

## Clinical signs in diffuse cerebral dysfunction

L. R. JENKYN, D. B. WALSH, C. M. CULVER,  
AND A. G. REEVES

*From the David Prosser Neurology Research Laboratories, Division of Neurology, Department of Medicine, and the Department of Psychiatry, Dartmouth-Hitchcock Medical Center, Hanover, New Hampshire, USA*

**SUMMARY** Abnormal responses to 13 questions from a typical mental status examination and 32 signs of neurological dysfunction were correlated with increasing degrees of cognitive impairment as measured by the Halstead-Reitan Neuropsychological Battery. Thirteen of these factors were found to be useful predictors of diffuse cerebral dysfunction when combined into a brief screening examination for application at the bedside.

The diagnosis of the presence or absence of diffuse cerebral dysfunction—that is, delirium (reversible) or dementia (irreversible)—is a frequent problem, most often encountered with elderly patients but by no means limited to them (Katzman, 1976). When the patient's cognitive integrity is in question, it is important to document the impairment accurately, rapidly, and economically in order to institute therapy for reversible disease processes (Marsden and Harrison, 1972). One tool for the immediate and objective measurement of cerebral function has been examination of the mental status at the bedside. Orientation, memory, problem-solving, and abstraction may be evaluated in a few minutes with a short collection of well chosen questions. These means of appraisal are popular and frequently valuable, but have certain prominent weaknesses. The tests and their administration and interpretation are difficult to standardise. Given a consistent examination of mental status, distinction between low intellect and genuine cortical impairment is subjective and is based on extensive experience with patients of all ages, capabilities, and levels of education. In addition, bedside examinations of mental status have not been correlated systematically with more fully documented measures of neuropsychological function.

Extensive psychometric testing represented by

Reitan's modification of the Halstead Battery (Reitan and Davison, 1974) provides a more precise estimate of cognitive function. This type of highly standardised testing evaluates many intellectual, problem-solving, and perceptual-motor abilities over a two to three hour testing period. The examination in many ways may be regarded as an extension and standardisation of certain parts of both the mental status and neurological examinations, and may help in making a more objective assessment. In many clinical situations the Halstead-Reitan Battery has proved very helpful. Its length and cost, however, preclude its use as a routine screening examination.

Clinicians tend to associate certain physical signs with diffuse cerebral dysfunction including the grasp, palmomental, and feeding reflexes. Many of these signs are present in infancy but become inhibited and unelicitable with increasing age and cortical maturity. Their reappearance later in life in the absence of focal lesions is felt to be secondary to release (disinhibition) from cortical suppression (Ingram, 1962; Humphrey, 1964; Paulson and Gottlieb, 1968; Villeneuve *et al.*, 1974). These physical signs are assessed routinely by some clinicians but apparently not at all by others. Their appraisal has the advantage of ease, rapidity, and economy of administration. However, their clinical value has not been standardised nor evaluated systematically (Kahn *et al.*, 1960; Joynt *et al.*, 1962; Hurwitz, 1968; Paulson and Gottlieb, 1968; Isaacs and Akhtar, 1972; Adams and Hurwitz, 1974; Villeneuve *et al.*, 1974; Jenkyn *et al.*, 1975).

The study reported here correlates 13 questions

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Address for reprint requests: Dr L. R. Jenkyn, Division of Neurology, Department of Medicine, Dartmouth-Hitchcock Medical Center, Hanover, New Hampshire 03755, USA.

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from a typical bedside mental status examination and 32 physical signs of neurological dysfunction with degrees of cognitive impairment measured by the Halstead-Reitan Neuropsychological Battery. Thirteen of these 45 factors correlated well with the degree of intellectual impairment and their validity was cross-validated on a second series of cases. Together, they make for a simple examination which may prove useful in screening for cortical dysfunction.

### Subjects and methods

Over a period of 12 months, 90 patients were selected randomly for inclusion in the study from the total patient pool referred to the Dartmouth-Hitchcock Neuropsychology Laboratory. These patients were referred in roughly equal numbers by the psychiatry, neurology, and neurosurgery services. Four patients were eliminated because it was apparent from their history and test results that they were mentally retarded and had no evidence of recently acquired cognitive dysfunction. Ten other patients were eliminated because both their neurological and neuropsychological results indicated that their cortical dysfunction was essentially focal in nature. Seventy-six patients remained whose neuropsychological results indicated either no impairment or some degree of diffuse, bilateral cortical dysfunction. Both inpatients (56) and outpatients (20) were represented. There were 43 males and 33 females with a mean age of 43.8 years (range 16–80). In the majority of cases the reason for referral was to determine whether significant cognitive impairment existed. In a minority of cases the existence of impairment was known or highly suspected and the reason for referral was to gauge its severity.

