Contribution of Psychosis and Depression to Behavioral Disturbances in Geropsychiatric Inpatients With Dementia

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Background. Specific behavioral disturbances in dementia may be associated with underlying disorders such as the presence of psychosis and depression. The objective of this study was to examine the association of depression and psychosis with behavioral disturbances in geropsychiatric inpatients with dementia.

Methods. All admissions between October 1993 and May 1995 were reviewed to identify those patients admitted to the Houston Veterans Affairs Geropsychiatry Unit with a diagnosis of dementia; 208 patients were included in the study. Hierarchical regression models were constructed to explore the contribution of depressive and psychotic symptoms, and depression and psychosis diagnoses to Cohen-Mansfield Agitation Inventory (CMAI) scores.

Results. Both depression and psychotic symptoms were significantly and positively correlated with behavioral disturbances. Psychotic symptoms were associated with aggressive behavioral symptoms, and depressive symptoms were associated with constant requests for help, complaining, and negativism. Dementia severity accounted for significant variance in CMAI scores and was positively associated with behavioral disturbance; thought disorder symptoms accounted for more behavioral disturbance variance than did depressive symptoms.

Conclusions. Both depressive and psychotic symptoms were associated with overall behavioral disturbances in patients with dementia. Psychotic symptoms and depressive symptoms were associated with different types of behavioral disturbances. Our findings support the contention that underlying depression or psychosis may partially account for different behavioral disturbances and that not all behavioral disturbances should be globally labeled “agitation.” Future studies should address symptom-specific treatment of behaviorally disturbed patients.

The behavioral disturbances that occur in approximately 80% of both community-based and nursing home patients with dementia (1–4) place these individuals and their caregivers at physical and psychological risk. Additionally, these behaviors are associated with high health care utilization and early institutionalization of the affected individuals (5–7). Because factors associated with behavioral disturbances are poorly understood, their treatments are often ill-conceived. Depression and psychosis are associated with behavioral disturbances in older adults suffering from dementia. A purpose of this study was to explore the relationship among depression, psychosis, and behavioral disturbance.

Two studies have reported that depression is associated with verbal agitation in nursing home and geropsychiatric inpatient populations (8,9), although another study found no association between depression and aggression when aggression was measured with a single 3-point scale question (10). Similarly, there is evidence to suggest that psychosis, which occurs in nearly 50% of patients with dementia (11–13), is also a contributor to behavioral disturbances. A recent study of 75 patients with Alzheimer’s disease reported that aggressive behavior was more frequent among those with hallucinations, but not among those with delusions (10). However, the investigation used only limited measures for physical aggression, verbal outbursts, and agitation. In a study of 33 outpatients with Alzheimer’s disease or multi-infarct dementia, the delusional patients were more aggressive, exhibited more severe activity disturbance, and had more cognitive impairment than nondelusional patients (13).

From our review of the existing literature (8,10,13–21) and our preliminary study (9), we hypothesized that behavioral disturbances in dementia are associated with specific factors such as psychosis or comorbid depression. In this study we examined the association of depression and psychosis with specific behavioral disturbances in geropsychiatric inpatients with dementia.

Method

We reviewed all admissions (using computerized medical records and the unit’s database) to the Houston VA Medical Center Geropsychiatry Unit between October 1993 and May 1995 to identify those with a diagnosis of dementia. Each patient admitted to the Geropsychiatry Unit receives a comprehensive evaluation by a multidisciplinary...
team including two geriatric psychiatrists, a geropsychologist, psychiatric nurses, a social worker, and a physician assistant. The diagnostic evaluation comprises a psychiatric history and mental status examination, a social history, a complete medical history and physical examination, blood chemistry panel, chest radiograph, electrocardiogram, electroencephalogram, magnetic resonance imaging or computed tomographic brain scan, and other tests as indicated by the patient’s history and physical examination.

