Published in final edited form as:

Int J Geriatr Psychiatry. 2010 June ; 25(6): 569–577. doi:10.1002/gps.2376.

Cognitive and daily functioning in older adults with vegetative symptoms of depression

Sergio Paradiso¹, Kevin Duff¹, Jatin G. Vaidya¹, Angela Hoth², and James W. Mold³

¹Department of Psychiatry, University of Iowa Carver College of Medicine, Iowa City, IA, USA

²Veterans Administration Medical Center, Iowa City, IA, USA

³Department of Preventive and Family Medicine, University of Oklahoma Health Sciences Center, Oklahoma City, OK, USA

Abstract

Objectives—In primary care 50–95% of patients with depression present with vegetative symptoms (VS). Based on the extant literature, older adults showing VS (but no dysphoria) may show functional impairment but this hypothesis has not been empirically tested. The goal of this study was to examine neurocognitive and daily functioning of elderly patients showing exclusively VS in comparison with patients presenting with VS and dysphoria.

Methods—Seven hundred and eighty-seven primary care patients received measures of neurocognition and daily functioning. Neurocognition was measured with the repeatable battery for the assessment of neuropsychological status (RBANS). Three groups were compared: (1) patients with two or more VS of depression without dysphoria (VS – D), (2) patients with at least one VS and dysphoria (VS + D), and (3) comparison patients without multiple VS or dysphoria.

Results—Nearly one third of the sample (31%) fell into the VS – D group, whereas 15% fell into the VS + D group. Both VS groups showed poorer neurocognition and activities of daily living than comparisons. Only one subtest of the RBANS (i.e., picture naming) showed a significant difference between VS + D and VS – D, and there was no significant difference on daily functioning. VS – D patients reported less frequent past history of depression and endorsed less anxiety compared to VS + D.

Conclusions—Elderly patients presenting with clusters of VS with or without dysphoria show poorer neurocognitive and functional performance. Relative poorer cognition and daily functioning in VS – D are potential harbingers of further decline and consistent with under-reporting of sadness in older age.

Keywords

vegetative symptoms; primary care; late-life depression; nondysphoric depression; neurocognition; right hemisphere functions; subthreshold depression

Conflict of interest

The authors have no conflicts of interest in this research.

Introduction

Clinical depression is nearly always associated with vegetative symptoms (VS) (American Psychiatric Association, 2000). These include fatigue, change in sleep, appetite and weight, disordered salivation and transpiration, cardiac arrhythmias and dyspnea, change in body temperature, altered sexual functions, and others (Kapfhammer, 2006). For almost a century, psychiatrists have known that some depressive conditions are predominantly characterized by VS and less so by affective disturbances (e.g., anhedonia, sad mood) (Kraepelin, 1921; Paskind, 1930; Keilholz, 1973; Klerman *et al.*, 1987; Judd *et al.*, 1994; Mossey *et al.*, 1996; Gallo *et al.*, 1997). A clinical picture with predominant VS is common in both inpatient and outpatient settings (Jones and Hall, 1963; Hamilton, 1989). The clinical importance of VS is also highlighted by the increased risk of suicide associated with them (Hagnell and Rorsman, 1978).

Between 50 and 95% of patients with depression present with VS to primary care providers (Schurman *et al.*, 1985; Simon *et al.*, 1999). Up to 11% of patients diagnosed with depression using structured interviews deny psychological symptoms upon direct questioning (Simon *et al.*, 1999). Many of these patients are elders (Unutzer *et al.*, 1999) who are notoriously at risk of underreporting sadness or loss of interest (Gallo *et al.*, 1997). Therefore, fatigue and other VS may be indication that an elderly person suffers from a depressive disorder (Gallo and Coyne, 2000).

Recent reviews have meritoriously remarked on the necessity to give appropriate weight to somatic symptoms when examining patients in primary care (Arnold, 2005; Kapfhammer, 2006). Nonetheless some older adults are not diagnosed with depression according to existing diagnostic criteria (American Psychiatric Association, 2000) because of their limited endorsement of emotional symptoms (Gallo *et al.*, 1997; Gallo *et al.*, 1999; Charney *et al.*, 2003). If these depressive conditions are not recognized, they are likely to go untreated leading to prolonged suffering for the patients and their families and other adverse outcomes (e.g., diminished vocational efficiency, comorbid medical conditions, and suicide).

Empirical research on the functional outcome of elderly individuals presenting *exclusively* with neurovegetative complaints is essentially absent (Kapfhammer, 2006). When examining older persons with typical depression, poorer cognitive performance is expected (Austin *et al.*, 1992; Paradiso *et al.*, 1997). However, it is currently not known whether individuals presenting exclusively with VS of depression show associated cognitive deficits. Perhaps more importantly, it is not known whether VS alone are associated with functional reduction in daily activities. This study aims at filling this gap by examining cognitive and daily functioning in older adults who presented for routine primary care visits with VS with or without dysphoria (VS + D and VS – D, respectively). The literature describing depressive conditions with insufficient number of symptoms or illness duration (i.e., 'subthreshold') to meet existing criteria for mood disorder (American Psychiatric Association, 2000) can help in the generation of the hypotheses for this study because up to 2/3 of individuals with subthreshold depression show limited capacity to endorse sad mood or anhedonia (Judd *et al.*, 1994) and therefore may present *predominantly* with VS. This body of research has shown that subthreshold conditions are prevalent (Broadhead *et al.*, 1990; Judd *et al.*, 1994; Gallo *et al.*, 1997; Penninx *et al.*, 1998) and confer significant risk for diminished daily functioning and cognitive competence leading to increased disability, poverty, and mortality (Gallo *et al.*, 1997; Penninx *et al.*, 1998; Chuan *et al.*, 2008). In this study, examining a large sample of community dwelling older adults who received a comprehensive cognitive assessment during routine medical visits allowed estimating the

prevalence of individuals with VS + D and VS – D in primary care, and test the hypothesis that VS – D is associated with functional impairment and cognitive dysfunction.

