Neurologic Factors Associated with Cognitive Impairment in a Rural Elderly Population in India: The Indo-US Cross-National Dementia Epidemiology Study

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ABSTRACT

Few reports exist of cognitive impairment and associated factors in developing countries. An age-stratified random sample of 388 men and women, 55 years and older, was drawn from a community-based population in the rural area of Ballabgarh in northern India. We classified as "cognitively impaired" those subjects who had scores below the 10th percentile of the population on a general mental status test (the Hindi Mental State Exam, HMSE) and, separately, on a memory test (Delayed Recall of a 10-Item Word List, DRWL). Three hundred seventy-six subjects also underwent a standardized neurologic history and examination. Neurologic factors associated with cognitive impairment, after adjusting for age, gender, and literacy, were history of impaired consciousness and findings of gait disturbance, diminished deep tendon reflexes, and the presence of at least one primitive reflex. We speculate that there may be unique risk factors in developing countries such as nutritional deficiencies leading to focal deficits and cognitive impairment. (*J Geriatr Psychiatry Neurol* 1998;11:11–17).

Few reports exist of cognitive impairment and associated factors in developing countries, where, however, the bulk of the world's elderly population resides. Cognitive impairment and minor neurologic morbidity may remain undetected in these populations, but may indicate the presence of underlying or incipient disorders including Alzheimer's disease (AD) and other dementias. Besides a chronic lack of resources, a major obstacle to studying these conditions has been the lack of standardized and appropriate screening and diagnostic methodology for use in developing countries.

In preparation for an epidemiologic study of dementia in a rural community in northern India, we developed a battery of cognitive tests to screen for and characterize dementing illness among the elderly in that community. We have previously described and reported normative scores on this test battery.[1,2] In this paper, we report preliminary findings on neurologic factors associated with cognitive impairment as defined by poor performance on these standardized, culture-fair tests.

METHODS

Background

The Indo-US Cross-National Dementia Epidemiology Study is a collaborative project of the University of Pittsburgh in Pittsburgh, Pennsylvania (USA) and the Centre for Ageing Research, India (CARI), in New Delh' (India). Its two primary goals are to investigate the ep demiology of the dementing disorders among the eld

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in the rural district of Ballabgarh in northern India, and to compare the results with those being obtained from the Monongahela Valley Independent Elders Survey (MoVIES project),[3] an ongoing study in a rural community in Pennsylvania (USA). The study is funded by a National Institute on Aging program in the expectation that epidemiologic similarities and differences will help identify new risk factors for dementia.[4] The first step of the cross-national study was to develop, for the Ballabgarh elderly, an appropriate cognitive screening battery, which would be psychometrically sound, reliable and valid; suffer from minimal cultural and educational biases; have optimal sensitivity and specificity for dementia,[5] and, eventually, allow meaningful comparisons to be made between the two populations. A considerable challenge was posed by the fact that the Ballabgarh population spoke only Haryanvi (the local dialect of Hindi) and was largely illiterate.

Cognitive Tests

We have previously described the development of the Hindi cognitive test battery[1,2] and reported normative scores on these tests from an age-stratified random sample of the Ballabgarh population. The Hindi battery is based on the English-language cognitive screening panel used by the MoVIES project,[6] which incorporates the neuropsychological battery developed by the Consortium to Establish a Registry for Alzheimer's Disease (CERAD).[7] The MoVIES battery includes a brief global cognitive scale (general mental status test), the Mini-Mental State Examination (MMSE)[8] and a set of other tests tapping several specific cognitive domains. For this paper, we have defined cognitive impairment based on performance on two tests in the Hindi battery: our general mental status test and our memory test.

Hindi Mental State Examination

Our Hindi adaptation of the MMSE[8] Hindi Mental State Examination (HMSE) has been described in detail elsewhere.[1] The major differences from the original are (i) orientation to the year (a piece of information which did not appear to be widely known among, or considered relevant to, these illiterate rural elderly), and for which we substituted "time of day"; (ii) the attention subtest requiring serial subtractions in the abstract, for which we substituted a story requiring serial subtractions; (iii) the attention subtest requiring spelling the word "WORLD" backwards, for which we substituted the task of naming the days of the week backwards; (iv) the "write a sentence" subtest for which we substituted an oral task, "tell me something about your house"; and (v) the praxis task (copying intersecting pentagons), for which we substituted a simpler drawing of a diamond shape within a square. The HMSE total score was calculated using the "days of the week" attention subtest, while the subtraction task was scored separately and not used in the analyses described in this report.