On admission to the Geropsychiatry Unit, the severity of cognitive impairment and behavioral symptoms of patients are rated with the following well-validated standardized instruments: (a) the Mini-Mental State Examination [MMSE; (22)], which is a valid and reliable measure of cognitive impairment; (b) the Hamilton Depression Rating Scale [HDRS; (23)], which has been shown to be a valid measure of depression in cognitively impaired older adults (24); (c) the Thought Disorder subscale [BPRS-THOT; (25)] of the Brief Psychiatric Rating Scale (BPRS), which assesses psychosis (hallucinations, delusions, thought disorder, and grandiosity); and (d) the Cohen-Mansfield Agitation Inventory [CMAI; (26)], which includes subscales measuring physical aggression (CMAI-1), nonaggressive physical agitation (CMAI-2), and verbal agitation (CMAI-3). Interrater reliability as measured by intraclass correlation coefficients was greater than 0.9 for the MMSE and HDRS; 0.76 for the CMAI; and 0.60 for the BPRS. Axis I psychiatric diagnoses by DSM-III-R [and later DSM-IV; (27,28)] criteria were established within 2 weeks of discharge at a consensus conference attended by two geriatric psychiatrists, a geropsychologist, and other members of the research team. Diagnoses are established using the objective tests described, information from clinical observation, and information from clinical interviews of patient and caregiver. Those patients diagnosed with coexistent depression met DSM-IV criteria for depression after a diagnosis of dementia was established [DSM-IV codes 290.13, 290.21, 290.43, 293.83]. A diagnosis of coexistent psychosis was made if a diagnosis of dementia was met and hallucinations or delusions were present [DSM-IV codes 290.12, 290.20, 290.42, 293.82, 293.81]. Finally, the number of active medical diagnoses listed on Axis III was included as a measure of medical burden.

Correlations were computed to explore the associations of depressive and psychotic symptoms with behavioral disturbance symptoms. Correlations of individual CMAI items to the HDRS and BPRS-THOT scales were calculated to investigate the specific CMAI items associated with depressive and psychotic symptoms. A Bonferroni correction of \( p < .001 \) controlled for error due to multiple comparisons. Hierarchical regression models were constructed to explore the contribution of depressive and psychotic symptoms, and depression and psychotic diagnoses, to CMAI scores.

RESULTS

The final sample of 208 inpatients with dementia included 204 men and 4 women. The mean age was 72 years (SD = 6.35; range = 58–96 years), and mean MMSE score was 17.6 (SD = 7.78). Forty-nine percent of the sample were married, 16% were widowed, 28% were either divorced or separated, and 7% were never married. The majority of participants were Caucasian (70%) or African American (24%). Thirty-three patients (16%) had vascular dementia, 31 (15%) had Alzheimer's dementia, 10 (5%) had alcohol-induced persisting dementia, 42 (20%) had other dementias, and 92 (44%) had mixed dementias. Forty-nine patients (24%) had diagnoses of coexistent depression and dementia, and 36 (17%) had diagnoses of coexistent psychosis and dementia. Only a small number (6%) of patients had a diagnosis of dementia coexistent with both depression and psychosis.

Table 1 shows the means, standard deviations, and ranges for the measures in this study. Patients were mostly at the moderately demented level and had an average of four medical illnesses. The BPRS-THOT indicates low to moderate levels of psychotic symptomatology, and the CMAI mean indicates severe agitation at admission in the majority of the sample; the majority of participants scored in the non-depressed range of the HDRS.

Table 2 shows the correlations of the HDRS, BPRS-THOT, and MMSE with the CMAI subscales and total score. Both depression and psychotic symptoms were significantly positively correlated with each type of behavioral disturbance, except for the lack of association between

<table>
<thead>
<tr>
<th>Measure</th>
<th>Mean (Standard Deviation)</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>17.64 (7.78)</td>
<td>0–30</td>
</tr>
<tr>
<td>Medical Burden</td>
<td>4.35 (2.67)</td>
<td>0–16</td>
</tr>
<tr>
<td>BPRS-THOT</td>
<td>8.01 (4.25)</td>
<td>0–22</td>
</tr>
<tr>
<td>HDRS</td>
<td>14.03 (8.40)</td>
<td>0–36</td>
</tr>
<tr>
<td>CMAI1</td>
<td>47.64 (21.30)</td>
<td>0–176</td>
</tr>
<tr>
<td>CMAI2</td>
<td>12.49 (6.49)</td>
<td>0–57</td>
</tr>
<tr>
<td>CMAI3</td>
<td>15.45 (9.31)</td>
<td>0–44</td>
</tr>
<tr>
<td>CMAI3</td>
<td>9.24 (5.45)</td>
<td>0–29</td>
</tr>
</tbody>
</table>

Notes: MMSE = Mini-Mental State Exam; Medical Burden = Number of medical diagnoses coded on Axis III; BPRS-THOT = Brief Psychiatric Rating Scale Thought Disturbance subscale; HDRS = Hamilton Depression Rating Scale; CMAI1 = Cohen-Mansfield Agitation Inventory factor 1 subscale (physical aggression); CMAI2 = Cohen-Mansfield factor 2 subscale (nonaggressive physical agitation); CMAI3 = Cohen-Mansfield factor 3 subscale (verbal agitation).