Methods

Study sample

The data used in the present study have been collected in the Oklahoma longitudinal assessment of health outcomes in mature adults (OKLAHOMA) study (Duff *et al.*, 2003). For comprehensive description of recruitment procedures and methods please refer to earlier publications (Duff *et al.*, 2003). Briefly, community-dwelling individuals 65 years or older who had a visit in the past 18 months with a primary care/ family practice physician were examined for health outcomes. Invitation letters were mailed to 2553 individuals; 1836 participants expressed an interest in participating and were contacted. Of these, 810 agreed to take part in the study. Eleven individuals were excluded for inability to give informed consent and 12 for they did not complete all key assessment procedures. The final sample was constituted by 787 individuals who received a packet of *ad hoc* questionnaires assessing demographic information, habits, medical conditions, physical and mental health symptoms, functional status (i.e., activities of daily living), and measures of health related quality of life. At the enrollment visit, participants were interviewed by a research nurse who obtained informed consent and reviewed the questionnaires for completeness and accuracy.

Assessment of psychiatric symptoms

Information on DSM-IV (American Psychiatric Association, 2000) criteria for major depressive episode (i.e., depressed mood, anhedonia, difficulty sleeping, weight and appetite changes, reduced energy, and subjective memory and concentration problems) was obtained from the responses on the questionnaires. A board certified psychiatrist (SP) and a licensed neuropsychologist (KD) scored all symptom categories as present or absent. Summation of depressive symptoms yielded an overall depression severity score. Anxiety was measured as excessive worry in the past 3 days and was also dichotomized (present/absent).

Assessment of cognition

Form A of the repeatable battery for the assessment of neuropsychological status (RBANS) (Randolph, 1998) was administered by a trained research nurse. The RBANS is an individually administered comprehensive neuropsychological battery consisting of 12 cognitive tasks that tap attention (including digit span, coding tasks), language (including semantic fluency, picture naming tasks), visual/spatial and constructional skills (including figure copy, line orientation tasks), and learning and memory (including list learning, list recall, list recognition, story memory, and story and figure recall tasks). The RBANS yields a total scale score ($M = 100$, $SD = 15$) reflecting overall neuropsychological status. RBANS total score and individual subtests were examined. As expected, some tasks require the engagement of common cognitive domains (e.g., attention for coding and list learning tasks). For this reason, factor analytically derived factors (Duff *et al.*, 2006) were also used in the analyses.

Assessment of other clinically relevant variables

Several other clinically relevant variables were measured. Medical burden was the summation of 48 medical conditions that participants rated as present or absent. Global functional status was attained from the summation of responses to an *ad hoc* questionnaire encompassing 14 activities of daily living (e.g., dress self, use telephone, handle money) rated by the participant as intact or needing some or total assistance. Assessment of alcohol

abuse was obtained by items from the CAGE scale (Ewing, 1984). These items were summed and then also dichotomized (absent = 0, present > 0).

Group composition

Subjects endorsing any two or more VS in the absence of sad mood or anhedonia [referred together as ‘‘dysphoria’’ (Gallo *et al.*, 1997) throughout this paper] were included in the VS – D group. Subjects with any two or more depressive symptoms, with at least one of the symptoms being sad mood and/or anhedonia and one being a VS, were included in the VS + D group. A threshold of two or more VS to classify subjects in the ‘vegetative symptoms without dysphoria’ group was chosen because multiple complaints appear to have greater predictive value for depression (Gerber *et al.*, 1989). The dysphoric comparison subjects (VS + D) were selected based on presence of sad mood or anhedonia and at least one VS so that this group would be comprised of subjects with two or more symptoms as in the VS – D group. This report focuses on VS described in the DSM-IV as criteria for diagnosing a depressive episode (e.g., fatigue, sleep disturbances, change in appetite/weight, and poor concentration) (American Psychiatric Association, 2000) because these VS appear to have the greater positive predictive value for underlying depression (Gerber *et al.*, 1989) (e.g., 61% for sleep disturbance, 60% for fatigue). Subjects with one or fewer symptoms constituted the non-VS comparisons.

Statistical analysis

For descriptive purposes, VS – D, VS + D, and comparison subjects were compared on demographic and clinical variables, and individual symptoms. Hypothesis testing was carried out on activities of daily living and cognitive functioning variables. Group effects on RBANS total score and individual subtests were computed controlling for age and education because of these variables’ potential independent effect on neurocognition. Group effects on individual RBANS subtests’ raw scores were preceded by an omnibus test (MANCOVA). Least-square differences (LSD) were used as *post hoc* tests. In addition, the three groups were compared on factor analytically derived RBANS verbal and visual spatial processing indices (Duff *et al.*, 2006, see below for details) using a MANCOVA (correcting for age and education). RBANS total score was also used in a regression model using sad mood and VS as independent predictors. Nominal data were analyzed with χ^2 tests.