Word List Learning and Recall Tests[9]

In the English-language version, the subject reads a lis of 10 words and then attempts to recall them. There ar three learning trials followed by delayed recall (and tw delayed recognition trials, not reported here). In thi paper, we focus on the results from the Delayed Recal of a 10-Item Word List (DRWL).

Because of the low level of literacy in the population we used the same format, but with auditory presentation and with words, which appeared to us (in the absence of formal word frequency norms for Hindi) to be roughly equivalent in terms of familiarity, concreteness, and imageability. The Hindi word list consists of the Hindi words for butter, arm, corner, letter, queen, ticket, grass, stone, book, and stick. With auditory (as opposed to visual) presentation, subjects appeared to be confused as to which "words" they were being asked to repeat on delayed recall, and appeared not to be able to distinguish these "words" from other "words" mentioned during testing (e.g., the three orally presented words for recall on the HMSE). A cueing strategy was devised to minimize source amnesia: the word list is typed on a sheet of green paper and the subject's attention is drawn to it during initial administration; subsequent oral instructions for learning and recall always refer to the "words on the green paper."

Study Population

The rural district of Ballabgarh in the State of Haryana, in northern India, is approximately 35 km from New Delhi and consists of 28 villages. The population follows largely agricultural occupations, and most of its currently elderly members, particularly the women, are illiterate. The community is the field-practice site of the Centre for Community Medicine of the All-India Institute of Medical Sciences (New Delhi), which operates a Comprehensive Rural Health Services Project in the area. The Project has, for over three decades, maintained an up-to-date census of the entire population of Ballabgarh. We were given access to this census for the purpose of identifying the older residents of the area and inviting their participation in our study. From the approximately 4800 individuals originally identified in the census database as being 55 years or older, a 10% age-stratified sample of 480 persons was drawn, to include 160 subjects in each age category 55–64, 65–74, and 75+ years. Field workers visited each subject at home and obtained informed consent according to procedures approved by the CARI Human Volunteers Protection Committee and the University of Pittsburgh Institutional Review Board.

As part of demographic data-gathering, age as recorded in the database was confirmed with the subject. When, as is often the case in rural areas of developing countries, an elderly subject was unaware of his exact age or date of birth, age was confirmed by asking the subject and family to estimate his/her age at the time of well-known historic events[10] as well as personal history (e.g., age at birth of oldest child, whose age is known). Among the 480, 8 were determined to be less than 55 years old, 53 had died, 22 had relocated outside the study area, 1 was a duplicate listing, and 8 refused cognitive testing. Field-testing was carried out among the remaining 388 individuals who were administered the cognitive tests described above. One of these subjects did not complete the HMSE and eight of them did not complete the DRWL.

Neurologic History and Examination

A standardized protocol was designed to obtain a standardized, semi-structured, detailed neurologic history from the subject and his/her next-of-kin, and to conduct general physical and neurologic examinations, and a further mental status examination (modified from the University of Pittsburgh Alzheimer's Disease Research Center, CERAD, and MoVIES protocols[3,7,11,12]). The standardized history includes information about specific current symptoms, level of function in activities of daily living, personality and behavior change, past history of specific symptoms and diseases, family history of neurologic diseases, history of specific exposures, and history of nutritional intake, smoking, alcohol use, and medication use. Mental status testing during the neurologic evaluation included tests of recall of recent and remote events, judgment and problem-solving, immediate and delayed recall (a modification of the Fuld Object Memory Test),[12] language, praxis, calculation, and a modified version of the Blessed Information-Memory Concentration Test.[13]

The standardized neurologic examination included cranial nerve examination, motor function testing (paresis/plegias, proximal/distal power, fine motor function, tone, involuntary movements), sensory function testing (neuropathy, radiculopathy, parietal lobe sensory function), cerebellar function, gait, dorsal column function, praxis, deep tendon reflexes, primitive reflexes, and Babinski's sign. All neurologic examinations were performed by the same US-trained neurologist (VC); further inter-rater diagnostic reliability was assured by assessments of the same patients in the United States and in India by investigators based in the United States (MG) and in India (VC).

