of the total sample, while 15(30%) were the spouses, 11(22%) were daughters, 3(6%) were daughters – in law and 5 (10%) were others related to the sample group, either their siblings or other paid caregivers

Table 5

CLINICAL DEMENTIA RATING FOR PATIENTS WITH ALZHEIMER'S DISEASE

CDR STAGE (SCORE)	N	%
Mild Dementia (CDR 1)	15	30.0
Moderate Dementia (CDR2)	22	44.0
Severe Dementia (CDR 3)	13	26.0

The sample group were classified in to three, based on their scores in the Clinical Dementia Rating Scale as mild (CDR 1), moderate (CDR 2) and severe (CDR 3). 15 (30%) fall in the mild group, 22(44%) in the moderate and 13(26%) in the severe group.

Table 6

COMPARISON OF AGE AND COGNITIVE STATUS OF PATIENTS IN THE THREE CDR GROUPS

CDR STAGE	AGE GROUP (YEARS)		CHI-SQUARE TEST
	66-70 N (%)	71-76 N (%)	
MILD	11(73.3)	4(26.7)	$\chi 2=15.10$ P=0.001 Significant
MODERATE	19(86.4)	3(13.6)	
SEVERE	3(23.1)	10(76.9)	

P value of 0.001 signifies that as age advances, the severity of the cognitive decline worsens.

Table 7

COMPARISON OF GENDER AND COGNITIVE STATUS OF PATIENTS IN THE THREE CDR GROUPS

CDR STAGE	GENDER		CHISQUARE TEST
	MALE	FEMALE	
	N(%)	N(%)	
MILD	7(46.7)	8(53.3)	$\chi 2=2.80$ P=0.24 NS
MODERATE	16(72.7)	6(27.3)	
SEVERE	7(53.8)	6(46.2)	

NS – Not Significant

There is no significant relationship between gender and cognitive decline.

Table 8

COMPARISON OF DURATION OF ALZHEIMER'S DEMENTIA AND COGNITIVE STATUS OF PATIENTS IN THE THREE CDR GROUPS

CDR STAGE	DURATION OF ILLNESS (YEARS)					CHI SQUARE TEST
	0.5	1	1.5	2	3	
	N (%)	N (%)	N (%)	N (%)	N (%)	
MILD	10(66.7)	3(20)	1(6.7)	1(6.7)	0	$\chi 2$=15.70 P=0.04 Significant
MODERATE	8(36.4)	9(40.9)	5(22.7)	0	0	
SEVERE	2(15.4)	7(53.8)	1(7.7)	2(15.4)	1(7.7)	

P value of 0.04 signifies that there is strong association between duration of Alzheimer's disease and cognitive decline.

Table 9

PERCENTAGE OF ALZHEIMER'S DISEASE PATIENTS WITH BEHAVIOURS PRESENT IN THE THREE STAGES OF DEMENTIA SEVERITY AS MEASURED BY CDR

BEHAVIOURAL DOMAINS	MILD N (%)	MODERATE N (%)	SEVERE N (%)	TOTAL N (%)
DELUSIONS	2(13)	5(23)	4(31)	11(22)
HALLUCINATIONS	2(13)	3(14)	1(7)	6(12)
AGITATION	7(47)	11(50)	11(85)	29(58)
DYSPHORIA	2(13)	10(45)	8(62)	20(40)
ANXIETY	4(26)	14(63)	7(54)	25(50)
ELATION	3(20)	0	1(7)	4(8)
APATHY	7(47)	17(77)	12(92)	36(72)
DISINHIBITION	5(33)	9(40)	4(31)	18(36)
IRRITABILITY	5(33)	9(40)	7(54)	21 (42)
ABERRANT MOTOR BEHAVIOUR	2(13)	6 (28)	7(54)	15(30)

The most common behaviour was apathy, which was exhibited by 72 %of patients, followed by agitation (58%), anxiety (48%), irritability (42%), dysphoria and aberrant motor behaviour (both 38%), disinhibition (36%), delusions (22%) and hallucinations (10%).

Table 10

COMPARISON OF MEAN COMPOSITE SCORES OF THE TEN BEHAVIOURAL DOMAINS WITH THREE STAGES OF DEMENTIA

	CDR			P VALUE
DOMAINS	Mild Mean	Moderate Mean	Severe Mean	ONE WAY ANOVA F TEST
DELUSION	7.33	9.67	9	0.47(NS)
HALLUCINATION	9	11	12	0.29(NS)
AGITATION	6.29	7.33	7.27	0.65(NS)
DYSPHORIA	9	7.5	6.13	0.25(NS)
ANXIETY	5.17	5.63	6	0.93(NS)
ELATION	7	.	8	0.67(NS)
APATHY	8.86	7.53	9.08	0.13(NS)
DISINHIBITION	6	8	8.25	0.03 significant
IRRITABILITY	6	8	8	0.03 significant
ABERRANT MOTOR BEHAVIOR	9	9.17	9.55	0.93(NS)

Disinhibition and irritability were the two behavioural problems found to be significantly associated with increasing severity of illness, with a p value <0.05. Although apathy, agitation and

aberrant motor behaviour were found to be more prevalent in the severe stages of illness, no significant results were obtained.

Table 11

COMPARISON OF MEAN FREQUENCY, SEVERITY AND COMPOSITE NPI SCORES IN MILD (CDR 1), MODERATE (CDR 2) AND SEVERE (CDR 3) ALZHEIMER'S DISEASE

Score	Mild	Moderate	Severe	One way ANOVA
Frequency Mean±SD	7.6 ± 1.43	7.38±2.14	8.32±1.7	F=1.09 P=0.34(NS)
Severity Mean±SD	2.91±0.34	2.82±0.51	3.21±0.39	F=3.42 P=0.04(Significant)
Composite Mean±SD	2.30±0.26	2.36±0.4	2.53±0.46	F=3.44 P=0.05(Significant)

Mean values for the total NPI scores increased across each CDR group with a significant difference between the mild and the severely impaired groups for the mean severity and the composite scores ($p<0.05$).

