Int J Clin Exp Med 2016;9(4):7374-7380
www.ijcem.com /ISSN:1940-5901/IJCEM0020744

*Original Article*

# Comparative study of damage to cognitive function and mental behavior in patients with general paresis of the insane, Alzheimer's disease, and frontotemporal dementia

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Received November 28, 2015; Accepted February 15, 2016; Epub April 15, 2016; Published April 30, 2016

**Abstract:** Dementia is a group of cognitive functional disorders with staggering worldwide morbidity and mortality. Recognition of the differences between types of dementia is important for clinical diagnosis and effective treatment. This study compared and analyzed differences in cognitive functions and mental behaviors of patients with three types of dementia: general paresis of the insane (GPI), Alzheimer's disease (AD), and frontotemporal dementia (FTD). The study cohort of 90 subjects included 30 subjects each in AD, GPI, and FTD groups. Clinical data of gender, age, duration of disease, education, family history of dementia, diagnosis of diabetes, diagnosis of hypertension, diagnosis of coronary heart disease, smoking habits, drinking habits, mini-mental state examination (MMSE) score, Montreal cognitive assessment (MoCA) score, neuropsychiatric inventory (NPI) score, and clinical dementia rating of patients were observed and compared. MMSE scores were significantly higher in the GPI group than AD or FTD groups. MoCA scores were significantly higher in the AD group than the FTD group. NPI scores were significantly higher in the FTD group than GPI or AD groups. Age, family history of dementia, and incidence of hypertension were significantly higher in AD and FTD groups than the GPI group. MMSE, MoCA, and NPI scores were significantly correlated with degree of dementia. In addition, degree of dementia was significantly correlated with age (OR = 1.845), family history of dementia (OR = 1.613), MMSE score (OR = 0.752), MoCA score (OR = 0.536), and NPI score (OR = 2.055). In brief, AD, FTD, and GPI patients display characteristic damage to cognitive function and mental behavior, and that damage correlates with the condition of disease. These characteristics can help effectively diagnose and classify types of dementia to improve patient prognosis. Clinicians should acknowledge such characteristic changes to ensure accurate diagnosis and allow early intervention for dementia patients.

**Keywords:** General paresis of insane, Alzheimer's disease, frontotemporal dementia, cognitive function, mental behavior, dementia

## Introduction

Dementia is a disorder of memory and other cognitive functions induced by genetic and environmental causes, and it has a relatively high morbidity rate in China [1, 2]. According to the World Health Organization (WHO), there are over 47.5 million cases of dementia worldwide, with 7.7 million new cases annually [3]. With rapid societal aging, especially in China, the number of patients with dementia is increasing. Recognizing, diagnosing, and intervening in early stages of dementia is increasingly important to maintain the health of society. In addition, accurately identifying the various types of dementia is critical for accurate treatment and intervention.

Alzheimer's disease (AD), also called senile dementia, is a degenerative encephalopathy characterized by hidden onset and progressive development [4]. AD is the most common type of dementia, accounting for 60%-70% of dementia cases. AD also has high morbidity, making it the sixth highest cause of death among Americans [5, 6]. Clinical features of AD include disorders of memory and other cognitive functions, such as alalia, apraxia, and agnosia.

During early stages of disease, patients can experience functional defects in motor skills, sensation, or coordination; with progression, patients can also suffer from abnormal mental behaviors and decreased social life [7]. In addition, AD pathogenesis is complicated, so there is currently no effective therapeutic method. Current clinical treatment systematically addresses patients' decreased cognitive function and mental symptoms, but it is difficult to prevent disease effectively or delay progression.

The second most common form of dementia is caused by frontotemporal degeneration, a clinical syndrome characterized by selective pathologic atrophy of the frontal lobe that mainly manifests as progressive mental degeneration and linguistic functional disorders. Frontotemporal degeneration has high clinical, pathologic, and genetic heterogeneity, and it is also the most prevalent cause of death for early-onset dementia. According to early clinical features of frontotemporal degeneration, international practice classifies the disease into frontotemporal dementia (FTD) or primary progressive aphasia (ppA). ppA is further classified into three subtypes: semantic dementia (SD), progressive non-fluent aphasia (PNFA), and logopenic progressive aphasia [8]. FTD is an early-onset type of progressive neurodegenerative disease that manifests as progressive behaviors and changes in personality and aphasia, making it difficult to diagnose. FTD pathology often shows abnormally folded protein accumulation and gliosis confined to the frontotemporal lobes. Recent research has shown that FTD has high genetic heterogeneity, although the disease does show a larger genetic predisposition than other neurodegenerative diseases. Mutation of 7 single genes, including *MAPT* genes, is correlated with onset of FTD [9-11].

