# Diagnosis and assessment of apathy in Chinese patients with Alzheimer's disease

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## ARTICLE INFO

## ABSTRACT

*Background:* Apathy is a major component of the behavioral and psychological symptoms of Alzheimer's Disease (AD) and other types of dementia. Most researchers have reached a consensus on a new set of diagnostic criteria for apathy (DCA) recently. However, no relevant reports on apathy exist for AD patients in Asian countries yet.
*Objectives:* To estimate the prevalence of apathy in Chinese AD patients.
*Methods:* 83 AD patients were recruited for a cross-sectional observational study. Following the new diagnostic criteria for apathy (DCA) and DSM-IV criteria for Major Depressive Disorder (MDD), each patient was assessed successively by Mini Mental State Examination (MMSE), the Neuropsychiatric Inventory-apathy subscale (NPI-apathy), the Geriatric Depression Screening scale (GDS), and the Caregiver Burden Scale (CBS).
*Results:* According to the DCA, we found that the frequency of apathy in Chinese AD patients reached 61.4%. The DCA had very good standard validity and internal consistency. The frequency of apathy was not significantly associated with that of depression, whereas there was a significant association between apathy and more severe cognitive deficits. Caregiver burden was significantly associated with severity of apathy.
*Conclusions:* From the symptoms of a group of Chinese AD patients, we summarized a set of effective methods for the diagnosis and assessment of apathy.

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## Introduction

The term, apathy, originally signified a virtuous state of indifference. Although frequently used in the neuropsychiatric literature, apathy is not included in current nosological classifications such as the DSM-IV [1] or ICD-10 [2] as an independent term. More recently, an advanced draft was discussed at a consensus meeting (during the EPA conference on April 7th 2008) and a unanimous agreement was reached on the diagnostic and assessment of apathy. Then, DCA were proposed by the French Association for Biological Psychiatry, the European Psychiatric Association, and the European Alzheimer's Disease Consortium [3]. The frequency of apathy in AD patients differed depending on the methods adopted to measure apathy. By using Apathy Evaluating Scale (AES), Clark et al. [4] showed that apathy was present in 43% of patients with AD. However, by using the Apathy Scale (AS) Starkstein et al. [5] reported that the frequency of apathy ranged from 19% to 76%. One possible reason is that standardized methods to diagnose apathy were not available until 2008, and apathy was mostly diagnosed using arbitrary cut-off scores on severity rating scales [6]. The NPI-apathy subscale is one of the most authoritative and commonly used scales [7]. It was developed by

Cummings et al. [8] to assess and quantify neurobehavioral disturbances in dementia patients and to quantify caregiver distress caused by such behaviors. NPI includes an apathy subscale, by which the overall frequency (1–4) and severity (1–3) of apathy are rated. Scores on the NPI apathy subscale range from 0 to 12, with higher scores indicating more severe apathy and an ordinary cut-off score of 4.0.

Severity of apathy correlated closely with cognitive function. Robert et al. [9] assessed 251 patients who met the criteria of amnestic Mild Cognitive Impairment (MCI) by using Apathy Inventory (IA), and checked the incidence of AD one year later. The results showed that cognitive function of MCI patients accompanied by apathy declined in the following years.

One example of unresolved nosological questions in behavioral neuroscience is that depression and apathy are difficult to distinguish from one another, despite the fact that many researchers have found clear-cut differences between apathy and depression. Levy et al. [11] performed a cross-sectional comparison of neuropsychiatric symptoms. They found that apathy did not correlate with depression in the combined sample and that apathy as measured by NPI, but not depression, correlated with lower cognitive function as measured by the MMSE. They concluded that apathy was a specific neuropsychiatric syndrome distinct from depression. Similarly, Starkstein et al. [9] reported that apathy was significantly associated with more severe cognitive deficits independent of depression.

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## Method

We performed a clinical cross-sectional observational study and recruited 83 AD patients from the Second Military Medical University's Changzheng Hospital Department of Neurology. All patients met the NINCDS-ADRDA criteria for AD. Excluded were patients with non-AD dementia, or other neuropsychiatric disorders, and those living independently without caregivers' support.

General information was collected from patients, including name, sex, age, years of education, address, and contact information. (Information was also considered valid if it was collected from caregivers, who took care of patients 2 days every week).

Each patient was diagnosed according to the DCA and the diagnostic criteria of MDD DSM-IV, and assessed by NPI-apathy, GDS, and CBS. Information was collected from caregivers if necessary. All assessments were conducted according to the Chinese version of the above guidelines, and data were organized and completed in the following 24 hours.

Chi-squared test was used to compare the frequencies of different symptoms in apathetic and non-apathetic patient groups. Concurrent validity of the DCA and correlations of the different symptoms were analyzed in way of distance correlation. Phi correlation was used to test the discriminant validity, and the Kruskal Wallis test was used to compare the frequencies of apathy among different types of depression. The significance threshold was set $P<0.05$ in all statistical tests. Analysis was carried out using Statistica 16.0 software.

## Results

According to the DCA, the frequency of apathy in Chinese AD patients was 61.4%. Table 1 shows the demographic characteristics of our subjects. The apathetic group scored 22.68 in MMSE, compared to 15.09 in the nonapathetic group. There were significant differences in the scores between apathetic and non-apathetic groups.