Table 12

2 TAILED PEARSON'S PRODUCT MOMENT CORRELATION OF AGITATION WITH OTHER BEHAVIOURAL DOMAINS

Domains	Correlation r	Significance	N
Delusion	-0.645	0.117	7
Hallucination	0.667	0.333	4
Agitation	1		30
Dysphoria	-0.094	0.797	10
Anxiety	0.132	0.64	15
Elation	0.866	0.333	3
Apathy	-0.171	0.460	21
Disinhibition	0.319	0.403	9
Irritability	-0.316	0.374	10
Aberrant motor behaviour	0.610	0.007	18

Agitation has significant correlation to aberrant motor behaviour ($r=0.610$, $p=0.007$).

Table 13

2 TAILED PEARSON'S PRODUCT MOMENT CORRELATION OF DISINHIBITION WITH OTHER BEHAVIOURAL DOMAINS

Domains	Correlation r	Significance	N
Delusion	0.483	0.187	9
Hallucination	0.000	1	5
Agitation	-0.319	0.403	9
Dysphoria	-0.359	0.484	6
Anxiety	-0.186	0.606	10
Elation	a	.	0
Apathy	0.045	0.884	13
Disinhibition	1	.	18
Irritability	1	0.000	18
Aberrant motor behaviour	-0.158	0.765	6

Disinhibition has positive correlation with irritability(r=1).

Table 14

2 TAILED PEARSON'S PRODUCT MOMENT CORRELATION OF IRRITABILITY WITH OTHER BEHAVIOURAL DOMAINS

Domains	Correlation r	Significance	N
Delusion	0.485	0.155	10
Hallucination	0.000	1	5
Agitation	-0.316	0.374	10
Dysphoria	-0.476	0.233	8
Anxiety	-0.221	0.489	12
Elation	a	.	0
Apathy	-0.049	0.858	16
Disinhibition	1	0.000	18
Irritability	1	.	21
Aberrant motor behaviour	-0.15	0.749	7

Although irritability has been positively correlated to disinhibition, it did not have significant correlation with other behavioural domains.

Table 15

2 TAILED PEARSON'S PRODUCT MOMENT CORRELATION OF ABERRANT MOTOR BEHAVIOUR WITH OTHER BEHAVIOURAL DOMAINS

Domains	Correlation r	Significance	N
Delusion	-0.500	0.667	4
Hallucination	0.866	0.333	2
Agitation	0.610	0.007	18
Dysphoria	0.190	0.598	10
Anxiety	0.042	0.897	12
Elation	1	0.000	2
Apathy	0.049	0.858	16
Disinhibition	-0.158	0.765	6
Irritability	-0.150	0.749	7
Aberrant motor behaviour	1	.	19

Aberrant motor behaviour has significant positive correlation with elation (r=1) and agitation(r=0.610).

DISCUSSION

The mean age of onset of Alzheimer ‘s disease in our study is 69.6 years (Table 1). This is supported by the study done by Antonio *et al*, in which the mean age of onset was 67 years. The male to female ratio in our study is 1.5: 1(Table 1). This varies from the other studies conducted by Judith *et al* in which the females outnumbered males. James *et al*, also found in his study that the male to female ratio was 1:2.

We find from Table 2 that only 10 % of the study group had completed tertiary education.40% of the patients with Alzheimer ‘s disease had no or only minimal education, which could indicate a increased prevalence of Alzheimer ‘s disease in patients with low education. Several studies have confirmed age and limited education as established risk factors for Alzheimer ‘s disease. Hall et al in his study in patients with Alzheimer ‘s disease in the African Americans found that low education is important risk factor in the causation of Alzheimer ‘s disease.

The mean duration of illness in patients with Alzheimer ‘s disease in our study is 0.97 years. It is evident from Table 3 that more than 40% of with Alzheimer ‘s disease are brought for treatment with in

0.5 to one year of onset of illness. Only one patient in the study had the illness for 3 years. This explains us that the caregivers are very sensitive to the behavioural changes observed in patients with Alzheimer ‘s disease. From Table 4, it is found that the offsprings and the spouse were the major caregivers accounting for 62%. Only one patient had a paid caregiver.

Of the 50 patients with Alzheimer ‘s disease, 15(30%) belonged to the mild stage of illness.22 (44%) were in the moderate group and 13(26%) in the severe group as rated by the Clinical Dementia Rating Scale (Table 5). This study tried to assess the significance of association between the age and the severity of cognitive decline. Table 6 shows that there exists significant association between advancing age and the decline in the cognitive status (P=0.001). Antonio et al, in his study has suggested advancing age as the most important risk factor for Alzheimer ‘s disease. This has been further supported by study by James *et al*. The age distribution of the patients with Alzheimer’s dementia in the three stages of illness is shown in figure1.

Similar attempts to find the association between gender and the cognitive status were made. However, no significant association was found between female gender and declining cognitive status (Table 7). The gender distribution across the three stages of Alzheimer ‘s disease is shown in figure 2.Although females are affected more with Alzheimer ‘s disease in older age group, in this study, males outnumbered females. This could be explained by the limited sample size.

Table 8 compares the duration of Alzheimer’s dementia and the cognitive status as assessed by the CDR scale. Pvalue of 0.04 signifies that there exists an association between increase in the duration of Alzheimer’s dementia and severe cognitive decline. Figure 3 shows the duration of Alzheimer’s dementia in patients in the three stages of illness.

The most common behavioural manifestation observed in the study group is apathy (72%), which is shown in Table 9 Findings from the Cache county study on memory in aging by Constantine *et al* showed that apathy was one of the most common mental and behavioural disturbances in participants with dementia

Irritability, a common behaviour in Alzheimer's disease, was present in less than one- half of the patients in this study (42%, Table 9). Irritability is distinct from agitation, being defined as rapid emotional fluctuations between frustration and impatience with the patient becoming easily disturbed. . In the study conducted by Mega and colleagues in patients with probable dementia, irritability was reported to be one of the most common troublesome behaviour.