#### NEUROPSYCHOLOGICAL TEST BATTERY

All subjects received a standard battery of tests (Reitan and Davison, 1974): The Wechsler Adult Intelligence Scale (WAIS); the Trails Test; the Halstead Battery (Category Test, Tactual Performance Test, Finger Tapping, Rhythm Test, and Speech Sounds Perception Test); the Dynamometer; an Aphasia Screening Test; a Sensory-Perceptual Examination; and the Reading part of the Wide Range Achievement Test.

On the basis of their neuropsychological testing results alone, patients were assigned to one of four categories of cognitive functioning: group 1 (no impairment), group 2 (mild impairment), group 3 (moderate impairment), group 4 (marked impairment). The neuropsychologist making this classification (CMC) had no knowledge of the

neurological tests described below and, in fact, never saw the patients personally since the neuropsychological testing was carried out by other technicians.

The basis for the fourfold classification was principally certain objective indices described below. These indices were used along with knowledge of the patient's age, education, and occupation to make a final judgment, and specific educational and occupational histories on each subject are available from the authors on request.

One of the objective indices is the Halstead Impairment Index, a decimal value ranging from 0.0 to 1.0 which represents that fraction of the five test measures of the Halstead test battery which lie in the 'impaired' range, (Reitan and Davison, 1974). The mean value, standard deviation, and range on this measure for each of the four groups are shown in Table 1.

Table 1 Mean value, standard deviation, and range on two objective measures for classifying patients

	Cognitive function of original subjects*			
	Normal	Impaired		
		Mildly	Moderately	Markedly
Halstead Impairment Index				
Mean	.21	.71	.93	1.0
SD	.13	.19	.09	0.0
Range	0.1–0.4	0.3–1.0	0.7–1.0	1.0
Index derived from Russell <i>et al.</i> 1970				
Mean	10.2	21.2	30.6	44.0
SD	3.6	3.4	4.1	2.6
Range	5–16	16–27	24–38	40–48

\*Determined by neuropsychological evaluation (see Methods).

The other objective index is based on normative scalar values given by Russell *et al.* (1970). They assign scale values between 0 (best performance) and 5 (worst performance) for various tests used in the battery. These scalar values were computed for 10 test measures in our battery of tests (Category Test; Tactual Performance Test: memory, location, total time; Rhythm Test; Speech Sounds Perception Test; Dominant and Non-dominant Finger Tapping; Trails A and B). The mean, standard deviation, and range on this measure for the four groups are also shown in Table 1.

#### PHYSICAL SIGNS AND MENTAL STATUS ITEMS

All patients were tested using the following 45 factors. Where bilateral responses were possible, a

unilateral abnormal response was considered a sign of diffuse dysfunction because subjects with focal lesions had been excluded from the subject population.

1. *Nuchocephalic reflex* (Jenkyn *et al.*, 1975) The shoulders of the standing subjects, whose eyes were closed, were turned briskly to the left and/or right, and the position of the head was noted. The reflex was inhibited and normal if the head actively turned in the direction of the shoulder movement after a lag period of approximately half a second. The reflex was present (disinhibited) and abnormal if the head held the original position. Movement of the head and shoulder en bloc, as may be seen with cervical spondylosis, obscured the reflex and prevented assessment of the response.

2. *Glabellar blink* (Klawans and Goodwin, 1969; Pearce, 1974b) The subject was directed to fix gaze on a point across the room. The examiner's index finger approached the patient from above the forehead outside the visual field. This eliminated visual threat as a stimulus. The glabellar region was then rapidly tapped eight to 10 times. The normal response was for reflex closure of the eyelids to be inhibited after two or three taps and the lids to remain open. Continuous reflex blinking of either the upper or lower eyelids, or both, with or without complete lid closure, constituted a disinhibited, abnormal response.

