Impact of behavioral symptoms on patients with Alzheimer's disease

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Background
Behavioral symptoms of dementia are noncognitive symptoms that occur commonly with Alzheimer's disease (AD). The characterization of the clinical profile of AD patients may help to better understand disease evolution and to improve diagnosis and treatment. Thus, the aim of our study is to describe the clinical profile of AD patients and to correlate the presence of behavioral symptoms with other variables of the disease.

Methods
Assessments of behavioral symptoms measured by the Revised Memory and Behavior Problems Checklist, the Mini Mental State Examination, the Clinical Dementia Rating, and the Disability Assessment for Dementia were performed for 40 AD patients.

Results
The Revised Memory and Behavior Problems Checklist scores were significantly increased in severe cases in comparison with mild cases. There were significant positive correlations between the Revised Memory and Behavior Problems Checklist with the Clinical Dementia Rating, and the Disability Assessment for Dementia. There was a significant negative correlation between the Revised Memory and Behavior Problems Checklist and the Mini Mental State Examination.

Conclusion
Our study shows that patients with AD have a high prevalence of behavioral and psychological symptoms measured by the Revised Memory and Behavior problems Checklist and that behavioral symptoms, cognitive impairment, and disease severity are correlated. Therefore, the Revised Memory and Behavior problems Checklist is a useful tool for evaluation in patients with AD.

Keywords:
Alzheimer's disease, behavioral symptoms, cognitive impairment, disease severity, prevalence

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Introduction

Dementias, and especially Alzheimer's disease (AD), are a growing public health problem associated with aging. The main symptoms of dementia are functional, cognitive, and behavioral manifestations [1]. Behavioral symptoms in AD are the first manifestations of the disease, which might precede cognitive alterations at some time during the course of the illness and differ according to disease severity [2].

Neuropsychiatric symptoms, previously known as behavioral and psychological symptoms of dementia, are now increasingly being considered as an important aspect of dementia because of their impact on the quality of life of both patients and their caregivers [3].

Behavioral symptoms such as depression, anxiety, and agitation occur commonly in AD, the most common form of dementia in late life. Evidence suggests that between 60 and 90% of individuals with AD present with at least one behavioral disturbance during the course of their illness [4]. They contribute toward greater caregiver and patient distress [5], more expensive and tedious interventions, and more rapid functional decline and cognitive impairment [6]. Considering these high rates of occurrence of behavioral symptoms and their adverse impact, it is important to understand what contributes toward their development in AD [7]. Behavioral symptoms are associated with a variety of negative effects on health, physical health problems, and death [8].

Recent evidence shows that good relationships and family understanding and functioning are associated with lower reactions level to behavioral problems and fewer family problems compared with individuals with unsatisfactory relationships and poor family functioning [9].

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Currently, behavioral symptoms can be assessed using standardized instruments such as the Neuropsychiatric Inventory [10], the Behavior Pathology in Alzheimer's Disease scale [11], the Alzheimer's Disease Assessment Scale (ADAS) [12], and the Revised Memory and Behavior Problems Checklist (RMBPC) [13].

Therefore, this study aimed to describe the behavioral symptoms of AD patients according to RMBPC and to correlate these symptoms to clinical variables of dementia such as age, sex, score of mini mental state examination (MMSE), severity, and presence of comorbid physical conditions.

Patients and methods

Forty patients diagnosed with AD according to the International Statistical Classification of Diseases, 10th revision (ICD-10) criteria were selected from the OPC of the Institute of psychiatry Ain Shams University and Geriatric department, Ain Shams University. The study included all patients diagnosed with AD according to the ICD-10 criteria in the period between June 2010 and December 2010, and this was an observational, cross-sectional, and qualitative study.

Within the study period, 55 patients were examined; only 40 of these patients fulfilled our criteria of diagnosis of AD and completed the study tools. All patients and their caregivers were provided oral information about the aim, content, and duration of the interviews; they were informed that the interviews and tools used in this study would be confidential and that refusal to participate would not influence their treatment. All patients and their caregivers who agreed to participate in the study and provided written consent were included.

Patients were subjected to the following assessments: comprehensive assessment including history, psychiatric and medical history, family history, physical examination, and interview of relatives as carers, and were screened using the MMSE [14].