Results

Prevalence, demographic, and clinical variables

Demographic and clinical information is provided in Table 1. Thirty-one per cent ($N=247$) of patients were classified as VS – D and 15% ($N=123$) as VS + D. Subjects with zero or one symptom (54%, $N=417$) constituted the comparison group. There was no significant group effect of age [$F(2, 784) = 1.1, p > 0.3$]. A significant effect of sex was found ($\chi^2(2) = 14.2, p = 0.001$). Women were more represented in both VS groups compared to comparisons [VS – D $\chi^2(1) = 9.3, p = 0.002$; VS + D $\chi^2(1) = 8.9, p = 0.003$], but VS groups showed similar sex composition [$\chi^2(1) = 3, p > 0.5$]. Education (dichotomized as ≤ 12 years vs. > 12 years) also showed a significant group effect [$\chi^2(2) = 10.6, p = 0.005$]. *Post hoc* tests showed that VS + D subjects were significantly less educated than comparisons [$\chi^2(1) = 9.9, p = 0.002$]. VS – D however did not significantly differ from VS + D or from comparison subjects (both $ps > 0.05$). The majority of the sample ($n = 694$ or 88.2%) was Caucasian, 69 (8.8%) persons were African American, 16 (2%) were Native American, 7 (0.9%) were Hispanic/Latino, and 1 person was Asian/Pacific Islander. Two different sets of analyses were carried out to examine the association between race and depression diagnosis. The first analysis included the two most represented racial groups (Caucasian and African-American). The two groups did not differ in depression diagnosis [$\chi^2(2) = 1.60, p = 0.45$].

In the next analysis, all groups were included (except for the one person who reported being Asian/Pacific Islander). The difference was not statistically significant [$F(2, 6) = 4.61, p = 0.60$].

Medical burden showed a significant group effect [$F(2, 784) = 45.1, p < 0.001$]. VS + D and VS - D showed greater medical comorbidity compared to non-cases (respectively $LSD = -1.82$ and $-1.47, p < 0.001$), but no difference between them ($LSD = .35, p > 0.1$). There was no significant group effect on severity of alcohol abuse [$F(2, 769) = .74, p > 0.4$]. Alcohol abuse was also analyzed as a dichotomous variable (median split: no symptom *vs.* any symptom). There were 36 patients (8.7%) among non-cases, 20 (8.3%) among VS - D, and 6 (5%) among VS + D patients with at least one CAGE symptom [$F(2, 2) = 1.8, p > 0.4$].

Psychiatric variables

An expected effect of depression severity ($F(2, 784) = 1174.7, p < 0.001$) was found, with both VS groups showing higher scores relative to comparisons (respectively VS + D $LSD = -2.6$, VS - D $LSD = -1.7, p < 0.001$). Compared to the VS - D group, VS + D subjects had greater symptom severity scores (with a mean difference of 0.9 points out of a possible total score of 5) ($LSD = -0.87, p < 0.001$). Consistent with the inclusion criteria, significant group effects were found for sad mood [$F(2, 2) = 717.5, p < 0.001$], sleep problems [$F(2, 2) = 167.4, p < 0.001$], fatigue [$F(2, 2) = 279.5, p < 0.001$], appetite and weight [$F(2, 2) = 227.8, p < 0.001$], memory and concentration problems [$F(2, 2) = 99.6, p < 0.001$] (Table 2). Compared to the VS + D group, VS - D subjects showed greater changes in appetite and weight [$F(2, 1) = 4.9, p = 0.027$], but no differences in sleep [$F(2, 1) = 1.6, p > 0.6$], or fatigue [$F(2, 1) = 1.3, p > 0.2$] or memory and concentration problems [$F(2, 1) = 1.1, p > 0.2$] (Table 2). There were 29 (11.7%) VS - D and 73 (59.3%) VS + D patients reporting anxiety (compared to 29 (7%) among non-cases) [$F(2, 2) = 194, p < 0.001$]. The difference was significant for the VS - D *versus* non-cases comparison [$F(2, 1) = 4.4, p < 0.04$], for the VS - D *versus* VS + D comparison [$F(2, 1) = 93, p < 0.001$] and for the VS + D *versus* non cases comparison as well [$F(2, 1) = 170, p < 0.001$].

History of depression showed a significant group effect [$F(2, 2) = 102.2, p < 0.001$] (Table 1). There were 15% of patients who had suffered depression in the past in the VS - D group but 44.7% in the VS + D group [$F(2, 1) = 38.8, p < 0.001$]. Approximately three times as many subjects with VS (-D and + D) compared to comparisons were treated with anti-depressants [$F(2, 2) = 16.7, p < 0.0001$] (Table 1). There were no differences in treatment between the two VS groups [$F(2, 1) = 0.04, p > 0.08$]. Close to 90% of all patients with VS did not receive or refused antidepressant treatment (Table 1).

