

# Neurological Abnormalities Associated with Severity of Dementia in Alzheimer's Disease

F. Jacob Huff and John H. Growdon

**ABSTRACT:** Abnormal findings on neurological examination were evaluated in 165 patients with a clinical diagnosis of Alzheimer's disease who attended a memory disorders clinic. Severity of dementia was measured by the Blessed Dementia Scale, and associations of abnormalities with dementia severity were evaluated using logistic regression. Presence of aphasia, apraxia, and primitive reflexes on neurological examination were strongly associated with severity, and weak associations were observed for abnormalities of muscle tone and gait. Among these associated neurological features, only aphasia and apraxia were present in mildly demented cases with sufficient frequency to suggest utility as diagnostic signs early in the course of the disease.

**RÉSUMÉ:** Les anomalies neurologiques associées à la sévérité de la démence dans la maladie d'Alzheimer. On a évalué les anomalies observées à l'examen neurologique chez 165 patients avec un diagnostic clinique de maladie d'Alzheimer qui fréquentaient une clinique pour les patients présentant des troubles de la mémoire. La sévérité de la démence a été mesurée au moyen de l'échelle "Blessed" pour la démence (Blessed Dementia Scale) et l'association des anomalies avec la sévérité de la démence a été mesurée au moyen de la régression logique. La présence d'aphasie, d'apraxie et de réflexes primitifs à l'examen neurologique était fortement associée à la sévérité de la démence et des associations faibles furent observées avec des anomalies du tonus musculaire et de la démarche. Parmi ces manifestations neurologiques associées, seulement l'aphasie et l'apraxie étaient présentes chez les patients légèrement déments avec une fréquence suffisante pour suggérer que ces signes peuvent être utiles au diagnostic dès le début de la maladie.

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In order to be useful in early diagnosis of Alzheimer's disease, a neurological abnormality must occur commonly in the early stage of the disease, and likelihood of its occurrence should increase in patients with greater severity of dementia. In an effort to determine whether features of the neurological examination show such relationships with severity, we examined the clinical records of a group of patients with Alzheimer's disease diagnosed by contemporary research criteria. We evaluated the association of dementia severity with presence of aphasia, apraxia, primitive reflexes, and other abnormal findings on neurological examination.

## METHODS

### Subjects

Data were collected over 5 years on 165 patients with a clinical diagnosis of Alzheimer's disease who attended a memory disorders clinic (Table 1). The diagnosis was based upon a history of gradual deterioration of cognitive functions that

impaired work performance or activities of daily living, and upon the results of physical examination. The diagnostic criteria have been published previously,<sup>1</sup> and correspond to those adopted by a recent Health and Human Services Task Force.<sup>2</sup> CT brain scan, EEG, and blood studies were done in order to exclude other causes of dementia. Patients with a Hachinski Ischemic Scale score of 5 or greater,<sup>3</sup> and those with a history of alcoholism, primary affective disorder, or symptoms of Parkinson's disease preceding the onset of dementia were excluded. Of these 165 patients, 8 have died; 6 brains were examined and all contained abundant senile plaques and neurofibrillary tangles characteristic of Alzheimer's disease. There were no clinical features that differentiated these autopsy-confirmed cases from the remainder of the patients diagnosed by the same clinical procedures.<sup>4</sup>

### Measurement of Severity and Age at Onset of Dementia

Severity of dementia was determined using the Blessed Dementia Scale.<sup>5</sup> Age at onset of dementia was estimated

From the Department of Psychiatry and Neurology, University of Pittsburg (Dr. Huff) and the Department of Neurology, Harvard Medical School at the Massachusetts General Hospital (Dr. Growdon)

Reprint requests to: Dr. Huff, Departments of Psychiatry and Neurology, University of Pittsburg, 617 Eye and Ear Hospital, 230 Lothrop Street, Pittsburg, PA U.S.A. 15213

retrospectively from reports of the duration of dementia obtained from a family member.