Agitation is broadly defined as non-compliance, refusal to co-operate with the caregiver, obstinence, resistance, crying, kicking and hard to handle in the Neuro psychiatric inventory. There was steady increase in agitation from 50 % to 85% of patients with worsening Clinical Dementia Rating scores (Table 9). Aberrant motor behaviour such as pacing, picking at clothing are scored separately in the Neuro psychiatric inventory, which also increases in patients with severe CDR stage. Cynthia *et al*, have suggested that agitation and depression were among the important predictors of institutionalization Because agitation, aberrant motor behaviour and irritability are major challenges in the care of demented patients, monitoring their individual response to treatment is important.

From Table 9,it is seen that dysphoria increased from more than 10% in the mild group to more than 60% in the severe group. This finding is consistent with the earlier observation by Mega and colleagues .The dysphoria domain of the Neuropsychiatric inventory excludes features common to both dementia and depression (eg, vegetative symptoms) and reflects the patient ‘s mood state more specifically than the commonly used rating scales for depression. Anhedonia, a core symptom of depression shares some features with apathy.

Delusions and hallucinations did not always occur together across the three groups. Although delusions increased in frequency, hallucinations declined in the more severely impaired group(Table 9). The independence of these symptoms may point to differing underlying pathophysiologic processes. . In one study, these phenomena were present around the time of diagnosis, perhaps even prompting referral for diagnosis, in 45% of patients. Other studies reported that hallucinations, more often visual than auditory, rarely manifest early in the illness but may be more common in severe dementia (Levy *et al*).

The earlier literature tended to group the study of delusions and hallucinations within the broader category of psychosis, in which either of the two would be considered a basis for the presence of a psychotic syndrome. In contrast, it has been proposed that delusions and hallucinations differ in their predisposing factors and etiopathogenesis. This position now has empirical support. A recent population-based study found that patients with Alzheimer's disease can be empirically classified into three groups on the basis of their neuropsychiatric symptom profile: a group with an affective disturbance, a group with a psychotic disturbance, and a group with no or other neuropsychiatric disturbances (Ballard *et al*). The presence of hallucinations predicted membership in the second group, whether or not delusions were present. In contrast, patients with delusions were present in all three groups. On the basis of this work, empirically derived criteria for an Alzheimer's disease-associated affective and psychotic syndrome have been proposed, with hallucinations being critical to the presence of the psychotic syndrome. In addition, Bassiony *et al*. found that delusions and hallucinations had different risk factors and consequences and that delusions, but not hallucinations, were closely associated with depression. Therefore, delusions and hallucinations may best be approached separately, with hallucinations

being most indicative of a psychotic syndrome and delusions being indicative of either a psychotic disturbance or an affective disturbance.

Table 10 shows that there is significant association between certain behavioural problems like disinhibition and irritability with worsening cognitive status. This finding differs from the earlier study by Mega *et al*, in which agitation, apathy and aberrant motor behaviour were found to be significantly associated with cognitive decline. Similar findings were observed in the Cache county study by Constantine *et al*, in which apathy correlated significantly with the cognitive decline.

The mean severity and the composite scores of the mild and the severe CDR group vary significantly (P= 0.04 and p=0.05 respectively) as seen from Table 11. This is consistent with the observations done by Mega *et al* in her study on 50 patients with probable dementia.

Table 12 shows that agitation has significant correlation with the aberrant motor behaviour(r=0.610.p= 0.007).

The correlation between disinhibition and irritability is shown in Table 13.In our study, there seems to be very significant correlation between these two behavioural domains, which is found in other studies too (Constantine *et al*). An attempt was made to assess the relationship between irritability with other domains (Table 14). Other than disinhibition, irritability did not have significant correlation with other behavioural domains.

As seen from Table 15, aberrant motor behaviour has positive correlation to elation (r=1) and agitation(r=0.61), consistent with earlier studies (Cummings *et al*)

The positive correlation between these behavioural domains as seen from the study emphasizes the importance of evaluation of these symptoms with appropriate assessment tools at the earliest and manage them with individually tailored interventions that includes both pharmacological and non pharmacological measures.

SUMMARY

In this Indian based hospital study on Alzheimer's disease, 33% of the study group was in the age group of 66-70 and the remaining 17% in the 71-76 groups. The male to female ratio was 1.5: 1, which is different from the usual observation, where females outnumber males. The mean duration of illness was 0.97 years. There is significant association between advancing age and cognitive decline. Increase in duration of Alzheimer's disease is associated significantly with severe cognitive decline.

Among the behavioural domains, 72% of the patients had apathy. However, unlike earlier studies, this did not have significant correlation to the worsening cognitive status. Similarly, agitation and aberrant motor behaviour also did not have significant correlation to the cognitive status. The mean composite scores of irritability and disinhibition were found to be significantly associated with poor cognitive functioning. There was significant difference in the mean composite scores of the behavioural problems between the mild and the severe CDR groups. Certain behavioural domains had positive correlation among them. Aberrant motor behaviour correlated with agitation and elation. Disinhibition correlated with irritability

CONCLUSION

From this study, the following conclusions are drawn:

1. Advancing age and increased duration of illness are significantly associated with severe cognitive decline.
2. Males with Alzheimer's disease were found to have severe cognitive decline than females.
3. Several behavioural problems occur simultaneously in patients with Alzheimer's disease.
4. The behavioural problems vary across the various stages of Alzheimer's disease.
5. Agitation, apathy, dysphoria, disinhibition and aberrant motor behaviour become more frequent in the severe stage of Alzheimer's disease.
6. Disinhibition and irritability have significant correlation to severe cognitive impairment.
7. With in the ten behavioural domains, agitation has significant correlation to aberrant motor behaviour and disinhibition has significant correlation to irritability.

With these results, it is possible to conclude that mental and behavioural problems are a central component of Alzheimer's disease, regardless of the stage of illness. Although the core feature of dementia is the disturbance in cognition, it seems clear that almost all individuals with dementia will exhibit behavioural problems at some point of their illness. The severity of the behavioural problems increases with the advancement of the illness.