Gait assessment was complex in this population. Factors potentially affecting ambulation (e.g., blindness, shortness of breath, degenerative joint disease, history of stroke) were recorded. Many subjects had suffered repeated trauma to the knees leading to arthritis. Prior to gait testing, the subjects' knees were examined for pain and crepitus on flexion/extension movements. Individuals who were completely blind and had to be led by the hand were excluded from detailed gait testing. These factors, along with focal neurologic deficits, were taken into consideration when evaluating gait.

Subjects reporting histories of episodes of impaired consciousness were assessed in detail for potential causes of such episodes. Particular emphasis was placed on differentiating seizures from pseudoseizures which are common in this population (see Discussion). Characteristics of episodes helpful in the diagnosis of pseudoseizures were attacks precipitated by a stressful event, no tongue biting or injury during the attack, no incontinence, bizarre movements of the body, eyes tightly closed, relief from the attack by noxious stimuli, immediate recovery with no postictal confusion, ability to hear and describe what was said during the attack. Differential diagnosis was determined only by clinical assessment.

Data Collection

Consenting subjects were cognitively screened by trained lay field workers under the supervision of the project neuropsychologist (SS) and medical officer (RP). All consenting subjects were also independently examined by the project neurologist (VC) and medical officer (RP) using the standardized neurologic protocol described above.

Twelve subjects did not undergo neurologic evaluation (five refused, one subject's family refused although the subject was in good health, one subject's family refused because the subject was too ill and blind, two relocated, and three who were gainfully employed did not have time to participate.) The data presented below are from the remaining 376 individuals who underwent both cognitive screening and neurologic examination.

Statistical Analysis

Neurologic history items that had a positive response from at least 5% of the study population, and neurologic examination items that had an abnormal finding in at least 5% of the study population, were included in the analysis. Multiple logistic regression models were fit to calculate odds ratios for the association between selected neurologic variables and scores below the 10th percentile cut point on (a) the HMSE and (b) the DRWL, adjusting for age, sex, and literacy. Two separate models were constructed for each neurologic history/exam item. In each model, the independent variables were age, sex, literacy, and the presence/absence of the abnormal neurologic item. The dependent variable in each model was a score below the 10th percentile on the cognitive test (HMSE or DRWL). Subjects were excluded from any model for which they did not have complete data on all variables; hence, the number of subjects varies slightly across models. Adequacy of the models was assessed using the Hosmer and Lemeshow goodness-of-fit statistic.

RESULTS

Demographic Characteristics

Of the 376 constituting the sample reported here, 120, 140, and 116 were aged 55–64 years, 65–74 years, and 75+ years respectively. Men and women constituted

Table 1. Distribution of Scores on HMSE and DRWL by Age, Gender, and Literacy

	Hindi Mental State Exam (HMSE) Mean (SD)*	*Delayed Recall of Word List (DRWL)† Mean (SD)*
Overall	25.4 (4.1)	4.8 (2.2)
Age		
55–64	26.3 (3.0)	5.6 (1.9)
65–74	25.6 (4.1)	4.9 (2.1)
75+	24.1 (4.7)	3.7 (2.1)
Gender		
Men	26.1 (4.0)	4.7 (2.4)
Women	24.5 (4.0)	4.9 (1.9)
Literacy		
Literate	27.9 (3.4)	5.6 (2.2)
Illiterate	24.6 (4.0)	4.5 (2.1)

*Max 30; 10th percentile: 19; †Max 10; 10th percentile: 2.

Table 3. Neurologic History/Exam Variables Associated with HMSE Total < 20 (Odds Ratios Adjusted for Age, Gender, and Literacy)

Neurologic Exam Item	*N*	*OR*	*95% CI*
History of impaired consciousness*	375	2.97	1.09–8.07
History of head injury with loss of consciousness	375	0.89	0.35–2.25
Peripheral neuropathy	373	2.04	0.80–5.18
Gait*	374	2.77	1.29–5.96
Diminished deep tendon reflexes	375	2.00	0.80–5.02
Plantar reflex	375	1.57	0.76–3.22
Glabellar reflex	375	1.62	0.73–3.59
Grasp reflex	375	0.90	0.41–1.97
Root reflex	375	1.00	0.46–2.18
Palmomental reflex	375	1.25	0.55–2.81
At least one abnormal primitive reflex	375	1.80	0.76–4.29

*Variables significantly associated with scores below the 10th percentile.