Psychiatric assessment included the following:

(1) ICD-10 Symptom Checklist [15]: The diagnosis of AD in the patients was confirmed according to a checklist that specifies two subtypes for the diagnosis of dementia of the Alzheimer's type according to the age of onset (early onset before 65 or late onset beyond the age of 65 years). The ICD-10 criteria also specify the severity of AD as mild, moderate, and severe.
(2) RMBPC [13]: This scale is used for assessment of behavioral problems in patients with dementia. Items were gathered from the original Memory and Problems Checklist [16], plus additional items; the main categories of the reported problems were memory, disruptive behaviors, and depression. It requires caregivers to rate the frequency of behavioral problems and memory difficulties in patients during the previous week and caregiver ratings of their own reaction to each of the reported problems. The rater should indicate whether any of these problems had occurred during the past week. It consisted of 24 items. Scoring was follows: 0 = never occurred, 1 = not in the past week, 2 = one to two times in the past week, 3 = three to six times in the past week, and 4 = daily or more often; the higher the total score, the more severe the behavioral problems.
(3) Clinical Dementia Rating (CDR) scale [17]: This is a scale for the global ratings of AD. Six domains are assessed: memory, orientation, judgment and problem solving, community affairs, home and hobbies, and personal care. CDR ratings are 0 for healthy individuals, 0.5 for questionable dementia, and 1, 2, and 3 for mild, moderate, and severe dementia as defined in the scale. The total CDR rating is obtained from the sum of boxes, which represents an aggregate score of each individual's areas.
(4) Disability Assessment for Dementia (DAD) [18]: This is an instrument used to describe the functional characteristics of AD patients and is intended specifically for the assessment of disability in individuals with cognitive deficits such as dementia. The scale consists of 10 main items. This scale can assess activities of daily living and monitor disease progression.

Statistical analysis

The results were analyzed using the statistical package for social science (version 10) (Levesque Company, SPSS Programming and Data Management, SPSS Inc., Chicago). Descriptive statistics was presented as means ± SD, number, and percentage (frequency distributions). Analytical tests used included the χ^2-test, cross tabs for contingency table analysis, and the Mann–Whitney *U*-test for two independent samples. Correlation analysis was also carried out using the Spearman correlation coefficient in a bivariate correlation procedure. Significance levels of 0.05 and 0.01 were used throughout all statistical tests in this study.

This research was approved by the Research Ethical Committee of Ain Shams University.

Results

Descriptive data

Analysis of data of 40 patients: the mean age of the patients was 71.12 ± 8.42 years, 12 men (30%) and 28 women (70%). Ten patients (25%) had early-onset AD and 30 patients (75%) had late-onset AD. According to the CDR scale, 20 (50%) of the cases were of mild severity and 20 (50%) of the cases were of moderate to severe degree. The mean score on the MMSE was 13.69 ± 8.1. The DAD scores were 31.16 ± 11.16. For RMBPC items, percent of occurrence of each item of the 24 items of RMBPC was calculated and indicated independent of other items according to their order in the scale and main category (memory, disruptive behaviors, and depression) to which each item belongs.

The mean number of problems in RMBPC was 10.23 ± 4.16, the mean reaction per problem was 1.49 ± 0.92, and the mean of the total reaction was 16.95 ± 13.62. In our study, 92% of the overall patients showed at least one behavioral problem during the previous week. The clinical characteristics of the patients are further presented in Table 1.

Description of behavioral problems

For RMBPC items, percent of occurrence of each item of the 24 items of RMBPC was calculated and indicated independent of other items according to their order in the scale; the main category (memory, disruptive behaviors, and depression) to which each item belongs is presented between brackets.

Percent of occurrence of repetitive questions in our sample was 70.95% (memory problem), remembering recent events (memory problem) was 86.73%, remembering significant events (memory problem) was 69.86%, losing things (memory problem) was 64.55%, forgetting day (memory problem) was 89.76%, not finishing tasks (memory problem) was 49.13%, difficulty in concentrating (memory problem) was 91.69%, destroying property (disruptive behavior) was 9.51%, embarrassing activities (disruptive behavior) was 33.77%, waking at night (disruptive behavior) was 45.49%, talking loudly and rapidly (disruptive behavior) was 31.28%, anxious or worried (depression) was 58.55%, dangerous behaviors (disruptive behavior) was 16.93%, threatened to hurt self (depression) was 3.11%, threatened to hurt others (disruptive behavior) was 10.84%, verbally aggressive (disruptive behavior) was 32.92%, sad or depressed (depression) was 88.34%, hopelessness (depression) was 34.22%, crying or tearful (depression) was 28.16%, comments about death (depression) was 20.92%, feeling lonely (depression) was 20.89%, worthless or burden (depression) was 28.78%, feelings of failure (depression) was 15.32%, and argumentative (disruptive behavior) was 45.19%.