These behavioural problems add substantially to the morbidity and the disability of the illness. They are the important source of burden to the caregivers. They play an important role in the diagnosis and management of Alzheimer's disease. Early detection and treatment of these behavioural problems may reduce the patient suffering, caregivers burden and delay hospitalization.

LIMITATIONS

1. The main limitation of the study is the lack of longitudinal assessment of behavioural changes in Alzheimer' s disease.
2. This is a hospital based study and not representative of the community.
3. Various subtypes of dementia have not been analysed in the study.
4. Other behavioural changes like eating disorders, sexual changes, vegetative symptoms and diurnal variation of behaviour are not assessed in this study.

SCOPE FOR FUTURE STUDIES

- Studying the patient longitudinally will allow the characterization of the temporal progression of the behavioural disturbances in Alzheimer's disease patients.
- Applying the Neuropsychiatric inventory to patients with other types of dementia such as vascular dementia, fronto temporal dementia and dementia in Parkinson's disease will clarify the patterns of behavioural changes related to various neuropathologies.

FIGURE 1-AGE DISTRIBUTION OF THE PATIENTS WITH ALZHEIMER'S DISEASE

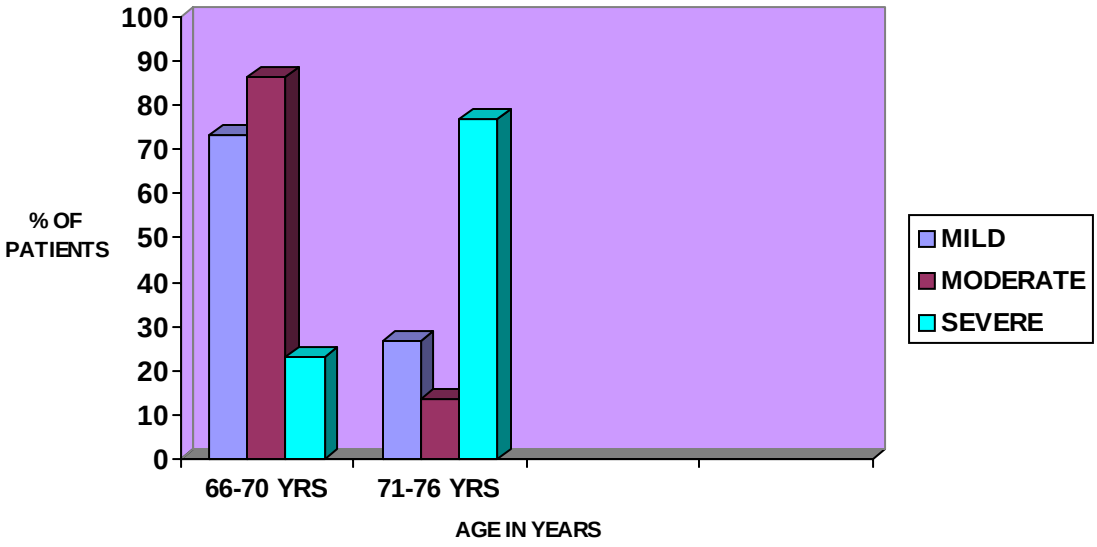


FIGURE 2- GENDER DISTRIBUTION OF PATIENTS WITH ALZHEIMER'S DISEASE

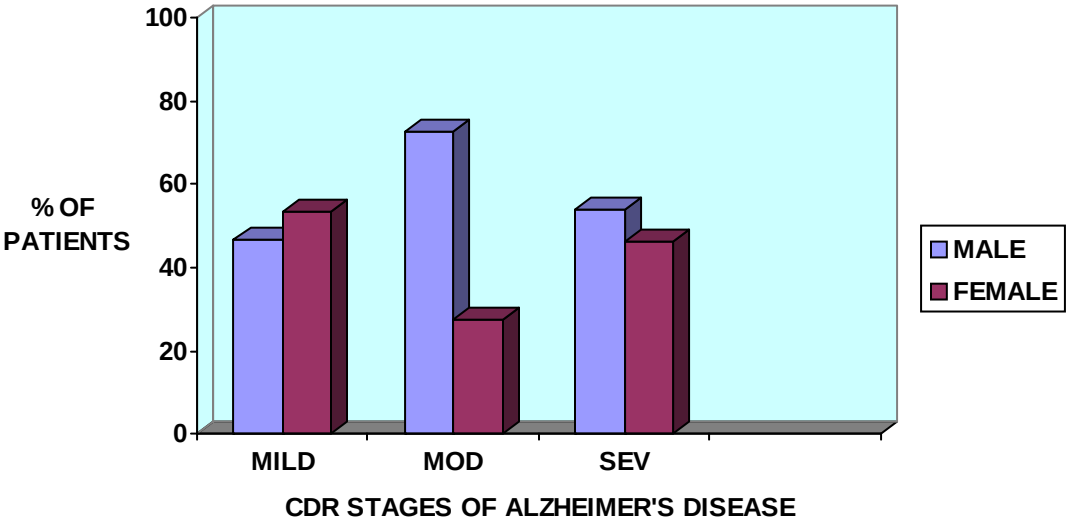


FIGURE 3- DURATION OF ALZHEIMER'S DISEASE IN THE THREE CDR GROUPS

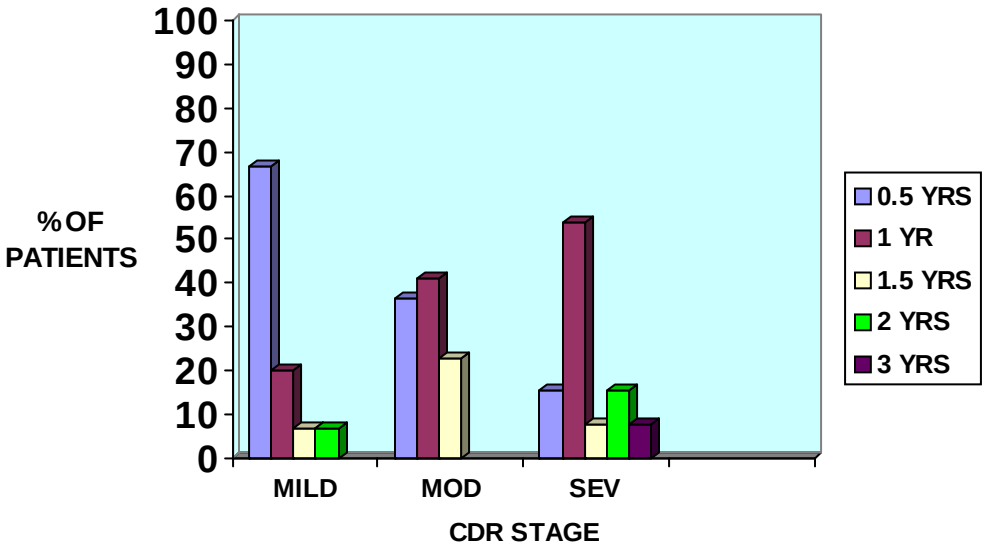
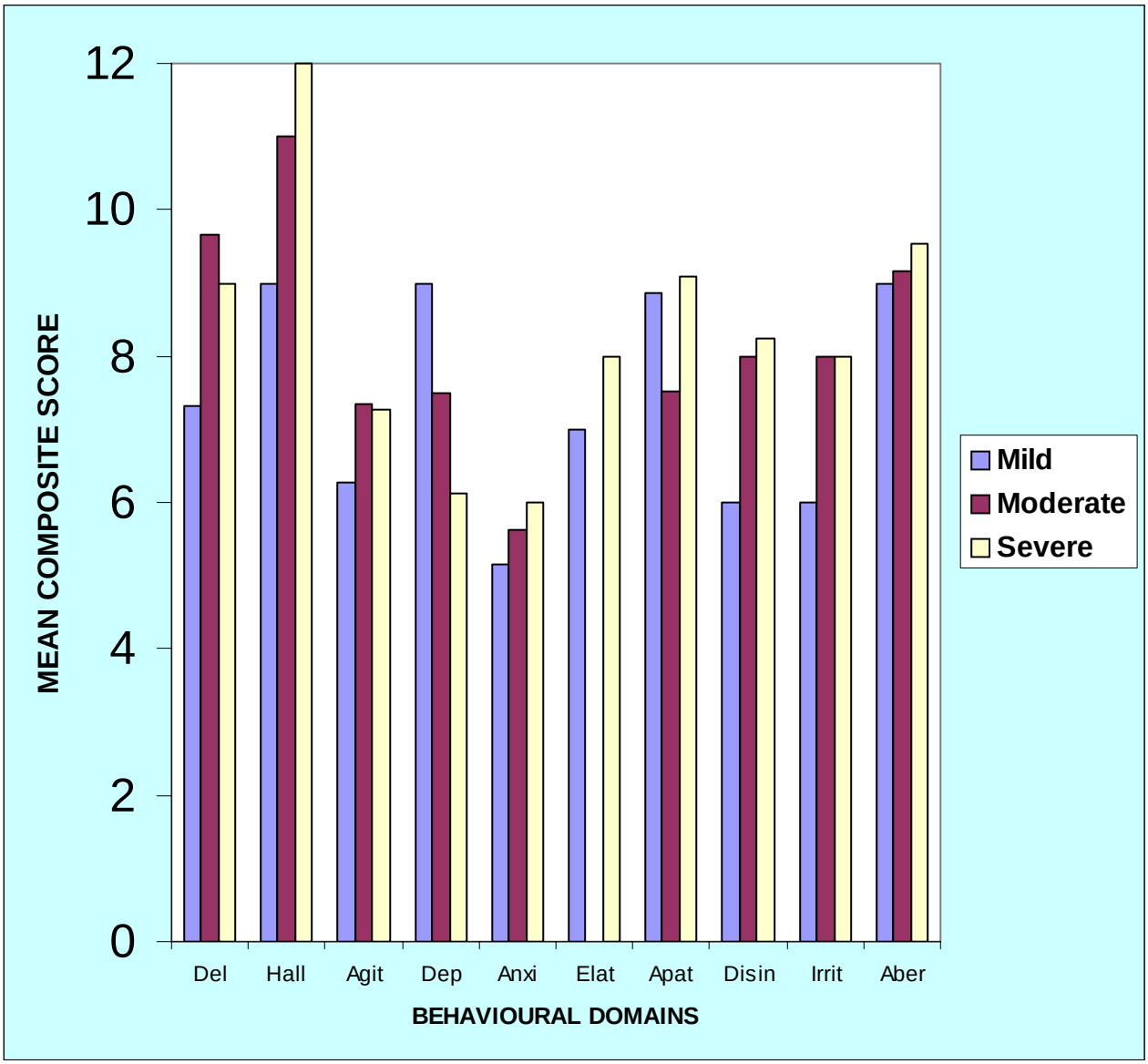


FIGURE 4- MEAN COMPOSITE SCORES OF TEN BEHAVIOURAL DOMAINS ACROSS THE THREE STAGES OF ILLNESS



BIBLIOGRAPHY

1. Alan Jacques, Graham A Jackson: Behaviour and dementia. Understanding dementia 3rd edition 2000; 166-167.
2. American Psychiatric Association. Diagnostic and Statistical Manual Of Mental Disorders, Fourth edition, text revision. Washington DC: American Psychiatric Association, 2000.
3. Antonio lobo, Pedro saz: Dementia. In: James L. Levenson ed. Textbook of Psychosomatic medicine.2005; chapter 7:131
4. Ballard C, Bannister C, Graham C, Oyebode F, Wilcock G: Associations of psychotic symptoms in dementia sufferers. British Journal of Psychiatry 1995; 167:537–540.
5. Bassiony MM,Steinberg MS, Warren A, Rosenblatt A, Baker AS, Lyketsos CG.Delusions and hallucinations in Alzheimer's disease: prevalence and clinical correlates. International journal of Geriatric psychiatry. 2000 Feb; 15(2): 99-107
6. . Bassiony M, Constantine G. Lyketsos: Delusions and Hallucinations in Alzheimer's disease. Review of the Brain Decade 2002