3–5. *Conjugate gaze* (Critchley, 1956; Hurwitz, 1968; Adams and Hurwitz, 1974) The subject was asked to follow the examiner's finger as it was moved to all extremes of vertical and horizontal gaze. A ruler was placed such that deviation of the edge of the cornea in either plane could be measured. *Upgaze* was considered abnormal if the deviation from the midposition did not equal or exceed 5 mm. *Downgaze* and *lateral gaze* were abnormal if deviation from the midposition was restricted to less than 7 mm. (1 mm equals 7° visual axis deviation, Hirschberg, 1885.)

6. *Visual tracking* (Rodin, 1964) The subject was instructed to hold his head still and follow the examiner's index finger as it was moved between both extremes of horizontal gaze. The eyes should have moved smoothly and without difficulty. Irregular, hesitant, or jerking saccades were considered abnormal.

7. *Snout reflex* (Schlezingner, 1938; Bieber, 1940; Ekbom *et al.*, 1952; Ansink, 1962; Ingram, 1962;

Paulson and Gottlieb, 1968; Klawans *et al.*, 1971; Villeneuve *et al.*, 1974) Using the middle phalange of the flexed index finger, the examiner firmly pressed the subject's relaxed lips, then drew the finger away. Any contraction of the orbicularis oris to this stimulus resulted in a puckering of the lips. This was considered a normal response if elicited by a sharp blow of the reflex hammer to the examiner's finger placed on the subject's lips. However, the presence of the response to minimal pressure without use of the hammer was considered abnormal.

8. *Suck reflex* (Schlezingner, 1938; Bieber, 1940; Ekbom *et al.*, 1952; Ingram, 1962; Paulson and Gottlieb, 1968) The examiner firmly placed the knuckle of the flexed index finger between the subject's lips. There should have been no response. Any pursing or sucking motion by the subject's lips was recorded as a disinhibited and abnormal response.

9–10. *Visual and tactile rooting* (Bieber, 1940; Ingram, 1962) In *visual rooting*, the examiner used an orally unfamiliar object—for example, pen, piece of paper—to approach the subject's mouth from within his visual fields. Absence of response was normal. Any anticipatory opening of the mouth, with or without turning toward the object, was considered disinhibited and abnormal. In testing *tactile rooting*, the examiner scratched each cheek of the subject with his index finger and observed for the same response.

11. *Forced biting* An orally unfamiliar object was placed in the mouth of the subject. Any tendency to bite down or hold onto the object was abnormal. Inability to release the object upon command by the examiner confirmed the response as abnormal.

12–13. *Grasp reflex* (Adie and Critchley, 1927; Bucy, 1931; Walshe, 1935; Bieber, 1940; Seyffarth and Denny-Brown, 1948; Paulson and Gottlieb, 1968; Shahani *et al.*, 1970; Villeneuve *et al.*, 1974) This reflex was tested both *with* and *without distraction*. First the subject was told, 'Do not hold on', while the examiner used his own finger to stroke the palmar surface of the subject's hand. Next, the subject was distracted by being instructed to spell a simple word such as 'fist' both forward and backward. Each hand was tested without distraction then with distraction. The addition of a second task ('spell fist backwards') to the first task ('do not hold on') increased the stress on the subject and allowed a disinhibited

reflex to become manifest. Absence of response of the subject's hands was normal. Flexion of the fingers in an attempt to grasp, or firm closure around the examiner's finger by the subject was considered disinhibited and abnormal.

14. *Palmomental reflex* (Blake and Kunkle, 1951; August and Miller, 1952; McLaughlin and Haines, 1953; Bracha, 1958; Ansink, 1962; McDonald *et al.*, 1963; Otomo, 1965; Hurwitz, 1968; Paulson and Gottlieb, 1968; Dalby, 1970; Adams and Hurwitz, 1974; Little and Masotti, 1974; Villeneuve *et al.*, 1974) The subject was instructed to look at the examiner's nose and remain quiet. Using the nail of his thumb, the examiner firmly stroked the thenar eminence of the subject's hand 10 consecutive times. The stimulus was noxious in intensity and not administered to the palm or hypothenar eminence where the response was less likely to be produced. The examiner observed the ipsilateral mentalis muscle of the chin for any degree of contraction with each stroke. Four or fewer consecutive mentalis contractions were considered within normal limits. Five or more mentalis contractions were considered disinhibited and abnormal. Each side was tested.