Another type of dementia can be caused by neurosyphilis, a central nervous system infectious disease induced by the microorganism *Treponema pallidum,* which invades meninges and/or the cerebral parenchyma. Neurosyphilis is generally classified into four types, which do not exist in isolation: asymptomatic, interstitial (meninges and vascular), cerebral parenchyma [general paresis of the insane (GPI) and myelanalosis], and gumma types. GPI is common 10-20 years after early *T. pallidum* infection and is characterized clinically by progressively decreased memory and mental abnormalities [12, 13]. Recent studies have verified that GPI patients experience characteristic electroencephalographic changes [14], including elevated chronic wave frequency band, decreased fast wave frequency band, maximum coherency of lead frequency bands between left and right hemispheres, and decreased corresponding frequency. Hydrogen proton magnetic resonance spectrum examination of hippocampus regions indicates that GPI patients can experience decreased N-aceytl aspartate (NAA)/creatine levels in bilateral hippocampus regions and elevated choline/NAA levels. This evidence indicates that GPI patients have neuron injuries in bilateral hippocampus regions that are similar to those of AD patients [15, 16]. However, early clinical manifestations of GPI patients are complicated and various. In addition to mental disease symptoms and decreased memory, some patients may concomitantly experience symptoms such as ataxia, which can confound diagnosis and lead to mistreatment.

Patients' detailed medical histories and auxiliary diagnosis methods, such as serum and cerebrospinal fluid syphilis antibody detection and imaging examination, are important for accurate diagnosis of dementia [17-22]. Recent standardization of the definition and classification of cognitive function disorders and wide application of oriented neuropsychological survey scales has allowed systematic analysis of risk factors and clinical characteristics of dementia and further provided reliable evidence for pharmaceutical and behavioral intervention. Progress in molecular genetics, protein chemistry, and immunohistochemical technology has revealed an important role for retrograde infection of the nervous system in neurodegenerative diseases, including AD and FTD [18]. Careful observation and analysis of differences between these diseases and secondary dementia, such as GPI, is important for clinical diagnosis and treatment. Therefore, this study compared and analyzed differences in cognitive functions and mental behaviors of patients with AD, FTD, and GPI.

## Materials and methods

### *Clinical data*

Patients admitted to Hongqi Hospital, Mudanjiang Medical University (Mudanjiang, Heilongjiang Province, China) from January

**Table 1.** Comparison of clinical information among subjects with general paresis of insane (GPI), Alzheimer's disease (AD), and frontotemporal dementia (FTD)

| | GPI group (n = 30) | AD group (n = 30) | FTD group (n = 30) | $F/\chi^2$ | $P$ |
|---|---|---|---|---|---|
| Age (years) | 52.4±9.8[b,c] | 68.2±7.4[a] | 66.8±6.5[a] | 38.126 | < 0.05 |
| Gender, male [n (%)] | 16 (53.3) | 18 (60.0) | 16 (53.3) | 1.031 | > 0.05 |
| Disease duration (years) | 3.23±0.68 | 3.61±0.53 | 3.16±0.71 | 0.812 | > 0.05 |
| Education (years) | 12.62±2.51 | 12.33±2.64 | 12.71±2.68 | 0.360 | > 0.05 |
| Family history of dementia [n (%)] | 1 (3.3)[b,c] | 8 (26.7)[a] | 9 (30.0)[a] | 7.917 | < 0.05 |
| Diabetes [n (%)] | 5 (16.7) | 3 (10.0) | 6 (20.0) | 1.184 | > 0.05 |
| Hypertension [n (%)] | 2 (6.7)[b,c] | 10 (33.3)[a] | 12 (40.0)[a] | 9.545 | < 0.05 |
| Coronary heart disease [n (%)] | 2 (6.7) | 3 (10.0) | 4 (13.3) | 0.741 | > 0.05 |
| Smokers [n (%)] | 5 (16.7) | 7 (23.3) | 9 (30.0) | 1.491 | > 0.05 |
| Drinkers [n (%)] | 5 (16.7) | 8 (26.7) | 10 (33.3) | 2.219 | > 0.05 |

[a]$P < 0.05$, vs. GPI group; [b]$P < 0.05$, vs. AD group; [c]$P < 0.05$, vs. FTD group.