53.7% and 46.3% respectively, consistent with the gender ratio of the base population. Literacy, defined as the ability to read, was reported as a characteristic of 86 (22.9%) of the subjects; the rest were classified as illiterate. Of those aged 75 years or more, 81.0 were illiterate, as compared to 75.9% of those aged less than 75 years. Among women, 94.8% were illiterate, as compared to 61.9% of men.

Cognitive Scores

Table 1 shows the distributions of scores on the HMSE and DRWL tests in the overall sample, and by age, gender, and literacy. The 10th percentile score for the overall sample on the HMSE was 19 out of a possible 30. The 10th percentile score for the overall sample on DRWL was 2 out of a possible 10.

Neurologic Variables

Table 2 shows the frequencies of neurologic history and examination variables by age, limited to those abnormalities which were present in at least 5% of the sample.

Neurologic Variables Associated with Cognitive Impairment

Results of logistic regression analysis are shown in Table 3 for the HMSE and Table 4 for DRWL.

Variables significantly associated with scores below the 10th percentile (<20/30) on the HMSE were history of impaired consciousness (odds ratio, OR = 2.97, 95% confidence interval, CI = 1.09, 8.07); and gait disturbance (OR = 2.77, 95% CI = 1.29–5.96). Greater age and female gender were significantly associated with low scores in all HMSE models, but literacy was not.

Variables significantly associated with scores below the 10th percentile (<3/10) on the DRWL were history of impaired consciousness (OR = 3.55, 95% CI = 1.36, 9.23); gait disturbance (OR = 2.21, 95% CI = 1.12–4.37); diminished deep tendon reflexes (OR = 2.75, 95% CI = 1.11–6.80); and at least one primitive reflex (OR = 2.32, 95% CI = 1.00–5.36). Greater age and illiteracy but not gender were significantly associated with low scores in all DRWL models.

Table 5 shows the frequencies of different causes of abnormal gait in this population, as determined by the examining neurologist. The causes of gait abnormality

Table 2. Frequency of Positive Response to Neurologic History and Frequency of Abnormal Findings during Neurologic Examination by Age

	55–64 Years Old (n = 120)	*65–74 Years Old (n = 140)*	*75 Years Old or Older (n = 116)*	*Total (n = 376)*
Neurologic History				
History of impaired consciousness	9 (7.5%)	9 (6.4%)	11 (9.5%)	29 (7.7%)
History of head injury with loss of consciousness	15 (12.5%)	21 (15.0%)	22 (19.0%)	58 (15.4%)
Neurologic Examination				
Peripheral neuropathy	23 (19.2%)	84 (60.0%)	94* (83.2%)	201 (53.9%)
Gait	14 (11.7%)	47 (33.6%)	60† (52.2%)	121 (32.3%)
Diminished deep tendon reflexes	29 (24.2%)	87 (62.1%)	97 (83.6%)	213 (56.7%)
Plantar reflex	21 (17.5%)	45 (32.1%)	59 (50.9%)	125 (33.24%)
Glabellar reflex	11 (9.2%)	54 (38.6%)	81 (69.8%)	146 (38.8%)
Grasp reflex	6 (5.0%)	35 (25.0%)	65 (56.0%)	106 (28.2%)
Root reflex	7 (5.8%)	36 (25.7%)	66 (56.9%)	109 (29.0%)
Palmomental reflex	19 (15.8%)	74 (52.9%)	91 (78.5%)	184 (48.9%)

*Peripheral neuropathy was not examined for three subjects.
†Gait was not examined for one subject.