Daily living and cognitive functioning

A significant group effect on activities of daily living was found [$F(2, 784) = 22.5, p < 0.001$] (Table 1). VS - D and VS + D showed significantly worse functioning compared to non-cases (respectively $LSD = -0.88$ and $-0.96, p < 0.001$). There was no significant difference between VS - D and VS + D ($LSD = -0.08, p > 0.6$). Analyses on the RBANS total score controlling for age and education showed a significant effect of group [$F(2, 782) = 6.91, p = 0.001$] with VS - D ($LSD = 3.3, p = 0.007$) and VS + D ($LSD = 5.0, p = 0.001$) performing significantly more poorly than the comparison subjects but being not different from each other ($LSD = 1.7, p = 0.30$) (Table 3). The omnibus test on the RBANS subtests controlling for age and education revealed a significant group effect [$F(24, 1542) = 2.16, p = 0.001$]. Significant between-subjects effects were found for list learning [$F(2, 787) = 3.52, p = 0.03$]; line orientation [$F(2, 787) = 6.02, p = 0.003$]; picture naming [$F(2, 787) = 6.27, p = 0.002$]; coding [$F(2, 787) = 11.56, p < 0.001$], figure recall [$F(2, 787) = 3.04, p = 0.048$]. All other RBANS subtests did not show significant group effects. *Post hoc* analyses revealed

that VS + D (LSD = 1.2, $p = 0.034$) and VS – D (LSD = 0.97, $p = 0.032$) performed more poorly on list learning compared to non-VS comparisons, but there was no significant difference between VS + D and VS – D (LSD = 0.26, $p = 0.6$). Line orientation showed a significant effect for VS + D *versus* comparison subjects (LSD = 1.2, $p = 0.001$). No other difference in line orientation was found to be significant (LSD < 0.73, $p > 0.06$). VS + D showed poorer picture naming scores compared to VS – D (LSD = 0.26, $p = 0.004$) and comparison subjects (LSD = 0.29, $p < 0.001$). VS – D and comparison subjects showed no significant difference in picture naming (LSD = 0.03, $p > 0.6$). Both VS + D (LSD = 3.8, $p < 0.001$) and VS – D (LSD = 2.9, $p < 0.001$) showed significantly poorer coding scores compared to non-VS comparisons. There was no statistically significant difference between the two VS groups (LSD = 0.8, $p > 0.4$). Performance on figure recall was significantly poorer in the VS + D group compared to non-VS comparisons (LSD = 1.0, $p < 0.02$) but no other group difference on this test was found to be statistically significant (LSD < 0.6, $p > 0.1$).

In summary, the VS+D group showed poorer performance on list learning, line orientation, picture naming, coding, and figure recall compared to non-VS comparisons. VS – D patients showed poorer performance on list learning and coding compared to non-VS comparisons. The only significant group effect between VS + D and VS – D was on picture naming.

The individual subtests suggested that performance on visual/spatial processing subtests was poorer in both VS + D and VS – D. To formally test this hypothesis, groups were compared on factor analytically derived verbal memory (including list learning, story memory, list recall, list recognition, and story recall) and visual/ spatial processing indices (figure copy, line orientation, coding, figure recall) (Duff *et al.*, 2006). A MANCOVA model (correcting for age and education) showed a significant overall group effect [$F(4, 1564) = 5.0$, $p < 0.001$]. Comparison on the verbal memory index showed no significant group effect [$F(2, 782) = 1.2$, $p > 0.2$]. A significant group effect on the visual/ spatial processing index [$F(2, 782) = 10$, $p < 0.001$] was found. *Post hoc* tests showed that VS + D (LSD = 5.8, $p < 0.001$) and VS – D (LSD = 3.4, $p = 0.002$) were both significantly poorer than comparisons in the visual/spatial processing domain. No difference was found between VS + D and VS – D (LSD = 2.3, $p > 0.1$). Analyses correcting exclusively for education yielded essentially the same results.

Based on the well-established notion that depressed mood carries risk for cognitive decline, two regression analyses were conducted to determine the relative impact of VS and sad mood on cognitive performance. In one model predicting RBANS total score, sad mood was entered first and VS second. The R value for sad mood was 0.11 [$R^2 = .012$, $F(1, 785) = 10.3$, $p = 0.001$], while the R value increased to 0.30 after adding VS [$R^2 = .09$, F change (4, 781) = 16.3, $p < 0.001$]. In the second model VS were entered first and the R value for VS was 0.29 [$R^2 = 0.084$, $F(4, 782) = 18$, $p < 0.001$], while adding sad mood only improved the R value to 0.30 [$R^2 = 0.09$, F change (1, 781) = 3.9, $p = 0.048$].

Discussion

This study examined daily functioning and cognitive abilities in elderly primary care patients with VS of depression with and without dysphoria. Several findings in this study add to our understanding of psychiatric symptoms in the elderly and to primary care geriatric medicine. Consistent with the subthreshold depression literature (Broadhead *et al.*, 1990; Judd *et al.*, 1994; Gallo *et al.*, 1997; Penninx *et al.*, 1998; Lyness *et al.*, 2006), VS – D and VS + D subjects showed poorer global functional abilities than comparison subjects. Irrespective of the concurrent presence of dysphoria, patients with VS showed mild but significantly poorer global cognitive function than non-VS comparisons. In agreement with

the literature (Marvel and Paradiso, 2004; Butters *et al.*, 2006), sad mood increased the risk for cognitive decline. Individuals endorsing exclusively VS also showed poorer cognitive function.