2013 to December 2014 were included in the study and were divided into AD group (n = 30), GPI group (n = 30), and FTD group (n = 30). AD diagnosis criteria were based on guidelines by the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) [19]. FTD and GPI diagnosis criteria were from the Guidelines for Diagnosis and Treatment of Chinese Dementia and Cognitive Handicap (2011 modified version). Diagnoses were confirmed by examinations of cranial computed tomography scans, magnetic resonance imaging, deoxyglucose positron emission computed tomography scans, and serum or cerebrospinal fluid syphilis antibody detection.

Clinical information, including gender, age, disease duration, education, family history of dementia, diagnosis of diabetes, diagnosis of hypertension, diagnosis of coronary heart disease, smoking habits, and drinking habits, was collected and compared. Mini-mental state examination (MMSE) and Montreal cognitive assessment (MoCA) scores were used to evaluate cognitive function, with lower scale values indicating more serious cognitive functional damage. Neuropsychiatric inventory (NPI) scores were used to evaluate neuropsychiatric behaviors. Clinical dementia rating (CDR) scores were used to evaluate dementia degree (1 point = mild; 2 points = moderate; 3 points = severe).

*Statistical methods*

SPSS 13.0 statistical software (IBM, Armonk, NY) was used to establish a database and perform statistical analysis. Single factor analysis of variance was used to compare multiple groups, and pairwise comparisons were made using the least significant difference (LSD) method. Spearman grade correlation analysis was used to analyze correlations between dementia and each score. Chi-square test was used to process materials without rank correlation, and Kruskal-Wallis method was used to rank materials in multiple groups to compare degree of dementia. Logistic multiple regression analysis was used to perform multiple-factor analysis of degree of dementia. Measurement data are expressed as mean ± standard deviation. Enumeration data are expressed as percentages. $P < 0.05$ was considered statistically significant.

## Results

*Comparison of clinical information among AD, GPI, and FTD group subjects*

AD, GPI, and FTD group subjects significantly differed in age (F = 38.126; $P < 0.05$), family history of dementia ($\chi^2 = 7.917$; $P < 0.05$), and incidence of hypertension ($\chi^2 = 9.545$; $P < 0.05$) (**Table 1**). Age, family history of dementia, and incidence of hypertension were significantly higher in AD and FTD groups than the GPI group. Other clinical information did not significantly differ among the three groups.

*Comparison of MMSE, MoCA, and NPI scores among AD, GPI, and FTD group subjects*

AD, GPI, and FTD group subjects had significantly different MMSE (F = 31.842; $P < 0.05$), MoCA (F = 53.938; $P < 0.05$), and NPI (F =

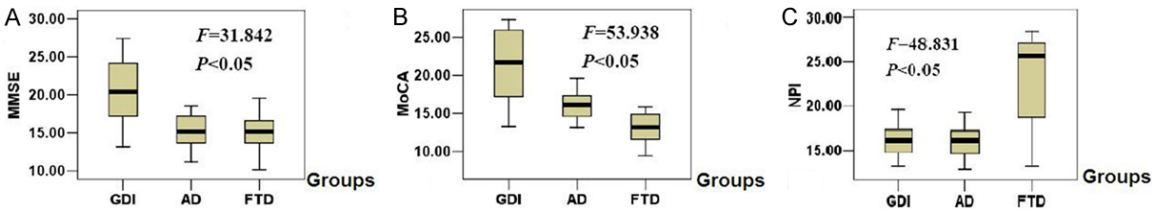


**Figure 1.** Comparison of MMSE, MoCA and NPI scores among GPI, AD and FTD. A. Mini-mental state examination, MMSE; B. Montreal cognitive assessment, MoCA; C. Neuropsychiatric inventory, NPI. Abbreviation: general paresis of insane, GPI; Alzheimer's disease, AD; frontotemporal dementia, FTD.

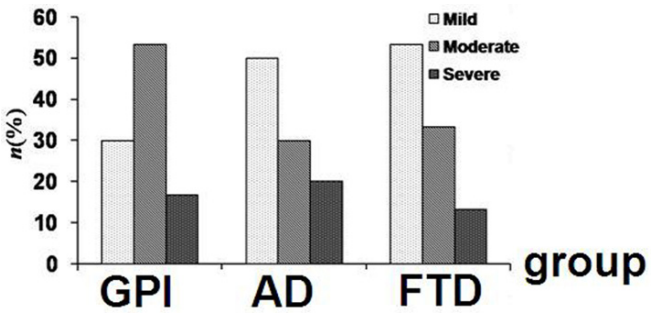


**Figure 2.** Comparison of degree of dementia among subjects with GPI, AD and FTD.

48.831; $P < 0.05$) scores (**Figure 1**). Specifically, MMSE scores were significantly higher in the GPI group than AD or FTD groups; MoCA scores were significantly higher in the GPI group than the AD group, which had significantly higher scores than the FTD group; and NPI scores were significantly higher in the FTD group than GPI or AD groups. MMSE scores did not significantly differ between AD and FTD groups, and NPI scores did not significantly differ between GPI and AD groups.