Table 2 shows the RMBPC subscales: memory problems, disruptive behaviors, and depression. Scores of each subscale are described as (mean ± SD) for number of problems, reaction to problem, and total reaction.

Table1 Clinical description of the patients and percent of occurrence of the seven most frequent behavioral symptoms (*n* = 40)

Clinical correlates	Mean ± SD or (%)
Age	71.12 ± 8.42
MMSE	13.69 ± 8.1
DAD	31.16 ± 11.16
Behavioral symptoms	
RMBPC (mean of problems)	10.23 ± 4.16
RMBPC (mean reaction per problem)	1.49 ± 0.92
RMBPC (total reaction)	16.95 ± 13.62
Difficulty in concentrating	91.69
Forgetting what day it was	89.76
Sad or depressed mood	88.34
Remembering recent events	86.73
Repetitive questions	70.95
Remembering significant events	69.86
Losing things	64.55

DAD, Disability Assessment for Dementia; MMSE, Mini Mental State Examination; RMBPC, Revised Memory and Behavior Problems Checklist score.

Clinical correlates of behavioral problems

Comparison of RMBPC total scores with the severity of AD showed that RMBPC scores were significantly increased in severe cases in comparison with mild cases ($P = 0.002$). RMBPC scores were not significantly different between men and women ($P = 0.12$); this is further shown in Table 3.

Also, a nonsignificant correlation was found between RMBPC scores with other variables such as age ($P = 0.83$), presence of diabetes ($P = 0.61$), hypertension ($P = 0.77$), osteoarthritis ($P = 0.08$), or coronary heart disease ($P = 0.75$); this is shown in Table 4. Therefore, the presence of a physical problem did not affect the prevalence of behavioral symptoms in this sample.

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RMBPC scores were significantly positively correlated with the score of CDR ($P = 0.003$) and among behavioral symptoms; lack of concentration showed the highest correlations, whereas a tendency was observed for dangerous behaviors. The rest of the behavioral symptoms alone did not show significant correlations.

RMBPC scores were also significantly positively correlated with the score of DAD.

Finally, RMBPC scores were significantly negatively correlated with the score of MMSE scores, $r = -0.821$ and $P = 0.001$; similarly, a significant positive correlation was found with CDR and DAD as r was 0.819 and 0.911 and $P = 0.003$ and 0.002, respectively.

Therefore, more severe dementia as rated by CDR was associated with significantly more behavioral problems as indicated by a higher total score of RMBPC and greater functional impairment as reported by DAD. In addition, greater functional impairment as reported by DAD was significantly associated with more behavioral problems as reported by RMBPC. Further, less severe cognitive impairment as reported by higher scores of MMSE was associated with less behavioral problems.

Discussion

The aim of the present study was to clarify the presence of behavioral symptoms according to RMBPC and to correlate these symptoms to clinical variables of dementia such as age, sex, score of MMSE, severity. and presence of comorbid physical conditions.

In our study, 92% of the overall patients showed at least one behavioral problem at the time of the study, in

Table 2 Descriptive data for the Revised Memory And Behavior Problems Checklist subscales ($n=40$)

	Number of problems			Reaction per problem			Total reaction		
Scale	Mean	SD	Range (min–max)	Mean	SD	Range (min–max)	Mean	SD	Range (min–max)
Memory problem	5.11	1.53	0–7	1.21	0.92	0–4	6.31	5.49	0–28
Disruptive behaviors	2.34	1.89	0–8	1.89	1.06	0–4	4.89	5.35	0–28
Depression	2.77	2.17	0–9	1.69	1.08	0–4	5.61	6.32	0–32
Total score	10.21	4.15	0–23	1.54	0.94	0–4	16.72	13.66	0–68

Max, maximum; min, minimum.

Table 3 Comparison between the severity of AD and RMBPC score

Clinical correlates	Mean	SD	*P* value
Severity			
Mild cases ($n=20$)	12.98	10.34	0.002**
Severe cases ($n=20$)	16.74	13.63	
Sex			
Men ($n=12$)	15.84	12.86	0.12
Women ($n=28$)	14.97	11.43	

AD, Alzheimer's disease; RMBPC, Revised Memory and Behavior Problems Checklist.
**Highly significant value.