Table 2. Association of Depressive and Psychotic Symptoms With Behavioral Disturbance

<table>
<thead>
<tr>
<th>Measure</th>
<th>CMAI1</th>
<th>CMAI2</th>
<th>CMAI3</th>
<th>CMAI3</th>
</tr>
</thead>
<tbody>
<tr>
<td>HDRS</td>
<td>.26*</td>
<td>.12</td>
<td>.29*</td>
<td>.28*</td>
</tr>
<tr>
<td>BPRS-THOT</td>
<td>.39*</td>
<td>.40*</td>
<td>.38*</td>
<td>.44*</td>
</tr>
<tr>
<td>MMSE</td>
<td>–.38*</td>
<td>–.58*</td>
<td>–.23*</td>
<td>–.49*</td>
</tr>
</tbody>
</table>

Notes: CMAI1 = Cohen-Mansfield Agitation Inventory factor 1 subscale (physical aggression); CMAI2 = Cohen-Mansfield factor 2 subscale (nonaggressive physical agitation); CMAI3 = Cohen-Mansfield factor 3 subscale (verbal agitation); HDRS = Hamilton Depression Rating Scale; BPRS-THOT = Brief Psychiatric Rating Scale Thought Disturbance subscale.

*p < .001.
HDRS and CMAI-2. MMSE was the largest univariate predictor and was significantly negatively correlated with the CMAI subscales and total score.

Correlations between the individual CMAI items and the HDRS and BPRS-THOT scores were also calculated to investigate the specific behavioral disturbance items associated with depression and psychosis. Psychotic symptoms were associated with aggressive behavioral symptoms, whereas depressive symptoms were associated with constant requests for help, complaining, and negativism (see Table 3).

In order to evaluate the contribution of depressive and psychotic symptoms and depression and psychotic diagnoses to behavioral disturbances while controlling for the possible effects of dementia severity and medication usage, hierarchical regression equations were calculated using the behavioral disturbance measures as the criterion variables. Separate equations were computed for each criterion variable: CMAI-1, CMAI-2, CMAI-3, and CMAI total score (CMSUM). Predictor variables were dementia severity, depression, and thought disorder symptoms, and depression and psychotic diagnoses. MMSE score was entered on the first step to control for the effects of dementia severity on behavioral disturbance. HDRS, BPRS-THOT, and depression and psychotic diagnoses (dummy coded following convention for use of categorical variables in linear regression) were entered together on the next step; the last step was an interaction between HDRS and BPRS-THOT.

Following convention for hierarchical regression analysis, if a step failed to contribute significant variance to the model, the step was then deleted from further analyses. Medication usage was nonsignificant, and therefore omitted from all models. In addition, the interaction variable was nonsignificant in all models and therefore omitted.

A power analysis for the regression analyses determined that with 208 subjects, five predictor variables, and a conservative $R^2$ estimation of 0.2, there was a 99% probability of rejecting the null hypothesis when the null hypothesis should be rejected (29).

All four regression equations were significant: CMSUM $[F(5,202) = 21.465, R^2 = .347, p < .001]$; CM1 $[F(5,202) = 13.013, R^2 = .244, p < .001]$; CM2 $[F(5,202) = 28.295, R^2 = .412, p < .001]$; CM3 $[F(5,202) = 10.708, R^2 = .210, p < .001$ (see Table 4). As expected, dementia severity was positively associated with behavioral disturbance and accounted for significant variance and significant incremental change in variance (5%–30%). Further, the addition of depression and thought disorder symptoms and depressive and psychotic diagnostic variables accounted for a significant amount of incremental change in variance (11%–18%) in all models. Examination of the standardized regression weights reveals that, with the exception of the model for CM2, the HDRS and BPRS-THOT scores accounted for the vast majority of the explained incremental variance in behavioral disturbance ($\beta = .21$ to .33), whereas depressive and psychotic diagnoses accounted for little of the variance ($\beta = .02$ to -.10). BPRS-THOT was the only independent variable with a large standardized regression weight in the CM2 model. The standardized regression weights describe a positive relationship between behavioral disturbance and increase in depression or psychosis symptoms, but show that having a diagnosis of depression or psychotic disturbance was associated with less behavioral disturbance—an unexpected direction of association.