Before discussing the results in this study some caveats need to be acknowledged. Results concerning past depression in this sample should be interpreted cautiously. Subjects answered one question about prior diagnosis which could be influenced by recollection. In addition, it is not known whether the past diagnosis was given by a clinician who used clinical judgment despite absence of the patient's endorsement of sad mood or anhedonia. In addition, not all DSM symptoms (e.g., guilt) were collected to identify a major depressive episode (American Psychiatric Association, 2000). The time frame of symptom duration ranged from 3 days to 1 month raising the possibility that some symptoms were shorter in duration than required in the existing diagnostic guidelines (American Psychiatric Association, 2000). While the RBANS is a comprehensive set of neuropsychological tests allowing domain specific measurement of neurocognition, it does not measure executive functioning, which might also be an important cognitive ability in geriatric depression (Lockwood *et al.*, 2002). In addition, functional activity was assessed with a self-report questionnaire. A negative bias may have influenced reporting of functional status in persons with dysphoria. Lastly, medications other than antidepressants were not reported. Medication adherence in the elderly is a significant problem. Medications are often taken in defect or excess from what was prescribed. Because of this generally poor compliance, ascertaining what medications (e.g., benzodiazepines, antihistaminics, and others) with potential of altering cognitive function, activities of daily living, or vegetative functions were indeed taken is challenging. The large sample size of the present study may help minimize these effects. Nonetheless, future studies should attempt to include this information.

Prevalence of vegetative symptoms

VS are frequent in older subjects presenting to primary care. During a routine visit, 31% of patients showed at least two VSs, while 15% complained of dysphoria and at least one accompanying VS. Only about 10% in each VS group received antidepressant treatment, signifying that presence of dysphoria did not change the frequency treatment was offered and/or followed by patients. Prevalence rates for VS in elderly primary care patients in our study were higher than rates of subthreshold depression (Judd *et al.*, 1994; Gallo *et al.*, 1997). For instance, Judd *et al.* (1994) reported 1-year prevalence rates of 11.8% in a community-dwelling sample of 9160. A recent study carried out in Germany showed a prevalence of 15.3% (Backenstrass *et al.*, 2006). Recruitment settings (primary care *vs.* community dwelling) and the older age in our sample may explain these differences. In addition, recruitment in the present study was not structured to be random. To promote compliance with the longitudinal component of the study (data not presented here) the requirement of a visit within the prior 18 months was adopted and this may have skewed the sample. Among patients who met this requirement some agreed to participate and others did not. The present study cannot determine to what extent persons who did not participate in the study differed from those who did.

Demographic and clinical variables

A recurrent theme in the findings of the present study is that older persons complaining of VS behave clinically quite similarly whether endorsing dysphoric mood or not. Female sex, greater medical comorbidity, and poorer daily functioning distinguished both VS groups from comparison subjects but not from each other. VS – D and VS + D patients did not differ in the global severity of their medical condition. In addition, sad mood excluded, the percentage of different depressive symptoms was similar across both VS groups and greater

than comparison subjects (Table 2). These similarities are consistent with the clinical lore that VS represent an extremely common presentation of depression in the elderly (Charney *et al.*, 2003). A possible mechanism for the presentation of isolated VS is individual differences in emotional awareness which has multiple determinants including education. It is therefore notable and consistent with prior studies (Kirmayer and Robbins, 1993) that VS + D patients were most educated among the three groups (albeit only the analysis against non-VS comparisons achieved statistical significance). More difficult is to explain why prior history of depression distinguished patients with VS with and without dysphoria. In fact, while 15% of patients with VS – D recalled having a prior diagnosis of depression, about half of the patients with VS + D had a positive history of depression. There are several possible explanations for these findings. First, VS – D represent a form of depression in a minority of cases (but compare with many similarities between VS – D and VS + D); second, differences in past depression diagnosis are related to poor recollection (but note the little objective memory differences between VS groups); third, current depression biased the recollection of past episodes of depression or dysphoria; or forth, these findings are the result of generally limited endorsement of sadness or anhedonia (Gallo *et al.*, 1999; Paradiso *et al.*, 2008a,b). The tendency of VS – D patients to report lower current anxiety relative to VS + D patients is consistent with the notion that elderly primary care patients with VS report low rates of psychological and emotional symptoms (Simon *et al.*, 1999).

Whereas the VS symptoms studied in the present manuscript are only those required for diagnosing major depressive episode (American Psychiatric Association, 2000), this research cannot definitively ascertain the nature of VS symptoms and their syndromic (or pathogenetic) association with the domain of dysphoria. The association VS – D and VS + D with medical burden does not help resolving this issue because depression is often associated with high rates of medical illnesses (Brown *et al.*, 2004).

Cognitive variables

Depression is among several factors affecting cognition in older age (Marvel and Paradiso, 2004). Cognitive impairment may be directly caused by sad mood (Paradiso *et al.*, 2001; Marvel and Paradiso, 2004) and/ or by the neurobiological consequences of the depressive illness (Paradiso *et al.*, 1997; Butters *et al.*, 2006). While showing on the one hand that depressed mood is a significant predictor for poorer neurocognition, this study confirmed that VS represent additional burden on the integrity of cognitive processes in later life. These findings are consistent with studies suggesting that subthreshold depression including both psychological and VS is a risk factor for cognitive impairment (Gallo *et al.*, 1997; Chuan *et al.*, 2008). Individual cognitive subtests analysis highlighted more similarities than differences between patients with VS – D and VS + D. In fact, while patients presenting with VS + D showed poorer cognitive performance in more subtests (5/12) than VS – D (2/12), there was only one significant difference between VS – D and VS + D subjects (i.e., picture naming). Performance on visual/spatial processing was poorer in both VS groups than comparisons supporting the notion that depressive conditions with *prevalent* VS affect neuropsychological competence subserved by right hemisphere functioning (Palmer *et al.*, 1996).