### Neurological Examination

All patients were examined by one of the five neurologists working in the clinic. Findings were abstracted by retrospective chart review. Abnormalities were classified using a pre-established list of abnormal findings. "Aphasia" was recorded in patients who manifested impaired confrontation naming or other expressive or receptive language deficits. "Apraxia" was defined by presence of either ideomotor or constructional apraxia. Presence of snout, suck, palmomental, and grasp reflexes was recorded separately. The remaining 46 abnormal findings were grouped into the following categories: cranial nerve signs, motor signs, sensory signs, abnormalities of balance and gait, involuntary movements, and coordination abnormalities. In analyzing the results, a patient was considered to have an abnormality in a particular category if any of the findings included in that category were present. Records for all 165 patients were rated by one neurologist (FJH), and a random selection of 40 patients was rated independently by a second neurologist (JHG). The two ratings for those 40 patients were compared. There were no significant differences between raters in the mean rating for any variable. Pearson product-moment correlation between raters was determined for each variable. The strength of these correlations was limited by the low prevalence of abnormalities for most variables. Coordination abnormalities were present in less than 2% of patients, and ratings of

coordination were not analyzed further. For the remaining variables, the average correlation between raters was .76.

### RESULTS

Patients were divided into four groups by severity of dementia on the basis of Blessed Dementia Scale scores at the time of initial examination: 1) scores ranging from 2 to 14, indicating mild dementia; 2) scores ranging 15 to 24; 3) scores ranging 25 to 36; and 4) scores 37 and higher, indicating severe dementia. Table 2 displays the percentage of patients in each severity group having each of the abnormal neurological findings examined in this study. In order to evaluate relationships among variables, logistic regression was performed using each examination feature in turn as a dependent variable with Blessed Scale score and age at the time of examination as the predictive variables.<sup>6</sup> Estimates of the coefficients for Blessed Scale score and patient age in the linear expression relating these variables to each examination finding, along with the chi-square ( $X^2$ ) value for each estimate, were determined across all 165 patients.

The following examination findings were positively related to severity of dementia but not to patient age: aphasia ( $X^2 = 20.3$ ;  $p < .001$ ), apraxia ( $X^2 = 15.5$ ;  $p < .001$ ), snout reflex ( $X^2 = 8.0$ ;  $p < .01$ ), suck reflex ( $X^2 = 12.8$ ;  $p < .001$ ), and grasp reflex ( $X^2 = 21.4$ ;  $p < .001$ ). A trend toward association of motor abnormalities with severity was observed ( $X^2 = 2.59$ ;  $p < .10$ ). The most common motor abnormality was increased muscle tone. Balance and gait abnormalities were marginally related to both severity of dementia ( $X^2 = 4.1$ ,  $p < .05$ ) and age ( $X^2 = 3.7$ ,  $p < .10$ ). The most frequent gait abnormalities were reduced stride length, decreased arm swing, and postural instability. Severity of dementia was not associated with cranial nerve abnormalities such as impaired range of gaze, involuntary movements such as postural tremor and myoclonus, or somatosensory deficits such as decreased sensitivity to vibration in the lower extremities. No examination finding other than balance and gait abnormality was related to patient age.

Among the clinical abnormalities that were related to severity of dementia, those that occurred most frequently in mildly

Table 1: Patient profile at first examination (N = 165)

Item	Mean or Total Number	Standard Deviation or Percentage
Age at First Examination	68.3	8.8
Age at Onset of Dementia	64.3	9.3
Duration of Dementia (years)	4.0	2.8
Number and Percentage Female	103	62%
Blessed Dementia Scale Score	24.3	13.5

Table 2: Neurological findings at first examination in subgroups based upon severity of dementia

Neurological Examination Findings	Range of Blessed Dementia Scale Scores Defining Subgroups of Different Severity <sup>a</sup>			
	2-14 (N = 47)	15-24 (N = 43)	25-36 (N = 46)	37-64 (N = 29)
Aphasia**	35	51	73	89
Apraxia**	27	37	59	79
Snout Reflex*	7	10	27	34
Suck Reflex**	7	2	7	28
Grasp Reflex**	0	2	13	34
Palmomental Reflex	2	14	13	14
Cranial Nerve Abnormalities	4	14	7	3
Motor Abnormalities†	13	17	13	28
Involuntary Movements	16	15	18	14
Somatosensory Deficits	11	14	11	4
Balance and Gait Abnormalities‡	13	19	27	41