15–17. *Paratonia* (Critchley, 1956; Paulson and Gottlieb, 1968; Wells, 1971; Adams and Hurwitz, 1974; Villeneuve *et al.*, 1974) The examiner tested the subject's resting muscle tone in the *arms and legs* by passive extension and flexion. Normal tone should have been present. An irregular opposition to the examiner's movements after instructions to relax resulted in a 'catching' sensation. This was considered abnormal and could be differentiated from the full range, regular rigidity, or cog-wheeling of Parkinsonism and the clasp-knife phenomenon of spasticity. A further variation of the test for paratonia was *limb placement*. The examiner held the subject's arm up and told him to relax, letting the examiner do all the work. Then the examiner dropped his hands. The subject's arm should have fallen at the same time. Any delay in dropping of the arm was considered abnormal after Parkinsonian rigidity and spasticity had been excluded.

18–19. *Perseveration* (Critchley, 1956; Allison, 1966; Hurwitz, 1968; Adams and Hurwitz, 1974; Villeneuve *et al.*, 1974) The examiner proceeded from irregular to regular cycles of passive extension and flexion of the subject's limb. After a few cycles, the subject's limb was released. Absence of movement was normal. Active continuation of the passive movement was considered abnormal

perseveration of motor activity. Both arms and legs were tested.

20–24. *Impersistence* (Berlin, 1955; Joynt *et al.*, 1962; Ben-Yishay *et al.*, 1968) The inability to sustain motor activity was tested in five ways: (i) the subject was instructed to close his eyes and keep them closed. The subject should have been able to maintain this activity for more than 15 seconds. Any eye opening in 15 seconds or less was abnormal (*impersistence on eye closure*); (ii–iii) the subject was instructed to protrude his tongue with eyes open and while blindfolded. The tongue should have been held out for more than 20 seconds. Inability to keep the tongue out for 20 seconds in either situation was abnormal (*impersistence on tongue protrusion, eyes either open or blindfolded*); (iv) the subject was instructed to fix his gaze on the examiner's finger at approximately the 45 degree angle in the horizontal plane of the right and left visual fields for 30 seconds. One deviation from the examiner's finger in each field or more than one deviation in one field was abnormal (*impersistence on lateral gaze*); (v) the subject was also instructed to protrude his tongue and close his eyes. Inability to sustain this activity for 10 seconds was considered abnormal (*impersistence on eye closure/tongue protrusion*).

25–26. *Face-hand stimulation* (Fink *et al.*, 1952; Bender *et al.*, 1954; Kahn *et al.*, 1960) The subject was instructed to close his eyes and describe where he had been touched by the examiner. The examiner alternately touched the right cheek, then left hand and right cheek together and simultaneously, right hand and left cheek together and simultaneously, and so on, recording the subject's response to each stimulation. Accurate localisation of all stimuli after three mistakes was considered normal. Improper localisation or extinguishing of one of the places stimulated was considered abnormal (*double simultaneous stimulation (DSS), either incorrectly localised or extinguished*).

27. *Plantar response* (Babinski, 1898; Brain and Curran, 1932; Goldstein, 1938; Wartenberg, 1945; Walshe, 1956; Brain and Wilkinson, 1959; Manfredi *et al.*, 1975) The lateral aspect of each foot was stimulated with a noxious instrument (pointed end of the reflex hammer) and the movement of the toes was observed. This technique was employed to avoid confusion with the tonic foot grasp evoked by stimulation placed more medially on the plantar surface. Plantar flexion of the great toe or no movement was considered normal.

Dorsiflexion of the great toe denoted the Babinski sign. Any uncertain response was described as equivocal.

28–29. *Vibration* (Klawans *et al.*, 1971) The sensory capacity of the arms and legs was assessed using a C128 tuning fork. Any reported decrease in sensation was considered abnormal.

30–31. *Post-hyperventilation apnoea* (PHVA) (Plum *et al.*, 1962; Jennett *et al.*, 1974) The subject was instructed to take five breaths as rapidly and as deeply as possible. The time between the fifth and sixth breaths was determined without informing the subject. If this interval exceeded 10 seconds, it was considered abnormal. Perseveration of inspirations beyond six breaths (number of breaths) forced the examiner to command the subject to stop, and responses of this kind were not recorded.