Treatment

Over 45% of our sample showed at least two depressive symptoms, but only about 20% of these were treated (and the present study cannot determine the extent to which these patients benefited from treatment). These rates were lower than those reported in studies of subsyndromal depression using enhanced treatment instructions (e.g., Lyness *et al.*, 2006 reported 28.9% treatment prevalence), but are unfortunately consistent with those of naturalistic primary care studies showing only 10–20% of depressed older adults being

treated (Gallo *et al.*, 1997; Unutzer *et al.*, 2000; Chuan *et al.*, 2008). While research has shown proactive treatment for depression in late-life to be effective (Hunkeler *et al.*, 2006), a remaining challenge for primary care clinicians will be the identification of older depressed persons not reporting sadness or loss of interest.

In summary, VS with or without dysphoria are frequent but undertreated, occur more frequently in women with less education and greater medical comorbidity and are associated with poorer than expected functional and cognitive performance. VS – D patients show less frequent past history of depression and current anxiety but poorer cognitive performance only on a single cognitive subtest compared to VS + D. Clusters of VS in the elderly may be associated with disability warranting in depth psychiatric evaluation and treatment.

Acknowledgments

This work was supported by the Edward J. Mallinckrodt Jr Foundation and by NIH/NIA grant 5K23AG027837 (Dr Paradiso), a National Alliance for Research in Schizophrenia and Affective Disorders Young Investigator's Award (Dr Duff), and a grant from the Presbyterian Health Foundation (Dr Mold).

References

- American Psychiatric Association. American Psychiatric Association: Diagnostic criteria from DSM-IV-TR. Washington, DC: American Psychiatric Press; 2000.
- Arnold LM. The nature of painful and somatic complaints in depressive disorders. *CNS Spectr.* 2005; 10:4–5. [PubMed: 18841596]
- Austin MP, Ross M, Murray C, et al. Cognitive function in major depression. *J Affect Disord.* 1992; 25:21–29. [PubMed: 1624644]
- Backenstrass M, Joest K, Frank A, et al. Preferences for treatment in primary care: a comparison of nondepressive, subsyndromal and major depressive patients. *Gen Hosp Psychiatry.* 2006; 28:178–180. [PubMed: 16516070]
- Broadhead WE, Blazer DG, George LK, Tse CK. Depression, disability days, and days lost from work in a prospective epidemiologic survey. *JAMA.* 1990; 264:2524–2528. [PubMed: 2146410]
- Brown ES, Varghese FP, McEwen BS. Association of depression with medical illness: does cortisol play a role? *Biol Psychiatry.* 2004; 55:1–9. [PubMed: 14706419]
- Butters M, Catterick D, Craig A, et al. Critical assessment of pharmaceutical processes-a rationale for changing the synthetic route. *Chem Rev.* 2006; 106:3002–3027. [PubMed: 16836307]
- Charney DS, Reynolds CF3RD, Lewis L, et al. Depression and bipolar support alliance consensus statement on the unmet needs in diagnosis and treatment of mood disorders in late life. *Arch Gen Psychiatry.* 2003; 60:664–672. [PubMed: 12860770]
- Chuan SK, Kumar R, Matthew N, Heok KE, Pin NT. Subsyndromal depression in old age: clinical significance and impact in a multi-ethnic community sample of elderly Singaporeans. *Int Psychogeriatr.* 2008; 20:188–200. [PubMed: 17888199]
- Duff K, Langbehn DR, Schoenberg MR, et al. Examining the repeatable battery for the assessment of neuropsychological status: factor analytic studies in an elderly sample. *Am J Geriatr Psychiatry.* 2006; 14:976–979. [PubMed: 17068320]
- Duff K, Patton D, Schoenberg MR, et al. Age- and education-corrected independent normative data for the RBANS in a community dwelling elderly sample. *Clin Neuropsychol.* 2003; 17:351–366. [PubMed: 14704885]
- Ewing JA. Detecting alcoholism. The CAGE questionnaire. *JAMA.* 1984; 252:1905–1907. [PubMed: 6471323]
- Gallo JJ, Coyne JC. The challenge of depression in late life: bridging science and service in primary care. *JAMA.* 2000; 284:1570–1572. [PubMed: 11000654]
- Gallo JJ, Rabins PV, Anthony JC. Sadness in older persons: 13-year follow-up of a community sample in Baltimore, Maryland. *Psychol Med.* 1999; 29:341–350. [PubMed: 10218925]