Table 4 Age and physical disorders in comparison with RMBPC

Clinical correlates	*P* value
Age	0.83
Diabetes	0.61
Hypertension	0.77
Osteoarthritis	0.08
Coronary HD	0.75

HD, heart disease; RMBPC, Revised Memory and Behavior Problems Checklist.

agreement with another study using the ADAS scale [18], which reported that 97% of all patients had some behavioral symptoms at the time of the study.

In our study, the most prevalent behavioral problems were those related to memory such as difficulty in concentration (91.69%) and forgetting what day it was (89.76%), followed by that related to depression as sad or depressed mood, 88.34% (Table 1), and the most severe were behavioral problems related to memory (5.11), followed by depression (2.77) and finally disruptive behavior (2.34) (Table 2). Our results were consistent with data of other researches that reported that lack of concentration and depressed mood are frequent in AD patients [19]. Similar results were obtained by Marin and colleagues on studying noncognitive disturbances in AD [19]. Concentration disturbances and lack of attention appear very early in AD patients [20], probably because of the bilateral tempoparietal degeneration that occurs in AD [21]. In addition to its high prevalence, decrease in concentration is positively correlated with CDR scale scores, suggesting that this symptom should be considered a central deficit in AD [22]. Meanwhile, percent of occurrence of other memory problems was high in our study such as forgetting what day it was (89.76%) and remembering recent events (86.73%), repetitive questions (70.95%), remembering significant events (69.86%), and losing things (64.55%). This could be because of the fact that half of our patients had severe AD according to CDR scale scores and also probably because of the bilateral tempoparietal degeneration that occurs in this disease [21].

However, depression is among the behavioral symptoms commonly present in AD patients, and its core symptom is depressed mood. In our study, sad or depressed mood was the third most frequent behavioral symptom, with a prevalence of 88.34%. These results are in agreement with those obtained in previous studies [23]. However, the frequencies of depression are variable [24]; although the relationship between dementia and depression is controversial, the latter constitutes an independent risk factor for AD [25]. Depressive symptoms are frequent among patients with AD in the absence of major depression [26].

The prevalence of hopelessness (34.22%) is similar to that reported in the literature [24]. Hopelessness is common among patients with AD and has an early onset in the course of the disease [25]. A comparative study including patients with AD, patients with depression, and healthy individuals showed that hopelessness may be found isolated or coexistent with depression, but it does not increase depression scores [18]. Similar to our study, other studies found that behavioral problems because of depression can occur at any stage of AD [27], indicating that the onset of depression might occur at any stage of the disease.

The proportion of patients showing increased awakening at night is 45.49% and this was comparable with previous studies [28]. Waking at night is especially annoying to caregivers [29] and, depending on the population series, its occurrence ranges from 10 to 60% in AD patients. Further, anxiety or worrying was prevalent in 58.55% of the patients studied. Reisberg *et al.* [30] showed that anxiety predominates during the initial phases of the disease, when patients become aware of their deficit. Similar to our results, various studies have shown that the frequency of anxiety in patients with AD ranges from 40 to 60% [31]. However, only 5–6% of the affected patients fulfill the *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. (DSM-IV) criteria for the diagnosis of generalized anxiety disorder [32].

Aberrant motor behavior, which can lead to psychomotor agitation, is frequent in patients with AD [30], and according to Cummings *et al.* [10], is present in 38 of 100 patients. In our study, verbal aggression reached a prevalence of 32.92%. Aggression may indicate a frontal

affectation and has a huge impact on caregivers [33]. Discordances in the prevalence of behavioral symptoms reported by different studies are probably because of the different scales used, as well as cultural differences [34]. In this study, according to RMBPC, we can categorize patients into high score RMBPC and low score RMBPC; both groups showed behavioral problems in the three domains of the scale (memory, depression, and disruptive). However patients with higher RMBPC scores showed more lack of concentration, which may represent a new subsyndrome that can be identified by inattention, loss of patience, frustration, and the lack of cooperation induced by deficient attention. The present study also provided additional evidence for the presence of neuropsychiatric sub syndromes in dementia, which have been reported previously by studies using the Neuropsychiatric Inventory [35]. In this study, although behavioral symptoms were found in 92% of patients with different severities, there were significantly more frequent behavioral symptoms associated with more severe ratings of dementia as reported by a significant correlation with CDR. In addition, more behavioral symptoms were reported with greater cognitive impairment as measured by MMSE. However, the results of other studies are controversial, so that several studies support this [33], whereas others do not [36]. In our study, a significant positive correlation was present between RMBPC scores and DAD scores, indicating that behavioral symptoms are often associated with functional disabilities in AD patients. This could be explained by the fact that behavioral symptoms are a manifestation of cognitive decline and constitute one of the most common causes of patients' disabilities. The proper management of these symptoms will therefore increase their well-being and quality of life [37]. A nonsignificant correlation was found between RMBPC scores with sex, age, and physical disorders including diabetes mellitus, hypertension, osteoarthritis, and coronary heart disease. This could be because the study was carried out in an outpatients' clinic with patients who had fewer physical disorders than inpatients.