Table 4. Neurologic History/Exam Variables Associated with DRWL Score < 3 (Odds Ratios Adjusted for Age, Gender, and Literacy)

Neurologic Exam Item	*N*	*OR*	*95% CI*
History of impaired consciousness*	371	3.55	1.36–9.23
History of head injury with loss of consciousness	371	0.76	0.31–1.85
Peripheral neuropathy	369	2.33	0.97–5.62
Gait*	370	2.21	1.12–4.37
Diminished deep tendon reflexes*	371	2.75	1.11–6.80
Plantar reflex	371	1.17	0.61–2.28
Glabellar reflex	371	1.89	0.91–3.93
Grasp reflex	371	1.37	0.68–2.77
Root reflex	371	1.44	0.71–2.89
Palmomental reflex	371	1.80	0.83–3.90
At least one abnormal primitive reflex*	371	2.32	1.00–5.36

*Variables significantly associated with scores below the 10th percentile.

Table 6. Events/Circumstances Surrounding Reported Episodes of Impaired Consciousness

Event	*Number (%)*
Pseudoseizure	7 (24.1%)
Seizure	5 (17.2%)
Dizziness/fall	3 (10.3%)
Diarrhea/dehydration	2 (6.9%)
Fainting	2 (6.9%)
Fever (typhoid, tetanus)	2 (6.9%)
Trauma	2 (6.9%)
Unknown single episode	2 (6.9%)
Poisoning	1 (3.4%)
Myocardial infarction	1 (3.4%)
Stroke	1 (3.4%)
Unknown illness	1 (3.4%)
Total	29 (100.0%)

were not mutually exclusive and many subjects had more than one cause, but the most common were pain, injury, degenerative joint disease, and peripheral neuropathy.

Table 6 shows the frequencies of different events and circumstances surrounding episodes of impaired consciousness, as reported to the neurologist by the subject and/or next-of-kin. No single circumstance or cause explained the majority of cases of impaired consciousness, but the single most common cause appeared to be pseudoseizures.

DISCUSSION

The bulk of the world's aging population resides in the developing countries, yet little is known about the distribution of, and risk factors for, dementia and cognitive impairment in these populations. It has been noted that similarities and differences in risk factors between different populations (e.g., in developed and developing countries) may help to narrow the search for etiologic clues.[5] In this paper we report some unusual findings from a pilot study in a population that has rarely been subjected to systematic study. These findings may help generate hypotheses for the future study of risk factors for cognitive impairment and dementia (including but not limited to AD) in developing countries.

In exploratory analyses, we have found that poorer cognitive functioning was associated with greater age, history of impaired consciousness, gait disturbances, diminished deep tendon reflexes, and the presence of primitive reflexes in a stratified random sample of a rural elderly population in India. The neurologic items remained associated with cognitive functioning even after adjustment for age, gender, and literacy. It is important to note that none of the subjects in this sample fulfilled diagnostic criteria for dementia.

Table 5. Causes of Gait Abnormalities

Cause	*Number (%)*
Pain, injury, arthritis, or backache	100 (82.6%)
Peripheral neuropathy	86 (71.1%)
Medical illness	29 (24.0%)
Senile gait (old age)	2 (1.7%)
Total	121 (100.0%)

Lower scores on the general mental status test (i.e., HMSE) were associated with female gender, while lower scores on the memory test (i.e., DRWL) were associated with illiteracy. In this population, illiteracy was strongly associated with both greater age and female gender.[2] The associations of cognitive test performance with age, gender, and literacy were as expected and consistent with findings in the MoVIES project, our sister study in the United States,[6] as well as several other studies in the world literature.[14,15,16]

The explanations are less clear for our findings of poor cognitive test performance being associated with certain neurologic abnormalities, listed above, but not with others (e.g., history of head trauma with loss of consciousness). Partly, the absence of other expected associations is due to lack of statistical power; relatively few elderly individuals in the sample reported or exhibited some of these abnormalities and we did not attempt to explore associations with abnormalities present in less than 5% of the sample (e.g., history or clinical evidence of previous stroke or transient ischemia). The low prevalence of reported stroke probably reflects the relative youth/lesser life expectancy of the population as compared to Western countries, or lesser survival after stroke; it is possible but less likely that it represents lower age-specific incidence of stroke.

Although a history of head trauma with loss of consciousness was present in 15% of our sample, it was not associated with poor cognitive scores. Based on the literature linking this factor with AD,[17,18] we had hypothesized that this factor would be associated with cognitive impairment. Head trauma is relatively common (due to, for example, road accidents or agricultural accidents) in this area, but emergency and high-technology health care is not readily available in this environment. Thus, survivors of head injury in our sample were probably those whose head injuries were minor, or at least not serious enough to cause premature deaths or significant disability.