*Correlation of MMSE, MoCA, and NPI scores with degree of dementia*

Distribution of CDR scores, measuring degree of dementia, significantly differed among the three groups (U = 7.727; $P < 0.05$) (**Figure 2**). In addition, CDR scores significantly correlated with MMSE, MoCA, and NPI scores. Correlations were evident when all study subjects were combined (**Figure 3**), but were even more evident when GPI (**Figure 4**), AD (**Figure 5**), and FTD (**Figure 6**) groups were analyzed separately.

*Correlation factor analysis of clinical information with degree of dementia*

With CDR score as a dependent variable and clinical information and MMSE, MoCA, and NPI scores as independent variables, logistic multiple regression analysis indicated that subjects' degree of dementia significantly correlated with age (OR = 1.845), family history of dementia (OR = 1.613), MMSE score (OR = 0.752), MoCA score (OR = 0.536), and NPI score (OR = 2.055) (**Table 2**).

## Discussion

This study of three types of dementia shows that AD, FTD, and GPI patients display characteristic changes in cognitive function and mental behavior. These characteristics can help effectively diagnose and classify these types of dementia to ensure accurate patient treatment and disease management. Most previous studies have used higher levels of testing (e.g., fMRI) to distinguish between types of dementia [17-23]. More specifically, this study shows that standard assessments of cognitive function and neuropsychiatric behavior can help identify dementia types. MMSE scores of GPI group subjects were significantly higher than those in AD or FTD groups; MoCA scores of AD group subjects were significantly higher than those in the FTD group; and NPI scores of FTD group subjects were significantly higher than those in GPI or AD groups. In addition, analyses showed that degree of dementia correlated with MMSE, MoCA, and NPI scores, indicating the value of these assessments to guide clinical parameters. Along with further characterization of these scores in additional patients and additional types of dementia, these trends can be used to help establish diagnostic criteria to distinguish dementia types. Further, since these assessments are already a part of standard clinical examinations, more accurate interpretation of the assessments' scores can have a significant impact on dementia patient diagnosis.

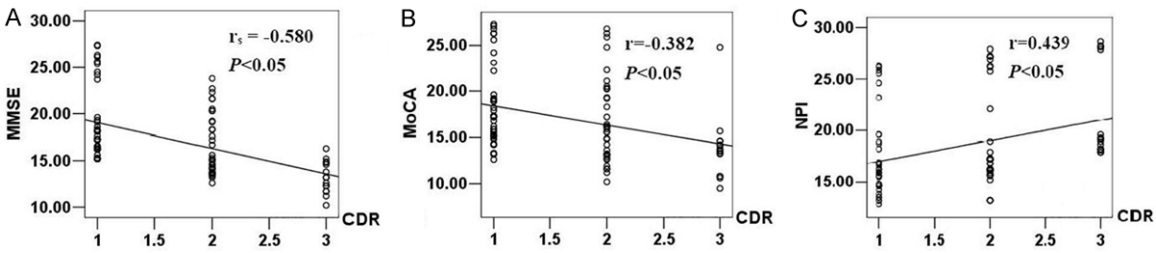


**Figure 3.** Correlation between MMSE, MoCA NPI and clinical dementia rating (CDR) scores among GPI, AD and FTD. A. MMSE; B. MoCA; C. NPI.

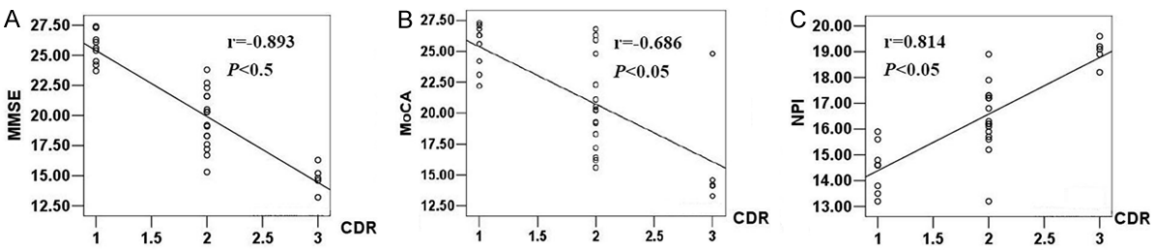


**Figure 4.** Correlation between MMSE, MoCA, NPI and clinical dementia rating (CDR) scores of GPI subjects. A. MMSE; B. MoCA; C. NPI.