7. Benoit M,Robert PH, Staccini P, One-year longitudinal evaluation of neuropsychiatric symptoms in Alzheimer's disease. The REAL.FR Study. Journal of Nutrition, Health and Aging 2005; 9(2): 95 –9
8. Burke WJ, Miller JP, Rubin EH et al: Reliability of Washington University Clinical Dementia Rating. Archives Of Neurology 1988; 45: 31-32.
9. Burns A, Jacoby R, Levy R: Psychiatric phenomena in Alzheimer's disease. British Journal of Psychiatry 1990; 157:72–94.
10. Cohen – Mansfield,J, Marx MS, Rosenthal AS. A description of agitation in a nursing home. Journal Of Gerontology and Medical Sciences 1989; 44:77-84.
11. Constantine G. Lyketsos, Martin Steinberg: Mental and behavioral disturbances in dementia: Findings from the Cache county study on memory in aging. American Journal Of Psychiatry 2000; 157:708-714
12. Constantine G.Lyketsos, Cynthia Steele: Physical aggression in dementia patients and its relationship to depression. American Journal Of Psychiatry 1999; 156:66-71
13. Craig AH, Cummings JL, Fairbanks L et al: Cerebral blood flow correlates of apathy in Alzheimer's disease. Archives Of Neurology 1996; 53: 1116-1120.

14. Cummings JL: The Neuropsychiatric Inventory: Assessing psychopathology in dementia patients. Neurology 1997; 48(suppl 6): S10-S16
15. Cummings JL, Mega M, Gray K, Rosenberg-Thompson S, Carusi DA, Gornbein J: The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. Neurology 1994; 44:2308–23
16. Cynthia Steele, Barry Rovner: Psychiatric symptoms and nursing home placement of patients with Alzheimer `s disease. American Journal Of Psychiatry 1990; 147:1049-1051.
17. Dag Aarsland, Jeffrey L. Cummings: Relationship of aggressive behaviour to other neuropsychiatric symptoms in patients with Alzheimer `s disease. American Journal Of Psychiatry 1996; 153:243-247
18. Deutsch LH, Bylsma FW, Rovner BW, Steele C, Folstein MF: Psychosis and physical aggression in probable Alzheimer's disease. American Journal Of Psychiatry 991; 148:1159–1163.
19. Devanand DP, Jacobs DM, Tang MX, Del Castillo-Castaneda C, Sano M, Marder K, Bell K, Bylsma FW, Brandt J, Albert M, Stern Y: The course of psychopathologic features in mild to moderate Alzheimer disease. Archives Of General Psychiatry 1997; 54:257–263

20. Eisdorfer C, Cohen D, Paveja GJ, et al. An empirical evaluation of the global deterioration scale for staging Alzheimer's disease. American Journal Of Psychiatry .1992; 140:190-194.
21. Engelborghs Maertens K, Nagels G: Neuropsychiatric symptoms of dementia: cross-sectional analysis from a prospective, longitudinal Belgian study. International journal of Geriatric psychiatry 2005 Nov;20(11):1028-37.
22. Farber NB, Rubin EH, Newcomer JW, Kinscherf DA, Miller JP, Morris JC, Olney JW, McKeel DW Jr: Increased neocortical neurofibrillary tangle density in subjects with Alzheimer disease and psychosis. Archives Of General Psychiatry 2000; 57:1165–1173
23. Finkel, Sl, Silva JC, Cohen G, et al. Consensus statement: Behavioural and psychological signs and symptoms of dementia: a consensus statement on current knowledge and implications on research and treatment. International Psychogeriatrics. 1996;(suppl 3): 497-500.
24. Flynn FG, Cummings JL Delusions in dementia syndromes: investigation of behavioral and neuropsychological correlates. Journal Of Neuropsychiatry and clinical Neurosciences 1991 Fall;3(4):364-70
25. Gormley N, Rizwan MR Prevalence and clinical correlates of psychotic symptoms in Alzheimer's disease. International journal of Geriatric psychiatry 1998 Jun;13(6):410-4

26. Greenwald BS, Kramer-Ginsberg E, Marin DB, Laitman LB, CK Hermann CK, Mohs RC, Davis KL: Dementia with coexistent major depression. American Journal of Psychiatry 1989; 146:1472-1478
27. Hall KS, Gao S, Unverzagt FW, et al:Low education and childhood rural residence:risk for Alzheimer's disease in African Americans. Neurology 2000; 54:95-99.
28. Haupt M, Kurz A, Janner M: A 2-year follow-up of behavioural and psychological symptoms in Alzheimer's disease. Dementia Geriatry and Cognitive Disorders 2000 May-Jun;11(3):147-52.
29. Hughes P, Leonard Berg et al: A new clinical scale for the staging of dementia. British Journal of Psychiatry 1982; 140:566-572
30. James A, Bourgeois, Jeffrey S Seaman, Mark E Servis: Delirium, Dementia and Amnestic Disorders. In: Robert E Hales, Stuart C Yudofsky eds: Textbook Of Clinical Psychiatry 4th edition,2003; chapter 7:259.
31. Judith A. Neugroschl, Alexander Kolevzon,Steven C. Samuels, Deborah B.Marin. Dementia. In: Benjamin A.Saddock, Virginia A.Saddock, eds, Comprehensive Textbook Of Psychiatry; 2005;Chapter 10:1069.
32. Lam CK, Lim PP, Low BL, Ng LL, Chiam PC, Sahadevan S: Depression in dementia: a comparative and validation study of four brief scales in the elderly Chinese. International journal of Geriatric psychiatry 2004 May;19(5):422-8.