Strengths, limitations, and clinical implications

This study used valid and specific tools to assess behavioral symptoms, cognitive function, daily function, and severity of AD patient. It was one of the few studies in an Arab context with a fairly adequate sample size that assessed and correlated behavioral symptoms in AD. From a qualitative perspective, the present results were similar to those obtained in other studies in which different evaluation tools were used. In fact, other tools probably assess behavioral symptoms in greater detail such as the ADAS scale, which includes the main behavioral symptoms for assessment in dementia. Nonetheless, the ADAS scale has the limitation of being scored on the basis of examiner impression. Consequently, the examiner might be overly influenced by his/her subjective impression of the patient at the time of the visit, which may not be representative of patient's behaviors during typical daily routines [38]. Another limitation in this study was the lack of adequate assessment of psychotic symptoms and correlation between this and RMBPC as in previous studies. Also, the previous use of antidementia and psychotropic agents in our sample could affect the frequency and total scores of RMBPC [39].

The present work has several implications for the treatment of AD. The high prevalence of behavioral symptoms in patients with AD implies that the assessment of behavioral symptoms is very important in clinical practice. In this respect, the use of scales such as RMBPC, which provides information from the patient and/or the caregiver in a short period of time, is recommendable in outpatient clinics.

Conclusion

The present study showed a high prevalence of behavioral symptoms in AD, as a huge percent of patients (92%) showed some behavioral symptoms at the time of exploration. The most important frequent symptoms were lack of concentration (91.69%), forgetting what day it was (89.76%), and sad or depressed mood (88.34%). 'Inattentional subsyndrome' was also identified in patients with higher RMBPC scores. Besides, strong correlations between behavioral disturbances and the severity of the disease, degree of cognitive impairment, and patients' disabilities have been found.

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Conflicts of interest

There are no conflicts of interest.

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الملخص العربى
تأثير الأعراض السلوكيه على مرضى ألزهيمر

د. دعاء هويدى، د. غاده حسن، د. عبير عيسى، د. هشام صادق، د. منى الشيخ

تعد المشاكل السلوكيه من أهم وأكثرالأعراض المزعجه لأهالى مرضى ألزهيمر وقد أوضحت الأبحاث وجود هذه الأعراض فى المراحل المختلفه للمرض.
أهداف البحث: وصف الأعراض السلوكيه فى عينه من مرض ألزهيمر وإيجاد العلاقه بينها وبين متغيرات المرض مثل أعراض المرض وشدته كذلك تأثير هذه الأعراض على الخلل الوظيفى لمرضى ألزهيمر.
وسائل البحث: تم عمل مقياس مشاكل الذاكره والمشاكل السلوكيه وكذلك مقياس الحاله الذهنيه المصغر ومقياس شدة الأعراض وأخيرا مقياس الخلل فى 40 مريض ألزهيمرمن العيادات الخارجيه لمركز الطب النفسى بعد أخذ الموافقه والتأكد من التشخيص.
النتائج: اتضح من خلال البحث وجود المشاكل السلوكيه فى أكثر من 92% من المرضى وكانت أكثر الأعراض شيوعا هى نقص التركيز ثم نسيان الأيام وكذلك الاكتئاب. كما اتضح زيادة هذه الأعراض كلما زادت شدة أعراض المرض خاصة الأعراض المعرفيه.
المناقشه: أثبتت الدراسه انتشار المشاكل السلوكيه عند مرضى ألزهيمر وارتباط هذه الأعراض بشدة المرض والأعراض المعرفيه للمرض وكذلك تأثيرها على قدرات المريض ووظائفه اليوميه ومن ثم تتضح أهمية قياس هذه الأعراض عند كل المرضى وعمل البرامج العلاجيه المختلفه للتغلب عليها.