32. *Oculocephalic reflex* (Szentagotthai, 1950; Plum and Posner, 1972) The subject in the supine or sitting position was instructed to keep his eyes open and not to fixate on anything in particular. The examiner rotated the head and observed the eyes. Deviation of the eyes in the direction of the head movement was normal. If the eyes held the original position the reflex was disinhibited and abnormal.

33–45. *Mental status examination* (Kahn *et al.*, 1960; Bender, 1966; Smith, 1967) Thirteen questions were given in the following order so that memory could be tested with distraction after three to five minutes.

i–ii. The examiner gave three items ('red, table, 23 Broadway') and asked the subject to repeat them. If there was difficulty with immediate repetition, the process was repeated to a maximum of three times. Then the subject was stressed to remember the items for later in the exam. The subject should have been able to repeat the items without error both at the onset (*immediate memory*) and termination (*recall memory*) of the mental status exam. It is important not to suggest how many items were given originally.

iii. *Where* are you? No error allowed.

iv. What *kind of place* is this? No error allowed.

v. What is the *date*? It was considered normal if the date was within three days of the actual date.

vi. What *day* of the week is this? No error allowed.

vii. What *time* is it? It was considered normal if the time was within one hour of the actual time.

viii. Who is the *present President* of the United States? No error allowed.

ix. Name the *past Presidents* of the United States in reverse order from the present one. The knowledge of past presidents is a function of age: a 20 year old should have known Ford, Nixon, Johnson, and a 40 year old should have known these plus Kennedy and Eisenhower, while a 60 year old should have known these plus Truman and Roosevelt.

x. In your opinion, what is the *largest city* in the country? Any large city was acceptable while states, local towns, and foreign cities were not.

xi. Subtract seven from 100 and continue subtracting seven from your answer (*serial sevens*). Serial sevens were abnormal if the subject made more than one error in subtraction. Abnormalities in the pattern of responses to serial sevens were not analysed because of lack of agreement on their meaning.

xii. Spell 'world' forward and backward (*reversal*, 'world'). Errors in forward spelling were ignored if the reverse sequence of the misspelled word was correct.

xiii. Give the days of the week forward and backward (*reversal*, *days of week*). No errors allowed.

## Results

Table 2 delineates some relevant characteristics of the subjects in the four cognitive categories. It also shows the number of abnormal responses found in each category during the examination of physical signs and mental status questions.

The number of abnormal responses increased directly with increasing degrees of cognitive im-

Table 2 *Characteristics of patients in four cognitive categories*

	Cognitive function of original subjects*				All
	Normal	Mildly	Moderately	Markedly	
Number	18	25	23	10	76
Mean age	29.2	38.7	52.8	66.4	43.8
(range)	(17–65)	(16–66)	(20–75)	(46–80)	(16–80)
Average number of abnormal responses per subject	2.9	6.0	13.9	19.1	9.4
Abnormal responses per category (%)	6.6	13.5	31.3	42.7	21.1

\*Determined by neuropsychological evaluation (see Methods).

pairment. A simple one-way analysis of variance reveals this to be a highly significant relationship ( $F=49.93$ ,  $df=3,71$   $P<0.001$ ).

Table 2, however, also reveals that the four groups differ in age. Could our data reflect an increased incidence of abnormal responses in older patients rather than a particular association between abnormal responses and cognitive impairment? The data were examined in two different ways to attempt to answer this question.

First, an analysis of covariance was performed in which the number of abnormal responses in the four groups was the criterion variable and age was the covariate. This analysis (Winer, 1962) served to eliminate statistically the correlation between age and number of abnormal responses (Pearson  $r=+.61$ ,  $P<0.01$ ), and then re-examined group differences with the effect of age removed. The analysis of covariance showed that the group differences were still highly significant with the effect of age removed ( $F=24.47$ ,  $df=3,71$   $P<0.001$ ).

A second related analysis was performed in which only the data for subjects between the ages of 40 and 65 years were considered. The number of such subjects in cognitive categories 1-4 were, respectively, five, 12, 11, and five. A one-way analysis of variance showed no significant difference in age among these four groups. The average number of abnormal responses in the four groups were respectively 3.6, 6.4, 16.0, and 19.8. A one-way analysis of variance showed these group differences to be significant ( $F=4.57$ ,  $df=3,28$ ,  $P<0.01$ ). Thus, there is good evidence that the total number of abnormal responses is directly related to the degree of cognitive impairment independent of age.