33. Lechowski L, Dieudonne B, Tortrat D, Teillet L: Role of behavioural disturbance in the loss of autonomy for activities of daily living in Alzheimer patients. International journal of Geriatric psychiatry 2003 Nov;18(11):977-82.
34. Levy ML, Cummings JL, Fairbanks LA, Bravi D, Calvani M, Carta A: Longitudinal assessment of symptoms of depression, agitation, and psychosis in 181 patients with Alzheimer's disease. American Journal Of Psychiatry 1996; 153:1438–1443
35. Levy ML, Cummings JL, Miller BL, Fairbanks L, Craig AH: Alzheimer's dementia and fronto temporal dementias: behavioural distinctions. Archives of Neurology 1982; 11: 121-126.
36. Litvan I, Mega MS, Cummings JL, Fairbanks L: Neuropsychiatric aspects of progressive supranuclear palsy. Neurology 1996; 47: 1184-1188
37. Lyketsos CG, Steele C, Baker L: Major and minor depression in Alzheimer's disease: prevalence and impact. Journal Of Neuropsychiatry and clinical Neurosciences 1997 Fall;9(4):556-61.
38. Marin DB, Green CR, Schmeidler J, Harvey PD: Noncognitive disturbances in Alzheimer's disease: frequency, longitudinal course, and relationship to cognitive symptoms. Psychiatry Service, Veterans Affairs Medical Center, Bronx, New York, USA.2005

39. McCarty HJ, Roth DL, Goode KT, Longitudinal course of behavioral problems during Alzheimer's disease: linear versus curvilinear patterns of decline. Journal Of Gerontology And Biological science and Medical science 2000 Apr; 55(4): 200-6.
40. Mega S, Jeffrey L. Cummings, Tara Fiorella, Jeffrey Gornbein: The spectrum of behavioural changes in Alzheimer’s disease. Neurology 1996;46: 130-135.
41. Miller BL, Cummings JL, Villaneuva – meyer J, et al: Frontal lobe degenerations: clinical, neuropsychological and SPECT characteristics. Neurology 1991; 41: 1374-1382.
42. Moriss RK, Rovber BW, Folstein MF,German PS : Delusions in newly admitted residents of nursing homes . American Journal Of Psychiatry 1990; 147:299-302
43. Morris JC, Ernesto C, Schafer K et al: Clinical Dementia Rating training and Reliability in multicenter studies: the Alzheimer's disease co operative study experience. Neurology 1997; 48:1508-1510.
44. Morris JC. The Clinical Dementia Rating (CDR): current version and scoring rules. Neurology 1993; 43:2412-2414.
45. Petry S, Cummings JL, Hill MA et al: Personality alteration in dementia of Alzheimer’ s type: Archives Of Neurology 1988; 45: 1187-1190.
46. Ramachandran G, Marder K, Tang M, Schofield PW, Chun MR, Devanand DP, Stern Y, Mayeux R: A preliminary study of

apolipoprotein E genotype and psychiatric manifestations of Alzheimer's disease. Neurology 1996; 47:256–259.

47. Ravetz RS: Psychiatric disorders associated with Alzheimer's disease. Journal Of American Osteopathic Association 1999 Sep;99(9 Suppl):S13-6.
48. Reisberg B, BorensteinJ,Salob SP et al:Behavioural symptoms in Alzheimer's disease: phenomenology and treatment .Journal Of Clinical Psychiatry 1987 ; 48 (suppl 5):9-15.
49. Rubin E, Kinscherf DA. Psychopathology of very mild dementia of Alzheimer’s type. American Journal Of Psychiatry 1989; 146: 1017-1021.
50. Sabrina paterniti, Marie- Helene Verdier-Taillerfer: Depressive symptoms and cognitive decline in elderly people. British Journal Of Psychiatry 2002; 181:406-410
51. Shaji KS, Smitha K, Lal KP, Prince MJ :Caregivers of people with Alzheimer's disease .a qualitative study from the Indian 10/66 Dementia Research Network. International Journal Of Geriatric Psychiatry 2003 Jan;18(1):1-6.
52. Steinberg M, Corcoran C, Tschanz JT, et al: Risk factors for neuropsychiatric symptoms in dementia: the Cache county study. International Journal Of Geriatric Psychiatry 2004; 19: 19-26

53. Stevens T, Livingston G, kitchen g, et al. Islington study of dementia subtypes in the community. British Journal of Psychiatry 2002; 180:270-6
54. The ICD-10 Classification Of Mental and Behavioural Disorders. Clinical descriptions and diagnostic guidelines. 2002
55. Zubenko GS, Moosy J: Major depression in primary dementia:Clinical and neuropathological correlates. Archives Of Neurology 1990; 47:209-214.
56. Zubenko GS, Moosy J, Martinez AJ et al:Neuropathological and neurochemical correlates of psychosis in primary dementia. Archives Of Neurology 1991; 48:619-624.

APPENDICES

PROFORMA

CASES:

1. NAME

2.AGE

3.SEX **1.FEMALE**

2. MALE

4.EDUCATION **1.NONE**

2.MINIMAL

3.COMPLETED PRIMARY

4.COMPLETED SECONDARY (MATRIC)

