

Criteria for Diagnosing Reversible Dementia Caused by Depression: Validation by 2-year Follow-up

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Summary: Eighteen patients fulfilling DSM-III criteria for both major depression and dementia were matched by age and sex to patients with a diagnosis of irreversible dementia and patients with a diagnosis of major depression. A past history of depression, self reports of depressed mood, self blaming, hopeless and somatic delusions, an appetite disturbance and subacute onset identified the patients suffering from dementia caused by depression. Two year follow-up confirmed the initial diagnosis and demonstrated that coexisting cognitive impairment and major depression are not usually precursory to a progressive dementing illness.

It has been known since the start of the century that depression can interfere with cognitive function (Kraepelin, 1921). In the past 20 years renewed interest has been shown in this phenomenon, in large measure because depression has been recognized as a reversible cause of dementia (Kiloh, 1961; Freemon, 1976; Folstein and McHugh, 1978; Rabins, 1981). One study in a neurological hospital, for example, found depression accounting for nine per cent of the admissions for dementia (Marsden and Harrison, 1972). While criteria for distinguishing depressed-demented patients from irreversibly demented patients have been suggested (Post, 1975; Wells, 1979), we know of no attempt to validate such criteria. The following study was undertaken to determine criteria which would distinguish these disorders, to determine the prognosis of co-existing cognitive impairment and depression, and to determine the difficulty (i.e. validity) of making such a diagnosis.

Method

Every patient 60 years of age and older and those younger patients with a suspect dementia hospitalized in a one year period (April, 1978-March, 1979) at the Henry Phipps Psychiatric Clinic were examined by P.V.R. All were administered the mini-mental state exam (MMSE), a reliable and valid indicator of cognitive disturbance (Folstein *et al.*, 1975; Tsai and Tsuang, 1979). Those scoring less than 24 and judged to be accessible, alert and performing at full effort were diagnosed as demented. The patients so identi-

fied fulfilled the DSM-III criteria for dementia. All patients were also examined for the presence of a sustained mood disorder and a negative change in self-attitude. Patients with these symptoms were diagnosed as depressed; all fulfilled the DSM-III criteria for major depression, except for the criteria which excludes co-existing organic mental disorder.

Eighteen patients were identified as suffering both major depression and dementia. These patients were matched by age (± 2 years or closest in age) and sex to patients hospitalized in the same one year period with a diagnosis of irreversible dementia. To determine if the course of their illness was similar to that of affectively ill patients, they were also matched by age and sex to a second group hospitalized during the same period suffering major depression but having normal cognition.

Patients were re-examined at two year follow-up. One depressed-demented patient had died. Two depressed-demented patients had moved out of state and could not be examined in person. By telephone they were fully oriented and aware of current events. Their families reported they were cognitively normal and we considered them fully recovered. One depressed-demented patient could not be located. Two irreversibly demented patients had died and three could not be located. One depressed subject had died and one was lost to follow-up.

Results

Fig 1 shows the range of MMSE scores at the time of

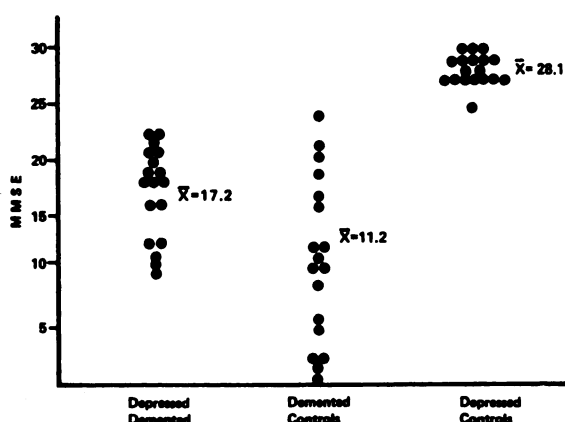


FIG 1.—MMSE scores on admission.