When we took the DCA as the diagnostic standard of apathy and used 4.0 as the NPI apathy cutoff score, the distance correlation reached 0.617. This indicated that the DCA exhibited good concurrent validity. In addition, we found that the DCA had high internal consistency because the Cronbach's alpha value reached 0.814. The severity of depression was evaluated by GDS. The Phi correlation of GDS score and the DCA was only 0.353, indicating a good discriminant validity.

The MMSE score was used to represent cognitive function. The correlation coefficient between MMSE and NPI-apathy was $-0.659$, which indicates that the severity of apathy has a negative correlation with cognitive function. On the contrary, the severity of depression was evaluated by GDS, and the correlation coefficient between MMSE and GDS was $-0.166$.

Diagnosis of depression in AD patients was based on the DSM-IV diagnostic criteria. MDD in our patients included Major Depressive Disorder Single Episode(MDE), Major Depressive Disorder Recurrent (MDR), and Dysthymia. Table 2 shows the relationship between depression and apathyin detail. The frequencies of apathy and depression were analyzed using Fisher's Chi-square test ($\chi^2/df=0.233$, $P>0.05$), which showed that apathy and depression had no significant correlation. Furthermore, Kruskal Wallis Test showed that the frequency of apathy was not different

**Table 1**
Overall characteristics of subjects.

|  | All (83) | Non-apathetic (32) | Apathetic (51) | P value |
|---|---|---|---|---|
| Age(years) | 73.98(8.25) | 76.15(6.58) | 72.62(8.94) | 0.771 |
| Male (%) | 51.8 | 50.7 | 50.2 | 0.051 |
| Duration (years) | 3.73(3.11) | 3.62(3.00) | 3.80(3.17) | 0.876 |
| Ed. level (years) | 8.72(4.04) | 9.87(4.30) | 8.00(3.73) | 0.206 |
| MMSE | 18.02(7.65) | 22.68(4.91) | 15.09(7.64) | <0.05 |
| NPI-apathy | 4.50(3.31) | 1.93(1.16) | 6.11(3.21) | <0.001 |

**Table 2**
Relationship between depression and apathy. The number of patients in each category is shown in the table and the percentage that they represent is shown in the parenthesis next to the patient number.

|  | Apathetic | Non-apathetic | Total |
|---|---|---|---|
| MDE | 2(2.40%) | 2(2.40%) | 4(4.80%) |
| MDR | 2(2.40%) | 3 (3.61%) | 5(6.02%) |
| Dysthymia | 3(3.61%) | 3(3.61%) | 6(7.22%) |
| Depression + | 7(8.43%) | 8(9.63%) | 15(18.07%) |
| Depression − | 44(53.00%) | 24(28.92%) | 68(81.92%) |
| Total | 51(61.45%) | 32(38.55%) | 83(100%) |

MDE = Major Depressive Disorder Single Episode, MDR = Major Depressive Disorder Recurrent.

among different types of MDD (P>0.05). The severity of depression was evaluated by GDS, and distance correlation of GDS score and NPI-apathy was only 0.104 which indicated a low correlation between apathy and depression.

Caregiver burden was indicated by CBS. The correlation coefficient between CBS score and NPI-apathy, MMSE, and GDS score was 0.712 −0.615, and 0.113, respectively. This indicated that caregiver burden was most closely correlated with patient's apathy.

## Discussion

In this series in a large teaching hospital in Shanghai, China, apathy was not only common among AD patients, but also correlated with loss of cognitive function. Although many have speculated on the pathophysiology of apathy, there is still not a generally accepted conclusion. Degeneration of the limbic lobe ventral striatal pallidal circuit has been invoked [12]. Because of overlap in anatomical position, apathy is believed to coexist in AD patients rather than being a by-product. For a long time, there were no unified international standards for the definition and assessment of apathy; assessment tools such as NPI-apathy and AES-C, were widely used [8]. In 2009, the wide acceptance of the DCA gave us a standard that could be used to accurately study apathy in Chinese AD patients. After the DCA was published, there have been several researchers applying it to study the frequency of apathy in different neurodegenerative diseases. Drijger et al. [13] recruited 122 Parkinson's Disorder (PD) patients and found that the frequency of apathy reached 17.2%, and that the concurrent validity between DCA and NPI-apathy was 0.76. Recently, Mulin et al. [14] performed a study in which they recruited patients suffering from different neuropsychiatric diseases diagnosed by the DCA. They reported that the frequency of apathy in AD patients was 55%. In our research, we used NPI-apathy as the gold standard to assess the validity of the DCA. We found that the DCA-diagnosed apathetic group had a higher NPI-apathy score than the nonapathetic group, and that the DCA had good concurrent validity. In addition, we found that the DCA had good high internal consistency. The frequency of apathy in Chinese AD patients was 61.7% in this study, which is consistent with the other reports.

The results of our study on Chinese AD patients are in agreement with many other reports that have demonstrated that the severity of apathy correlates with cognitive impairment in AD patients. Starkstein et al. [5] found that apathy in AD is a behavioral marker of more aggressive dementia, characterized by faster progression of cognitive, functional, and emotional impairment than those without apathy. Levy et al. [11] concluded that apathy correlated with lower cognitive function, as measured by MMSE. In our study, we concluded that apathy is, negatively correlated with cognitive function in AD patients in China, as in other countries.

Separating apathy and depression may be conceptually difficult [10, 14], but in our sample probably because it was limited to AD patients, there was little overlap between apathy and depression as