Table 3 summarises for each factor the rate of abnormal responses in subjects with normal cortical function (group 1): the false positive rate; and the rate of normal responses in cortically impaired individuals (groups 2, 3, and 4): the false negative rate. All 45 factors could not be tested in every subject for a variety of technical reasons.

The statistical significance of the relationship of each factor to normal or impaired cortical function was evaluated by a  $\chi^2$  test. This was performed on a two by four table which contained the frequency of the presence or absence of the abnormal response for each cognitive category. The factors are listed in Table 3 in order of decreasing significance of their  $\chi^2$  values. When the chi squared value is greater than or equal to 16.3, the significance is  $P<0.001$ . When it is greater than or equal to 11.3, the significance is  $P<0.01$ .

Table 3 Summary of rate of abnormal responses in subjects with normal cortical function

Response tested	$\chi^2$	Number tested	False positive (%)	False negative (%)
<b>P &lt; 0.001</b>				
Paratonia (arms)	32.01	75	5.6	47.4
Uppgaze	30.29	76	11.1	37.9
Paratonia (legs)	27.40	75	0	56.1
Oculocephalic	26.37	68	0	63.5
Nuchocephalic	25.29	75	5.6	48.3
PHVA (number of breaths)	24.56	73	5.6	83.6
Serial sevens	24.52	75	22.2	70.2
Visual tracking	24.11	76	16.1	46.6
Reversal (days of week)	23.18	73	0	91.1
Limb placement	21.41	75	5.6	52.6
Lateral gaze	20.86	76	5.6	62.1
Recall of past presidents	16.47	75	22.2	42.1
Suck	16.30	76	0	56.9
<b>P &lt; 0.01</b>				
DSS (extinguish)	16.14	76	0	81.0
Grasp (without distraction)	16.10	76	0	87.9
Kind of place	15.07	74	0	96.5
Snout	14.23	76	11.1	60.4
Grasp (with distraction)	14.11	76	0	79.3
Downgaze	13.18	76	11.1	56.9
PHVA (time to sixth breath)	12.53	69	5.6	84.3
Glabellar blink	12.49	75	29.4	27.6
Impersistence on lateral gaze	11.74	68	29.4	39.2
<b>P &lt; 0.05</b>				
Reversal ('world')	10.50	74	23.5	50.9
Time	10.13	74	0	83.9
Memory (recall)	9.11	75	38.9	24.6
Impersistence on eye/tongue protrusion	8.47	75	5.6	87.7
Palmontal	8.02	75	5.6	70.2
<b>Not significant</b>				
Motor perseveration (arms)	7.43	75	0	98.3
Vibration sense (legs)	6.72	73	5.6	89.1
Date	6.68	75	5.6	84.2
Largest city	6.23	74	0	93.0
Babinski	5.86	71	5.9	85.2
Impersistence on tongue protrusion (eyes open)	5.60	75	5.6	84.2
Where	5.47	75	5.6	93.0
Impersistence on eye closure	4.65	75	0	96.5
Recall of present president	4.32	75	0	93.0
Motor perseveration (legs)	3.90	75	0	96.5
Day	3.56	75	11.1	84.2
DSS (incorrectly localised)	3.36	75	0	91.2
Impersistence on tongue protrusion (eyes blindfolded)	3.32	72	5.9	89.1
Forced bite	2.34	76	0	98.3
Memory (immediate)	1.70	76	0	100
Vibration sense (arms)	1.70	73	0	100
Root (visual)	1.70	75	0	100
Root (tactile)	1.70	75	0	100

When it is greater than or equal to 7.8, the significance is  $P < 0.05$ . A chi squared value of less than 7.8 indicates that the results obtained for that factor are not significantly different from chance. Twenty-seven of the factors were significantly related to the level of cognitive impairment while 18 were not.

The significant factors ( $P < 0.05$ ) with the lowest false negative rates were selected in order to assemble an effective battery of tests to screen for diffuse cortical dysfunction. Factors with false negative rates greater than 60% were arbitrarily considered to be poor predictors. The false positive rates for all 27 significant factors were considered acceptable. The 13 factors listed in Table 4 represent those with false negative rates less than 60%.