admission in the three groups. While the depressed-demented subjects were less cognitively impaired as a group than demented patients ($t = 2.99, P < .005$), many patients in the two groups had identical scores. Features of the history and mental status examination in the depressed-demented and irreversibly demented controls are shown in the Table. A past history of affective disorder and a subacute onset were more

common in the depressed-demented. Depressed mood was reported more often by depressed-demented patients but four individuals in this group did not describe their mood as depressed. One such patient could not describe her mood but appeared agitated and fearful, another stated he felt "terrible", and two reported feeling something was wrong with themselves but denied sadness or depression. The depressed-demented also suffered delusions more frequently than the demented group, and it is of note that the delusions were depression specific; that is, unfounded ideas of self-blame, poverty or physical deterioration were present only in the demented-depressed group, while persecutory delusions were seen in both groups.

All depressed-demented subjects were treated with either tricyclic antidepressants or electroconvulsive therapy. While all showed some improvement in their mood, three of the eighteen subjects remained cognitively impaired (MMSE less than 24) on discharge. These three subjects did not differ in length of illness or type of symptoms from those who did recover.

The cognitive performance at two year follow-up emphasizes the distinction between the depressed-demented and irreversibly demented groups (Fig 2). Two of the depressed-demented who had not fully recovered remained demented, while the third patient

TABLE
Patients characteristics

Variable	Demented depressed (n = 18)	Demented controls (n = 18)	P value*	Predictive value (%)
Family history of affective disorder	4	1	NS	80
Past history of:				
Depression	9	1		
Mania and depression	1	0		
Depression and alcoholism	1	0		
Total	11	1	<.001	92
Alcoholism	2	1	NS	67
Depressed mood	13	4	<.003	76
Delusions	15	3	<.001	83
Type:				
Persecutory	5	3	NS	62
Self-blaming	5	0	<.02	100
Hopeless	4	0	<.02	100
Poverty, loss	2	0	NS	100
Somatic	7	0	<.004	100
Guilt	3	0	NS	100
Sleep disturbance	7	7	NS	50
Appetite disturbance	10	4	<.04	71
Length of symptoms				
Median	2 months	5 years		
Range	1 week – 6 years	5 months – 7 years		

*Fisher's exact probability test

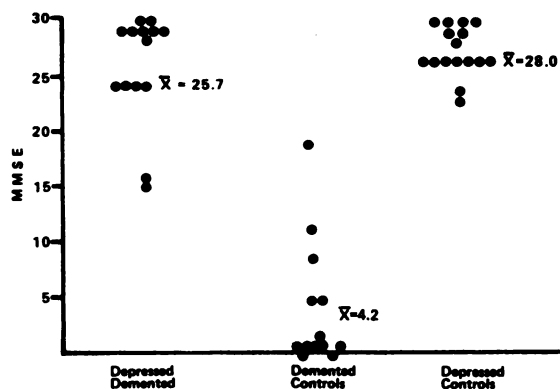


Fig 2.—MMSE scores at 2 year follow-up.

who had not fully recovered had died. The remaining subjects were cognitively normal as were 15 of the 16 tested depressed subjects. The MMSE in the demented-depressed were not lower than in the depressed ($t = 1.37$, NS). In the demented group, on the other hand, all but one patient had deteriorated cognitively and the mean MMSE remained lower than in the demented-depressed ($P < .005$).

Discussion

The two-year follow-up validates the initial diagnoses. Patients diagnosed as irreversibly demented had deteriorated while the depressed-demented and depressed cognitively intact controls generally remained cognitively intact. Had any patients with major depression been put in the irreversibly demented category, it is quite likely they would have had a spontaneous remission and improved cognitively (Ron *et al*, 1979; Nott and Fleminger, 1975). Thus, as Felix Post (1975) has suggested, concomitant dementia and depression are not precursors to a dementing illness in most individuals. However, those suffering from these disorders did not all have good prognoses since three of the 18 subjects remained cognitively impaired. Several others (Wells, 1979; Shraberg, 1978; McAlister and Price, 1982) have also reported that not all depressed-demented patients recover cognitively.