However, we found unexpectedly that individuals who reported previous episodes of impaired/altered consciousness (not associated with trauma) were significantly more likely to perform poorly on both the mental status test and the memory test. In a previous survey[19] of neurologic disorders in this community, we found the question about impaired consciousness to be highly sensitive to the presence of partial seizures. Repeated seizures, as well as chronic use of anticonvulsant drugs (including folk remedies which can include heavy metals and unknown herbal preparations) could conceivably contribute to cognitive impairment. We had hypothesized that seizures might account for the bulk of these episodes of impaired consciousness, but the circumstances surrounding them were in fact quite variable, ranging from dehydration to pseudoseizures (hysterical conversion symptoms), and suggested no particular common etiology. Pseudoseizures are relatively common responses to stress in uneducated/unsophisticated populations, and are frequently encountered by neurologists and psychiatrists in developing countries. Keshavan et al.[20] reported conversion disorder to be the most common type of psychopathology in their cases. In the absence of further information, we speculate that perhaps what these individuals had in common was a tendency to suffer alterations of consciousness in response to various disease states and other forms of stress. This tendency might reflect a variety of underlying subclinical disease states (including perhaps subclinical cerebrovascular disease and/or unknown psychopathology) which in turn might reflect, or reduce, "cognitive reserve,"[21] lowering cognitive scores.

This elderly population was similarly heterogeneous for gait disturbance. The most common causes were degenerative joint disease and peripheral neuropathy, although peripheral neuropathic signs by themselves were not associated with cognitive impairment. The standard diet of most of these elderly individuals is vegetarian and comprises largely unleavened wheat flat breads, lentils, and tea, with little intake of green leafy vegetables. Further, a large proportion of the elderly are edentulous and lack dentures, thus precluding the dietary intake of items which require significant chewing. Various diarrheal diseases are common, presumably resulting in malabsorption. Nutritional supplements (e.g., vitamin pills) are not taken unless prescribed by a physician. Thus, micronutrient (e.g., Vitamin B and antioxidant) deficiency could be present and could contribute to neurologic conditions (e.g., subacute combined degeneration) associated with gait abnormalities as well as cognitive impairment. Iron deficiency anemia is common in India (88.3% in rural areas near Calcutta[22] and 57% in New Delhi[23] in individuals aged > 44 years), both from dietary deficiencies and from parasitic infestations (hookworm and malaria).

As deep tendon reflexes were symmetrically diminished in most of our subjects, it is possible that they were also the result of peripheral neuropathy, and that their association with cognitive impairment has the same implications as discussed above. The presence of primitive reflexes can suggest diffuse forebrain dysfunction but may also be seen in asymptomatic elderly; their association with cognitive impairment in our sample may suggest that they are markers of incipient dementing illness. Huff et al[11] found that AD patients were significantly more likely to have primitive reflexes than were healthy controls.

We are not aware of any previous reports, from developing countries, examining relationships between neurologic abnormalities and cognitive impairment or dementia. Studies in the United States have shown that mild extrapyramidal signs can predict the development of dementia in elderly individuals,[24] and that AD patients with myoclonus or extrapyramidal signs had greater intellectual decline and functional impairment.[25] However, in another series of AD patients, cognitive changes were more common, and more likely to predict progression of disease, than were neurologic findings.[11]

In summary, in a pilot study with carefully standardized neurologic assessment and cognitive screening methods, we have found cognitive impairment in a rural elderly Indian sample to be associated with the expected demographic variables and also with certain unexpected neurologic abnormalities. Further follow-up of our study population, which is ongoing, will allow us to determine whether the same neurologic factors predict the development of dementia. We hypothesize that risk factors for cognitive impairment (and, by implication, for dementing disorders) in this population may include nutritional deficiencies and certain common infectious diseases. To test these hypotheses, specific screening for these conditions may be worthwhile to include in prospective epidemiologic studies of dementia. It also appears that risk factors for dementia seen in more affluent societies, such as stroke and head trauma, may be less important in developing countries because survival after these events is less likely. Thus, different risk factors may be found for cognitive impairment, and possibly for dementia, across populations, suggesting that different strategies may be indicated for prevention and treatment.

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