<sup>a</sup>Numbers in the Table represent percentage of patients in each group having each abnormal finding

Significant results from Logistic Regression analysis:

\*\*Presence of finding related to Blessed Scale Score ( $p < .001$ ) but not to Age ( $p > .10$ )

\*Presence of finding related to Blessed Scale Score ( $p < .01$ ) but not to Age ( $p > .10$ )

†Presence of finding related weakly to Blessed Scale Score ( $p < .10$ ) but not to Age ( $p > .10$ )

‡Presence of finding related to Blessed Scale Score ( $p < .05$ ) and weakly to Age ( $p < .10$ )

demented patients (Blessed Scale Scores 2 to 14) were aphasia (35%), apraxia (27%), motor abnormalities (13%), and balance and gait abnormalities (13%). Although the prevalence of abnormal reflexes was related to severity of the disease, they were infrequently present in mildly demented patients (Table 2).

#### DISCUSSION

A cross-sectional analysis of findings on initial examination revealed that aphasia, apraxia, and primitive reflexes were all associated with dementia severity, but only aphasia and apraxia were present in mild cases with sufficient frequency to suggest utility as diagnostic signs early in the course of the disease. The Blessed Dementia Scale, which was used in this study to measure severity of dementia, is sensitive to impairments in functional activities of daily life, social interactions, orientation, memory, and attention. Scores on this test correlate with post-mortem counts of senile plaques,<sup>5</sup> and it thus has an established association with severity of the pathological changes in Alzheimer's disease.

Among the features of the mental status examination performed during the neurological evaluation of a patient with dementia, aphasia and apraxia are major features that are not directly assessed by the Blessed Scale, and therefore represent relatively independent measures of higher cortical function. In the present study, aphasia and apraxia were nevertheless strongly associated with severity of dementia as determined by the Blessed Scale. Other aspects of the neurological examination were either not strongly associated with dementia severity, or (in the case of the primitive reflexes) were associated with severity but present infrequently in mild cases. These results indicate that impairments in mental status are more important than other neurological features in early diagnosis of Alzheimer's disease.

The snout, suck, and grasp reflexes were associated with dementia severity independently of patient age in the present study. Tweedy and co-workers<sup>7</sup> reported correlation of snout and grasp reflexes, but not the suck reflex, with impaired performance on cognitive tests in demented patients. Koller and colleagues<sup>8</sup> reported that a snout reflex was elicited with equal frequency in patients with Alzheimer's disease as in age-matched control subjects, and that the reflex was more prevalent in older subjects in both groups. Discrepancies among these studies may reflect differences in the patient populations studied. The general conclusion to be drawn from them, however, is that primitive reflexes are not useful as early diagnostic markers of Alzheimer's disease.

Among the other features of the neurological examination, only motor abnormalities (chiefly, increased muscle tone) and impairments of balance and gait showed an association with severity of dementia, and impaired balance and gait was associated with age as well as dementia severity. Increased muscle tone was observed by Sjogren<sup>9</sup> in 14 of 18 cases of autopsy-confirmed Alzheimer's disease that had been examined clinically. A disorder of gait was present in 13 of Sjogren's cases. The features of the gait disorder commonly observed in the

present study (reduced stride length, decreased arm swing, and postural instability) were also described by Sjogren. Impairments of gait and balance have been reported to occur more frequently in patients with Alzheimer's disease than in age-matched control subjects,<sup>10</sup> but qualitatively similar changes in gait appear with normal aging.<sup>11</sup> Gait abnormalities thus cannot be used to diagnose Alzheimer's disease.

The method of retrospective review of clinical records used in this study is vulnerable to errors due to differences among examiners in technique or in reliability of recording abnormalities, and to misclassification of recorded abnormalities by the reviewer. The fact that strong relationships between severity of dementia and specific neurological abnormalities were nonetheless detected suggests that these relationships represent robust clinical features of the disease. The observation that mental status abnormalities are more sensitive than other neurological findings in detecting early dementia, however, will require confirmation by prospectively designed investigations.

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