**DISCUSSION**

This study found that depressive and psychotic symptoms were associated with the same general clusters of behavioral disturbance symptoms in dementia patients, but

| Table 3. Cohen-Mansfield Items Significantly Associated With Depression and Psychosis |
|----------------------------------|----------------|-----------------|
| CMAI Item                        | BPRS-THOT      | HDRS            |
| 1. Pacing and aimless wandering  | .29            | .23             |
| 2. Inappropriate robing or disrobing| .27            |                 |
| 4. Cursing or verbal aggression  | .32            |                 |
| 5. Constant unwarranted requests for attention or help |                |
| 7. Hitting                       | .35            |                 |
| 8. Kicking                       | .25            |                 |
| 9. Grabbing                      | .27            |                 |
| 10. Pushing                      | .36            |                 |
| 11. Throwing things              | .27            |                 |
| 12. Making strange noises        | .24            |                 |
| 13. Screaming                    | .23            |                 |
| 16. Trying to get to a different place| .26            |                 |
| 17. Intentional falling          |                |                 |
| 18. Complaining                  | .23            |                 |
| 19. Negativism                   | .31            | .24             |
| 21. Hurting self or other        | .45            |                 |

**Notes:** CMAI = Cohen-Mansfield Agitation Inventory; HDRS = Hamilton Depression Rating Scale; BPRS-THOT = Brief Psychiatric Rating Scale Thought Disturbance subscale. All correlations $p < .001$.

| Table 4. Regression of Depression and Psychosis on Behavioral Disturbance |
|----------------------------------|----------------|-----------------|
| CMAI Item                        | BPRS-THOT      | HDRS            |
| CMSUM                            | β   -329       | .208            |
| $R^2\Delta$                      | .165*         | .182*           |
| CMAI1                            | β   -247       | .211            |
| $R^2\Delta$                      | .097*         | .147*           |
| CMAI2                            | β   -470       | .075            |
| $R^2\Delta$                      | .301*         | .111*           |
| CMAI3                            | β   -154       | .196            |
| $R^2\Delta$                      | .047*         | .162*           |

**Notes:** MMSE = Mini Mental State Exam; HDRS = Hamilton Depression Rating Scale; BPRS-THOT = Brief Psychiatric Rating Scale Thought Disturbance subscale; DEP = Depression diagnosis; PSYC = Psychosis diagnosis; CMSUM = Cohen-Mansfield Agitation Inventory total score; CMAI1-CMAI3: Cohen-Mansfield Agitation Inventory subscales 1-3. *$p < .001; \dagger p < .005$. $R^2\Delta$ for Step 2 includes HDRS, BPRS-THOT, DEP, and PSYC.
that the individual behavioral items accounting for these associations differed. Psychosis and depression were each associated with the construct of agitation, but psychotic symptoms were associated with aggressive behavioral symptoms, whereas depressive symptoms were associated with constant requests for help, complaining, and negativism. These findings support the contention that underlying depression or psychosis may partially account for different behavioral disturbances, and that not all behavioral disturbances should be conceptually combined under the global rubric of “agitation.” We conclude that patients with dementia and aggressive symptoms warrant in-depth assessment for psychosis, and patients presenting with frequent requests for help and negativism warrant in-depth assessment for depression.

To our knowledge, this is the first study to examine the associations between both depressive and psychotic symptoms in geropsychiatric inpatients with dementia. In contrast to earlier studies reporting depression to be associated only with verbal agitation (8,9), we found that depressive symptoms were correlated with physical as well as verbal agitation. This may be a result of our larger sample size or our sample of mostly male geropsychiatric inpatients. Psychosis was moderately positively correlated with physical aggression, nonaggressive physical agitation, and verbal agitation. This result agrees with several studies that have reported psychosis to be associated with physical aggression (13,16), or with both physical and verbal aggression (30,31).