5. COMPLETED TERTIARY (COLLEGE)

5. RELATIONSHIP OF THE CAREGIVER

1.SPOUSE

2.SON/DAUGHTER

3. SON IN LAW/DAUGHTER IN LAW

4.SIBLING

5.OTHERS

6.DURATION OF ILLNESS

CAREGIVERS

1. **NAME**
2. **AGE**
3. **SEX**
4. **ADDRESS**
5. **EDUCATION**
6. **OCCUPATION**
7. **INCOME**

CLINICAL DEMENTIA RATING SCALE

Category	healthy CDR 0	questionable dementia CDR 0.5	mild dementia CDR 1	moderate dementia CDR 2	severe dementia CDR 3
Memory	No memory Loss	Mild consistent forgetfulness; partial Recollection of events	Moderate memory loss, more marked for recent events; defect interferes with daily activities	severe memory loss; only highly learned material retained; new material rapidly lost	severe memory loss; only fragments remain
Orientation	fully Oriented	fully oriented	some difficulty with time relationships; Oriented for place & person at examination, but may have geographic disorientation	usually disoriented in time; often to place	orientation to person only
Judgment & problem	solves every day	only doubtful impairment in	moderate difficulty in handling complex	severely impaired in handling	unable to make

solving	problems well	solving problems, similarities, differences	problems, social judgement usually maintained	problems; similarities, differences; social judgement usually impaired	judgements or solve problems
Community affairs	independent function at usual level in job, shopping, business& financial affairs, volunteer & social groups	only doubtful or mild impairment, if any, in these activities	unable to function independently at these activities though may still be engaged in some;may still appear normal to casual inspection	no pretence of independent function outside home	no pretence of independent function outside home
Home &Hobbies	life at home hobbies, intellectual interests well maintained	life at home hobbies, intellectual interests well maintained or slightly impaired	mild, but definite impairment of function at home; more difficult chores abandoned; more complicated hobbies & interests abandoned	only simple chores preserved; very restricted interests, poorly sustained	no significant function in home outside of own room

Personal Care	fully capable of self care	fully capable self care	needs occasional prompting	requires assistance in dressing, hygiene, keeping of personal effects	requires much help with personal care, often incontinent

SCORING BOX FOR CDR SCALE

Score	0	0.5	1	2	3
Memory					
Orientation					
Judgement & Problem solving					
Community affairs					
Home &Hobbies					
Personal care					

NEUROPSYCHIATRIC INVENTORY

A. DELUSIONS: Y N N/A

Frequency ___ severity ___

1. Fear of harm
2. Fear of theft
3. Spousal affair
4. Phantom boarder
5. Spouse impostor
6. House not home
7. Fear of abandonment
8. Talks to TV, etc.
9. Other

B. HALLUCINATIONS: Y N N/A

Frequency ___ severity ___

1. Hears voices
2. Talks to people not there
3. Sees things not there
4. Smells things not there
5. Feels things not there
6. Unusual taste sensations
7. Other

C. AGITATION/AGGRESSION: Y N N/A

Frequency ___ severity ___

1. Upset with care giver
2. Stubbornness
3. Uncooperative; resists help
4. Hard to handle
5. Cursing or shouting angrily
6. Slams doors; kicks, throws things
7. Hits, harms others
8. Other

D. DEPRESSION: Y N N/A

Frequency ___ severity ___

1. Tearful and sobbing
2. States, acts as if sad
3. Puts self down, feels like failure
4. Bad person, deserves punishment
5. Discouraged, no future
6. Burden to family
7. Talks about dying, killing self
8. Other

E. ANXIETY: Y N N/A

Frequency ___ severity ___

1. Worries about planned events
2. Feels shaky, tense
3. Sobs, sighs, gasps
4. Racing heart
5. Phobic avoidance
6. Separation anxiety
7. Other

F. ELATION/EUPHORIA: Y N N/A

Frequency ___ severity ___

1. Feels too good, too happy
2. Abnormal humor
3. Childish, laughs inappropriately
4. Jokes &remarks not funny to others
5. Childish pranks
6. Talks big, grandiose
7. Other

G. APATHY/INDIFFERENCE: Y N N/A

Frequency ___ severity ___

1. Less spontaneous or active
2. Less likely to initiate conversation
3. Less affectionate, lacking emotions
4. Contributes less to household chores
5. Less interested in others
6. Lost interest in friends or family
7. Less enthusiastic about interests
8. Other

H. DISINHIBITION: Y N N/A

Frequency _____ severity _____

1. Acts impulsively
2. Excessively familiar with strangers
3. Insensitive or hurtful remarks
4. Crude or sexual remarks
5. Talks openly of private matters
6. Inappropriate touching of others
7. Other

I. IRRITABILITY:Y N N/A

Frequency ____ severity _____

1. Bad temper
2. Rapid changes in mood
3. Sudden flashes of anger
4. Impatient, trouble coping with delays
5. Cranky, irritable
6. Argues, difficult to get along with
7. Other

J.ABERRANT MOTOR BEHAVIOUR

Y N N/A

Frequency _____ severity _____

1. Paces without purpose
2. Opens or unpacks closets or Drawers
3. Repeatedly dresses &undresses
4. Repetitive activities or habits
5. Handling, picking behavior
6. Excessive fidgety
7. Other

NEUROPSYCHIATRIC INVENTORY SCORING SUMMARY

DOMAIN	ABSENT	FREQUENCY	SEVERITY	FREQUENCY X SEVERITY
DELUSIONS	☐	1 2 3 4	1 2 3	☐ ☐
HALLUCINATIONS	☐	1 2 3 4	1 2 3	☐ ☐
AGITATION	☐	1 2 3 4	1 2 3	☐ ☐
DYSPHORIA	☐	1 2 3 4	1 2 3	☐ ☐
ANXIETY	☐	1 2 3 4	1 2 3	☐ ☐
ELATION	☐	1 2 3 4	1 2 3	☐ ☐
APATHY	☐	1 2 3 4	1 2 3	☐ ☐
DISINHIBITION	☐	1 2 3 4	1 2 3	☐ ☐
IRRITABILITY	☐	1 2 3 4	1 2 3	☐ ☐
ABERRANT MOTOR BEHAVIOUR	☐	1 2 3 4	1 2 3	☐ ☐
TOTAL SCORE				☐ ☐ ☐

NEUROPSYCHIATRIC INVENTORY RATING SHEET FOR INFORMANT

FREQUENCY:

1. Occasionally-less than once per week
2. Often-about once per week
3. Frequently- several times per week, but less than every day
4. Very frequently-daily or essentially continuously present

SEVERITY:

1. Mild- produces little distress
2. Moderate-more disturbing to the patient, but can be re directed by the caregiver
3. Severe- very disturbing to the patient and difficult to re direct

The score for each domain is: frequency x severity.