- Gallo JJ, Rabins PV, Lyketsos CG, Tien AY, Anthony JC. Depression without sadness: functional outcomes of nondysphoric depression in later life. *J Am Geriatr Soc.* 1997; 45:570–578. [PubMed: 9158577]
- Gerber PD, Barrett J, Manheimer E, Whiting R, Smith R. Recognition of depression by internists in primary care: a comparison of internist and “gold standard” psychiatric assessments. *J Gen Intern Med.* 1989; 4:7–13. [PubMed: 2915277]
- Hagnell O, Rorsman B. Suicide and endogenous depression with somatic symptoms in the Lundby study. *Neuropsychobiology.* 1978; 4:180–187. [PubMed: 622217]
- Hamilton M. Frequency of symptoms in melancholia (depressive illness). *Br J Psychiatry.* 1989; 154:201–206. [PubMed: 2775946]
- Hunkeler EM, Katon W, Tang L, et al. Long term outcomes from the IMPACT randomised trial for depressed elderly patients in primary care. *BMJ.* 2006; 332:259–263. [PubMed: 16428253]
- Jones D, Hall SB. Significance of somatic complaints in patients suffering from psychotic depression. *Acta Psychother Psychosom.* 1963; 11:193–199. [PubMed: 14061248]
- Judd LL, Rapaport MH, Paulus MP, Brown JL. Subsyndromal symptomatic depression: a new mood disorder? *J Clin Psychiatry.* 1994; 55(Suppl):18–28. [PubMed: 8077164]
- Kapfhammer HP. Somatic symptoms in depression. *Dialogues Clin Neurosci.* 2006; 8:227–239. [PubMed: 16889108]
- Keilholz, P. *Masked Depression.* Hans Huber: Bern; 1973.
- Kirmayer LJ, Robbins JM. Cognitive and social correlates of the Toronto alexithymia scale. *Psychosomatics.* 1993; 34:41–52. [PubMed: 8426890]
- Klerman GL, Budman S, Berwick D, et al. Efficacy of a brief psychosocial intervention for symptoms of stress and distress among patients in primary care. *Med Care.* 1987; 25:1078–1088. [PubMed: 3695638]
- Kraepelin, E. *Manic-depressive insanity and paranoia.* Edinburgh, UK: Livingstone; 1921.
- Lockwood KA, Alexopoulos GS, Van Gorp WG. Executive dysfunction in geriatric depression. *Am J Psychiatry.* 2002; 159:1119–1126. [PubMed: 12091189]
- Lyness JM, Heo M, Datto CJ, et al. Outcomes of minor and subsyndromal depression among elderly patients in primary care settings. *Ann Intern Med.* 2006; 144:496–504. [PubMed: 16585663]
- Marvel CL, Paradiso S. Cognitive and neurological impairment in mood disorders. *Psychiatr Clin North Am.* 2004; 27:19–36. vii–viii. [PubMed: 15062628]
- Mossey JM, Knott KA, Higgins M, Talerico K. Effectiveness of a psychosocial intervention, interpersonal counseling, for subdysthymic depression in medically ill elderly. *J Gerontol A Biol Sci Med Sci.* 1996; 51:M172–M178. [PubMed: 8681000]
- Palmer BW, Boone KB, Lesser IM, et al. Neuropsychological deficits among older depressed patients with predominantly psychological or vegetative symptoms. *J Affect Disord.* 1996; 41:17–24. [PubMed: 8938201]
- Paradiso S, Hermann BP, Blumer D, Davies K, Robinson RG. Impact of depressed mood on neuropsychological status in temporal lobe epilepsy. *J Neurol Neurosurg Psychiatry.* 2001; 70:180–185. [PubMed: 11160465]
- Paradiso S, Lamberty GJ, Garvey MJ, Robinson RG. Cognitive impairment in the euthymic phase of chronic unipolar depression. *J Nerv Ment Dis.* 1997; 185:748–754. [PubMed: 9442186]
- Paradiso S, Vaidya J, Tranel D, Kosier T, Robinson RG. Nondysphoric depression following stroke. *J Neuropsychiatry Clin Neurosci.* 2008a; 20:52–61. [PubMed: 18305284]
- Paradiso S, Vaidya JG, McCormick LM, Jones A, Robinson RG. Aging and alexithymia: association with reduced right rostral cingulate volume. *Am J Geriatr Psychiatry.* 2008b; 16:760–769. [PubMed: 18697882]
- Paskind H. Manic depressive psychosis in private practice. *Arch Neurol Psychiatry.* 1930; 23:787–794.
- Penninx BW, Guralnik JM, Ferrucci L, et al. Depressive symptoms and physical decline in community-dwelling older persons. *JAMA.* 1998; 279:1720–1726. [PubMed: 9624025]
- Randolph, C. *The Repeatable Battery for the Assessment of Neuropsychological Status.* San Antonio, TX: Harcourt; 1998.

- Schurman RA, Kramer PD, Mitchell JB. The hidden mental health network. Treatment of mental illness by nonpsychiatrist physicians. *Arch Gen Psychiatry*. 1985; 42:89–94. [PubMed: 3966857]
- Simon GE, Vonkorff M, Piccinelli M, Fullerton C, Ormel J. An international study of the relation between somatic symptoms and depression. *N Engl J Med*. 1999; 341:1329–1335. [PubMed: 10536124]
- Unutzer J, Katon W, Russo J, et al. Patterns of care for depressed older adults in a large-staff model HMO. *Am J Geriatr Psychiatry*. 1999; 7:235–243. [PubMed: 10438695]
- Unutzer J, Simon G, Belin TR, et al. Care for depression in HMO patients aged 65 and older. *J Am Geriatr Soc*. 2000; 48:871–878. [PubMed: 10968289]

Key points

- VS of depression including changes in energy, sleep, appetite, and weight are extremely common in older adults presenting to primary care but no study has examined the extent to which they are associated with functional and cognitive impairment.
- In our study of 787 community-dwelling elderly presenting to routine primary care visits, 31% were found to have exclusively VS (two or more) and 15% at least one VS with associated sadness or loss of pleasure.
- Persons with clusters of VS with but also without sadness or loss of pleasure showed poorer cognition and functional performance in daily activities compared with persons without VS.
- Modest differences between patients with VS alone and VS with depression suggest that the presence of VS in the elderly warrants psychiatric attention.