As a matter of interest, the original data were re-examined using only these 13 factors. Table 5 shows the average number of abnormal responses per subject in this screening battery for each cognitive category (groups 1-4). The number of abnormal responses per person increases with increasing degrees of cerebral dysfunction, and more than two abnormal responses was usually associated with impaired cognitive function. The 76 subjects were classified as normal (two or less abnormal factors on the screening battery) or

impaired (three or more abnormal factors). The results are shown in Table 6. The screening

Table 6 Results of classification of patients by selected screening battery

Prediction of cognitive function	Cognitive function of original subjects*			
	Impaired			
	Normal	Mildly	Moderately	Markedly
Normal	16	8	1	0
Impaired†	2	17	22	10
Total	18	25	23	10
% correct	89	64	96	100

\*Determined by neuropsychological evaluation (see Methods).

†Three or more abnormal responses.

battery correctly predicted normal cognitive function in 89% of those subjects with normal cortical function. Therefore, the rate of prediction of abnormal cortical function in normal subjects (the false positive rate) was 11%. With increasing degrees of impairment, the screening battery correctly predicted cortical dysfunction in 64% of mildly impaired subjects, in 96% of moderately impaired subjects, and in 100% of markedly impaired subjects. The rate of prediction of normal cognitive function among all cortically impaired subjects (the false negative rate) was 16%.

The above analysis suffers from being circular in that the 13 factors were derived from the same data on which the subsequent analysis was based. For this reason a small cross-validation study was performed. Twenty-three new subjects were selected randomly from those referred to the Neuropsychology Laboratory, and the short battery of 13 factors was given to them. Again, no patient was selected with neurological or neuropsychological evidence of focal cortical dysfunction. Each patient was independently assigned to one of the four cognitive categories on the basis of his or her neuropsychological test results alone. The resultant data are shown in Table 7. Table 8 shows the relationship between cognitive function and the presence of two or less abnormal factors (predicted to be normal) or three or more abnormal factors (predicted to be impaired). The association is just as strong in the cross-validation as in the original data.

## Discussion

This study assessed the usefulness of a number of physical signs and mental status questions associated with the clinical recognition of diffuse cortical dysfunction. Each factor was examined

Table 4 List of factors selected for an effective battery of screening tests for diffuse cortical dysfunction

Factors with false negative rates less than 60%
Nuchocephalic reflex
Glabellar blink
Suck
Upgaze
Downgaze
Visual tracking
Lateral gaze impersistence
Paratonia of both arms
Paratonia of both legs
Limb placement
Accurate spelling of 'world' in reverse
Accurate order of past presidents in reverse
Accurate recall of three items over time with distraction

Table 5 Average number of abnormal responses per subject in selected screening battery by cognitive category

Screening battery responses (maximum = 13)	Cognitive function of original subjects*			
	Impaired			
	Normal	Mildly	Moderately	Markedly
Number of abnormal responses per person (range)	1.78 (0-6)	4.32 (1-8)	7.00 (1-12)	8.70 (4-13)

\*Determined by neuropsychological evaluation (see Methods).

Table 7 Classification of new subjects by results of neuropsychological tests alone

	Cognitive function of new subjects*				
	Impaired				Total
	Normal	Mildly	Moderately	Markedly	
Number	5	10	7	1	23
Number of abnormal responses on screening battery for each subject	3	6	10	8	
	2	6	9		
	1	6	7		
	1	4	7		
	0	4	6		
		4	5		
		3	5		
		3			
		2			
		2			
Average number of abnormal responses per subject	1.4	4.0	7.0	8.0	4.4

\*Determined by neuropsychological evaluation (see Methods).

Table 8 Relationship between cognitive function and the presence of abnormal factors

Prediction of cognitive function by screening battery	Cognitive function of new subjects*			
	Impaired			
	Normal	Mildly	Moderately	Markedly
Normal	4	2	0	0
Impaired†	1	8	7	1
Total	5	10	7	1
% correct	80	80	100	100

\*Determined by neuropsychological evaluation (see Methods).

†Three or more abnormal responses.

individually for its ability to predict impairment as measured by the Halstead-Reitan Neuropsychological Battery. It is significant that the subjects evaluated were those who represent the population at risk for mild diffuse cortical impairment—that is, those referred for neuropsychological evaluation—and not the population with severe and obvious diffuse cortical dysfunction.