The literature contains conflicting reports of the association between dementia severity and behavioral disturbances. Several studies (8,17–21) reported a strong association between the two variables, whereas Aarsland and colleagues (10) did not find significant differences in behavioral disturbances between severity levels of dementia as measured by the Global Deterioration Scale. We found dementia severity to be moderately positively correlated with all types of behavioral disturbance, and regression analyses found dementia severity to account for a large amount of the variance in behavioral disturbance. These results suggest that future researchers should consider controlling for dementia severity in their analyses of other contributing factors to behavioral disturbance. Interestingly, the importance of dementia severity appears to vary with the type of behavioral disturbance. The MMSE accounted for 30% of the variance in physical nonaggressive agitation, 16% of the variance in physical aggression, and only 5% of the variance in verbal aggression. Perhaps this discrepancy between types of behavioral disturbance explains Aarsland and colleagues’ (10) nonsignificant finding, as their measure of aggressive behavior combines both verbal and physical aggression.

After controlling for the effect of dementia severity, depressive and psychotic symptoms and diagnoses together accounted for a modest amount of variance in all types of behavioral disturbances. Psychotic symptoms consistently accounted for relatively more variance than depressive symptoms; in particular, depressive symptoms contributed relatively little to the nonaggressive physical agitation score. As reflected in individual items, it may be that psychosis produces more active symptoms whereas depression is more likely to produce passive symptoms. Behavioral scales such as the CMAI place more emphasis on these active symptoms.

Surprisingly, psychosis and depression diagnoses were much less important than symptoms in accounting for all types of behavioral disturbances. Further, the association between the diagnoses and behavioral disturbances was in the direction of diagnoses being associated with less behavioral disturbance. This finding appears contradictory to the results concerning psychiatric symptoms, but may be an artifact of the DSM-IV diagnostic system used in the consensus conference. Delusions or hallucinations must be prominent and predominant in order to meet diagnostic criteria for dementia with delusions or dementia with a coexistent psychotic disorder; similarly, depressive symptoms must be severe enough to meet the criteria for a major depressive episode, and be predominant, in order to meet diagnostic criteria for dementia with depression. In contrast, the continuous nature of the depressive and psychotic symptom rating scales allows for the detection of a positive association between behavioral disturbances and depressive and psychotic symptoms that are not severe enough to meet criteria for depression and psychosis diagnoses. Thus, the results may reflect an association between behavioral disturbances and psychosis and depression, but at lower levels of severity than warrant a DSM-IV diagnosis of psychosis or depression.

This study had several limitations that must be acknowledged. First, the generalizability of this study is probably limited. The sample consisted only of inpatient veterans, the majority of whom were male. In addition, the relative prevalences of dementia subtypes differ from those reported for the general population. This is probably due to the higher prevalences of alcohol abuse, strokes, and heart disease in our population. In addition, this may be due to the investigators’ policy of systematically including more than one DSM-IV dementia diagnosis if there was substantial evidence to support multiple presumed etiologies. Secondly, this study utilized a mixed sample of dementia diagnoses; however, there is no consensus in the literature about the importance of pure dementia samples. Too few patients in these pure subgroups prevented separate analyses. Finally, although our measure of psychotic symptoms is reliable and valid, more comprehensive scales exist (32). Although our models accounted for significant amounts of variance, even our best model failed to account for 59% of the variance in behavioral disturbances. The limitations of this study may have contributed to the amount of variance unexplained. It may also be that specific cognitive deficits, such as severity of frontal lobe deficits, may be modulating the association between behavioral disturbances and depression and psychosis. Thus, future studies should sample both men and women, examine different types of dementias, examine specific cognitive deficits, and utilize more in-depth scales for the assessment of psychiatric symptoms.

The results of this study underscore the importance of careful screening for depressive and psychotic symptoms in patients with dementia and behavioral disturbances. Attention to specific psychiatric symptoms may have important
treatment implications. In the absence of any gold standard for treating behavioral disturbances in patients with dementia, this study adds credence to treating patients with depressive symptoms with antidepressants and those with psychotic symptoms with antipsychotics. Future studies should address the effect of treating behaviorally disturbed dementia patients experiencing depressive symptoms with antidepressant agents and those experiencing thought disorder symptoms with antipsychotic agents.

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REFERENCES