Table 1

Demographic and clinical variables

	VS–D (N=247)	VS + D (N=123)	Non-VS comparisons (N=417)
Age	73.8 (6.1)	73.3 (5.8)	73.1 (5.8)
Sex ^{**} (% female)	62.8	65.9	51.6
Education [*] (% 12 years)	56.3	47.2	57.2
Depression score ^{***}	2.3 (.54)	3.2 (.96)	.59 (.49)
History of depression ^{***} (% positive)	15.0	44.7	7.2
Treatment ^{***} (% positive)	11.3	10.6	3.6
Functional status (ADLs) ^{***}	1.56 (2.1)	1.65 (2.3)	.68 (1.61)
Medical burden ^{***}	5.2 (2.6)	5.5 (2.6)	3.7 (2.2)
CAGE	0.17 (0.62)	0.12 (0.51)	0.19 (0.68)

Note: Percentages, means, and standard deviations are reported. Statistical comparisons are reported in the text. VS – D = subjects endorsing any two vegetative symptoms or more but no sad mood or anhedonia; VS + D = subjects endorsing any two depressive symptoms or more, with at least one of the symptoms being sad mood and/or anhedonia and one being a vegetative symptom. Non-VS comparisons = subjects endorsing one or fewer symptoms. ADLs = activities of daily living; CAGE = CAGE questionnaire, a measure of alcoholism. Treatment = per cent of subjects treated with antidepressant at the time of office visit. Depression score: sum of depression symptoms. Significant group effects (see text for statistical details and pair-wise comparisons):

^{*}
 $p = 0.005$;

^{**}
 $p = 0.001$;

^{***}
 $p < 0.001$.

Table 2

Depressive symptoms

	VS-D (n = 247)	VS + D (N=123)	Non-VS comparisons (n = 417)
Sad mood *	0 (0)	123 (100)	10 (2.4)
Sleep problems *	122 (49.4)	58 (47.2)	32 (7.7)
Fatigue *	236 (95.5)	114 (92.7)	156 (37.4)
Appetite/weight *	160 (64.8)	65 (52.8)	43 (10.3)
Concentration *	56 (22.7)	34 (27.6)	7 (1.7)

Note: Number and percent participants (in parentheses) endorsing the symptom in the total sample are presented. VS – D = subjects endorsing any two vegetative symptoms or more but no sad mood or anhedonia; VS + D = subjects endorsing any two depressive symptoms or more, with at least one of the symptoms being sad mood and/or anhedonia and one being a vegetative symptom. Non-VS comparisons = subjects endorsing one or fewer symptoms. Significant group effects (see text for statistical details and pair-wise comparisons):

* $p < 0.001$.

Table 3

RBANS subtests

	VS-D (n = 247)	VS + D (N = 123)	Non-VS comparisons (n=417)
RBANS total **	95.5 (14.9)	93.0 (15.6)	99.6 (16.6)
Digit span	11.5 (2.8)	11.3 (2.9)	11.6 (2.7)
Semantic fluency	16.9 (4.5)	16.9 (4.8)	17.7 (4.9)
List learning *	23.7 (6.0)	23.5 (5.3)	25.1 (5.9)
List recall	4.8 (2.4)	4.6 (2.6)	5.1 (2.7)
List recognition	18.8 (1.6)	18.9 (1.5)	18.8 (1.8)
Story memory	15.4 (4.5)	15.2 (4.6)	16.1 (4.7)
Story recall	7.7 (2.9)	7.3 (3.0)	7.9 (3.0)
Figure copy	18.0 (2.4)	18.1 (2.2)	18.3 (2.1)
Figure recall *	12.5 (4.5)	11.9 (4.5)	13.1 (4.2)
Line orientation **	15.7 (3.4)	14.8 (3.9)	16.3 (3.5)
Coding ***	33.5 (10.6)	32.7 (10.7)	37.4 (10.9)
Picture naming **	9.5 (0.9)	9.3 (1.0)	9.6 (0.7)

Note: Means and standard deviations are presented. RBANS =repeatable battery for the assessment of neuropsychological status; VS-D = subjects endorsing any two vegetative symptoms or more but no sad mood or anhedonia; VS + D = subjects endorsing any two depressive symptoms or more, with at least one of the symptoms being sad mood and/or anhedonia and one being a vegetative symptom. Non-VS comparisons = subjects endorsing one or fewer symptoms. Significant group effects corrected for age education (see text for statistical details and pair-wise comparisons). Individual significant *post hoc* analyses: list learning: CTRLS > VS + D = VS-D; line orientation: CTRLS > VS + D, VS + D = VS-D, CTRLS = VS-D; picture naming: CTRLS = VS -D > VS + D; coding: CTRLS > VS + D = VS -D; figure recall: CTRLS > VS + D, VS + D = VS-D, CTRLS = VS-D.

*
 $p < 0.05$;

**
 $p < 0.01$;

 $p < 0.001$.