The results show that 18 factors had no significant statistical association with the presence or absence of diffuse dysfunction. These included such commonly used mental status questions as the date, day of the week, geographic location, present president, and immediate memory (the ability to repeat three items immediately without distraction). Also, the 'regressive' signs of motor perseveration, visual and tactile rooting, and forced biting were not significant predictors. Other

factors were significantly associated with cognitive impairment but were of little predictive value because of prohibitively high false negative rates. These included such physical signs as the grasp (both with and without distraction), palmomental, snout, and oculocephalic reflexes as well as motor impersistence and post-hyperventilation apnoea. Also, frequently used mental status questions such as serial sevens, kind of place, time of day, and saying the days of the week in reverse order were associated with very high false negative rates.

The remaining 13 significantly associated factors were combined to assess their predictive value as a short test battery. They were initially applied to the original data (from which they came) and found to be highly accurate in their prediction of normal or impaired cognitive function. Subsequently, a cross-validation study was performed with a new sample of patients and it confirmed the predictive utility of the 13 item battery.

The screening battery possesses several interesting characteristics. All 13 factors have clearly identifiable present or absent responses. Ten of the 13 factors require no verbal response from the subject. The relationship of the nuchocephalic reflex to diffuse cerebral dysfunction has been described previously. It was shown that, whether inhibited or disinhibited, the nuchocephalic reflex predicted correctly the state of higher cortical function in 75–80% of all subjects older than 16 years of age (Jenkyn *et al.*, 1975). It is interesting that the presence of a glabellar blink, previously associated with Parkinson's disease, is also related to the presence of diffuse cerebral dysfunction. This suggests that diffuse cortical impairment may be an integral part of the degenerative process of Parkinsonism, or that diffuse disease involves the basal ganglia or their connections (Pearce, 1974a, b; Drachman and Stahl, 1975). Among the infantile feeding reflexes to reappear with diffuse cortical dysfunction, the suck reflex is notable for its predictive value. The snout reflex, which appears to differ from the suck reflex only in the strength of the eliciting stimulus, was excluded from the battery because its false negative rate (60.4%) was just greater than the arbitrary 60% rate that was set as the acceptable upper limit.

Of great interest is the usefulness of observing extraocular movements in this battery. Innervation of normal voluntary vertical gaze (both upward and downward) is associated with both hemispheres, is not localised to any particular cortical areas, and might be impaired with diffuse dysfunction (Critchley, 1956; Hurwitz, 1968; Hoyt and Daroff, 1971; Adams and Hurwitz, 1974). Contralateral horizontal gaze, a function that may



be elicited from cortical stimulation of most areas of the hemisphere, but especially area 8 of Brodman (Carpenter, 1971), had a false negative rate of 62.1% and, like the snout reflex, just missed the cutoff for inclusion in the screening battery. Impersistence on lateral gaze may be secondary to organic dysfunction of the horizontal gaze centres of the cerebral cortex, or more likely results from the psychological need to maximise sensory input in an individual who is finding it increasingly more difficult to maintain control over and contact with the environment. Visual tracking, thought to be a function of the occipital lobes, may be impaired bilaterally in a diffuse process, or may require bilateral hemispheric innervation for smooth pursuit (Rodin, 1964).

Paratonia (*gegenhalten*) of arms and legs, and perseveration of limb placement (a phenomenon also described as *catatonia*) may be the result of loss of the capacity to inhibit resting muscle tone. Poor recall of past presidents and three items over time with distraction, and inaccurate reverse spelling of 'world' confirm that both remote and recent memory and learning capabilities are disrupted in diffuse cerebral dysfunction.

One significant attribute of the screening battery is the ease with which it may be incorporated into the physical examination without increasing the expenditure of time. The nuchocephalic reflex may be evaluated while the Romberg test is performed. The glabellar blink and suck are tested while examining the head and mouth. Conjugate vertical gaze and visual tracking require only observation during the routine examination of extraocular movements. Impersistence on lateral gaze is observed while checking for nystagmus. Paratonia may be elicited while evaluating muscle tone and the limb placement manoeuvre is easily added at this point. The mental status examination is sufficiently adaptable to include the recall of past presidents, reverse spelling of 'world' (having proof that the subject can spell it accurately forward), and the recall of three items over time (three to five minutes) with distraction. It is only necessary to tally the number of abnormal responses in order to have a rapid indication of the state of higher cortical function at the bedside.

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