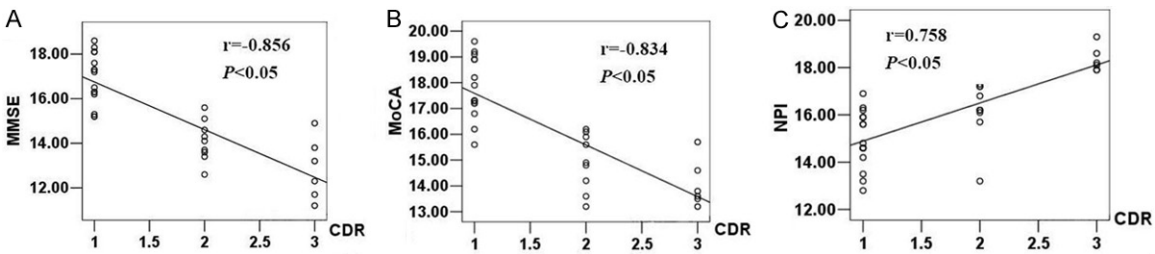


**Figure 5.** Correlation between MMSE, MoCA, NPI and clinical dementia rating (CDR) scores of AD subjects. A. MMSE; B. MoCA; C. NPI.

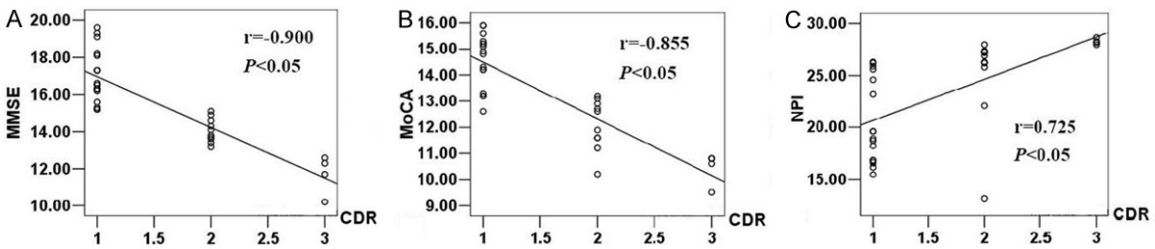


**Figure 6.** Correlation between MMSE, MoCA, NPI and clinical dementia rating (CDR) scores of FTD subjects. A. MMSE; B. MoCA; C. NPI.

Age, family history of dementia, and incidence of hypertension were significantly higher in AD and FTD group subjects. Previous work shows that AD and FTD have strong genetic components and familial histories, while GPI originates from infection. However, while AD risk is known to increase with age, FTD is considered an early-onset type of dementia. In addition, although previous studies have identified a relationship between hypertension and AD [20], other studies have identified no correlation between FTD and hypertension [21]. These

**Table 2.** Correlation factor analysis of clinical information with degree of dementia

| Variable | β | OR | Wald $\chi^2$ | *P* |
|---|---|---|---|---|
| Age | 0.692 | 1.845 | 4.698 | < 0.05 |
| Family history of dementia | 0.775 | 1.613 | 7.035 | < 0.05 |
| MMSE score | -0.106 | 0.752 | 5.638 | < 0.05 |
| MoCA score | -.0113 | 0.536 | 4.916 | < 0.05 |
| NPI score | 1.032 | 2.055 | 6.113 | < 0.05 |

results indicate that, among the three types of dementia examined, cognitive functional and behavioral damages are mildest in GPI group subjects. In contrast, FTD patients manifest relatively severe cognitive functional and behavioral damages.

In addition, further logistic multiple regression analyses indicated that degree of dementia correlated with age, family history of dementia, MMSE score, MoCA score, and NPI score, indicating that CDR scores reflect the degree of damage in subjects' cognitive function. These results indicate that age and genetic factors play a significant role in generation and development of dementia diseases such as AD and FTD. Together, these diagnostic parameters represent a powerful tool to help assess, characterize, and guide treatment for dementia patients.

Damage to cognitive functions and mental behaviors of GPI, AD, and FTD patients have specific quantifiable characteristics that correlate with the patient's degree of dementia. Clinicians should master these characteristic changes to enable accurate early diagnosis and ensure effective intervention to improve the prognosis of dementia patients.

## Acknowledgements

This work was supported by Natural Science Foundation of Heilongjiang Province of China (No. QC2013C102).

## Disclosure of conflict of interest

None.

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