Miller (1980) has examined the converse issue, mood disorder in a group of irreversibly demented patients, and found high levels of depression. Her aim was to examine symptom levels and the question of whether any of the subjects met specific diagnostic criteria for depression was not raised. Reifler *et al* (1982) have recently reported that 23 per cent of patients diagnosed as suffering senile dementia of the Alzheimer type met Research Diagnostic Criteria criteria for definite or probable primary or secondary depression even though their dementia was irrevers-

ible. They emphasized that such symptoms require treatment. The three patients reported here who did not fully recover cognitively, but did show mood improvement illustrate this. Neither Reifler *et al* nor the present study has presented criteria which identify patients who will show partial cognitive recovery if their depression is treated. Further study of this question is warranted.

One might wonder whether the interest in the dementia of depression as a treatable cause of dementia has exaggerated its clinical importance. Is there evidence that misdiagnosis happens? Marsden and Harrison's study from the National Hospital, Queen Square, London (1972), in which nine per cent of the patients referred for evaluation of dementia suffered from depression, is notable since all patients had been pre-screened by a neurologist or psychiatrist, presumably for treatable dementia. In another British study, Kendell (1974) found that 8.2 per cent of patients who were diagnosed as demented were re-diagnosed as depressed at follow-up. Some misdiagnosis is likely to have occurred in the U.S. as well. The U.S.-U.K. diagnostic study (Duckworth and Ross, 1975), for example, demonstrated that older individuals were more likely to be diagnosed as suffering from dementia (organic brain syndrome) by American psychiatrists, and from an affective disorder by United Kingdom psychiatrists.

Because of the predictive validity of the history and mental status examination, we conclude that patients who suffer dementia caused by depression can be recognized with a standard clinical examination. We do not believe that the dementia of depression is a mysterious disorder which only experts can detect. This study suggests that if patients presenting with symptoms of dementia undergo a thorough family and past psychiatric history as well as a search for the signs and symptoms of major affective disorder, then most with depression causing dementia will be recognized (Wells, 1982). A past history of affective disorder, a sub-acute onset, a persistently depressed or dysphoric mood, a history of poor appetite and weight loss, and delusions of self-blame, hopelessness or physical ill health suggest that the patient is suffering a treatable cause of dementia.

The interest in these coexisting disorders goes beyond the diagnostic aspect. We believe their co-existence may offer new insights into brain structure-function relationships. It seems plausible to us that the reversible cognitive disorder seen in some depressed patients might be explained as a neurophysiological unmasking by depression of the subtle structural brain changes or abnormalities such as those seen in normal aging or undetected stroke. In most individuals cognition fully recovers because the lesions themselves

are not of a magnitude to cause dysfunction. In others, however, the structural lesions continue causing cognitive impairment after the affective disorder resolves, but the patient does recover the cognitive dysfunction secondary to the neurophysiological impairment of the depression. Support for this hypothesis comes from three sources. Hemsli *et al* (1968) reported that some recovered elderly depressives have barbiturate sleep induction thresholds similar to those of demented subjects suggesting subtle underlying structural pathology. Tomlinson *et al* (1968) have examined the neuropathology of cognitively normal elderly depressives and found neuritic plaques, neurofibrillary tangles, granulovacuolar degeneration and softening, although in the same amounts as the cognitively normal elderly. More recently, PET scan studies have shown physiological abnormalities in depressed individuals (Mathew *et al*, 1980) while Jacoby and co-workers (1983) have shown that the CT scan determined brain tissue density of depressed elderly resembles that of demented patients more than normals.

While the clinical history and examination can identify patients suffering depression causing cognitive impairment, there may be occasional patients for whom such an examination is difficult or impossible, or patients in whom such features are lacking. This makes the search for biological markers of depression such as brain metabolism abnormalities revealed by the PET scan (Uytendhoef *et al*, 1983) important. However, the recently reported failure of the dexamethasone suppression test to distinguish between Alzheimer's disease and depression (Spar and Gerner, 1983) emphasizes that the clinical examination is the most specific diagnostic procedure now available.

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