

FOCUS: PSYCHIATRY AND PSYCHOLOGY

Late-life Onset Bipolar Disorder Presenting as a Case of Pseudo-Dementia: A Case Discussion and Review of Literature

Alok Banga^{a*}, Tsewang Gyurmey^b, David Matuskey^c, Daniel F. Connor^a, Richard F. Kaplan^a, and David C. Steffens^d

^aDepartment of Psychiatry, University of Connecticut Health Center, Farmington, Connecticut; ^bPACE Organization of Rhode Island, former fellow in the Department of Geriatrics, University of Connecticut Health Center, Farmington, Connecticut; ^cDepartment of Psychiatry, Yale University, New Haven, Connecticut; ^dChair of the Department of Psychiatry, University of Connecticut Health Center, Farmington, Connecticut

Depression and comorbid cognitive impairment in the elderly can be difficult to distinguish from dementia. Adding to the complex differential is that depression may be part of a bipolar illness rather than a unipolar mood disorder. A diligent workup and close monitoring of patients can inform appropriate treatment and can make the difference between recovery and persistence of symptoms. The present case will illustrate how a comprehensive workup utilizing extensive data gathering, laboratory workup, use of neuropsychological testing, neuroimaging, and timely treatment can lead to successful clinical outcomes that can be sustained for many years.

INTRODUCTION

The elderly can present with two different patterns of mixed affective-cognitive disturbances. The first refers to a primary mood disturbance accompanied by a cogni-

tive disturbance, while the second refers to a primary dementing illness that is accompanied by a secondary major depression [1]. When severe, the first type has also been called pseudodementia or dementia of depression. Several overlapping features make

*To whom all correspondence should be addressed: Alok Banga MBBS (MD), MPH, Assistant Professor, Department of Psychiatry, UConn Health Center, 263 Farmington Avenue, Farmington, CT 06030; Tele: 860-679-2730; Fax: 860-679-1296; Email: banga@uchc.edu.

†Abbreviations: MMSE, Mini Mental Status Examination; NOS, Not Otherwise Specified; PTH, parathyroid hormone; PTHrp, parathyroid hormone-related protein; CRP, C-Reactive Protein; ESR, erythrocyte sedimentation rate; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; PET, Positron Emission Tomography; SPECT, Single Photon Emission Computed Tomography; ECT, Electro Convulsive Therapy.

Keywords: pseudo-dementia, late life onset bipolar disorder

it hard to differentiate between the two. A major difference, however, is that pseudodementia is a reversible cognitive impairment. This differential prognosis of pseudodementia requires a timely diagnosis and adequate treatment of depression, which can represent the difference between recovery and the persistence of symptoms. The diagnosis and treatment of this type of depression can be even more complex if it is part of a bipolar spectrum rather than a unipolar illness [2].

We discuss a case that illustrates the difficulties in distinguishing between these two presentations.

CASE PRESENTATION

The patient is a 76-year-old Caucasian male, a successful professional who was working full time until about 2 months prior to admission to our hospital. He was first admitted to another psychiatric hospital for a month after he reportedly made a suicide gesture by pointing a gun to his head and firing two shots into the ceiling. In recent months, the patient had been very concerned about developing Alzheimer's dementia after one of his close friends was sent to a nursing home for advanced dementia. Over the prior 6 months, he was reported to have become very confused, paranoid, and distrusting of other people. He was often tearful at times and had reported significant "guilt" to his wife. Per him and his family, he was working 12 to 15 hours a day, but his work output was significantly diminished. He was also described as sleeping only 2 to 3 hours at night. The patient was admitted to a community psychiatric hospital where, over a period of 1 month, he exhibited fluctuating orientation levels, cognitive deficits such as anomia, grossly disorganized speech and thinking, and severe memory loss. His Folstein Mini Mental Status Examination (MMSE†) score varied between 13 and 23 points (out of 30) during this hospitalization. He would rarely eat because of his depressed mood as well as significant paranoia that someone had poisoned his food. He reportedly suffered a weight loss of 20 pounds in 60 days. He displayed marked impairment in his activities

of daily living as well. A diagnosis of Psychotic Disorder Not Otherwise Specified (NOS) and possible Alzheimer's dementia was made, and he was initially given a trial of haloperidol and olanzapine for 3 to 4 days but developed extra pyramidal side effects and hypotension from these medications, respectively. He was then started on sertraline 50 mg, with the dose gradually titrated up to 150 mgs a day, and risperidone, gradually titrated to 2 mgs BID. His family reported that his paranoia increased despite these medications. Because the patient had made no improvement in clinical status after an almost 30-day stay in a community hospital and treating doctors recommended a transfer to a nursing facility in the future, he was transferred to our academic teaching hospital as per his family wishes.

Hospital Course at our Facility

After his admission to our hospital, he continued to have cognitive impairment as well as affective symptoms. We interviewed his family and obtained permission to interview his work staff extensively to get a detailed longitudinal history. We found out that he had a history of a "breakdown" about 20 years prior to the current episode, after working "long hours for many days" where he "couldn't slow down." During that episode, he flew for an impromptu trip across the country with his friends. On the trip, he had an anxiety attack, and he was firmly convinced that it was a heart attack. He received alprazolam to "slow his mind down" in the emergency room of a hospital, where he was worked up for what he believed was a myocardial infarction. After a reportedly normal cardiology workup, the patient was discharged from the hospital with PRN alprazolam. He had no other psychiatric or substance abuse history and until recently had been a very successful and productive professional who would often work extra-long hours without feeling tired. Personality wise, he was described to us by his staff and family as a very flamboyant, boastful, and charming individual, who was "full of energy" and "extremely driven." In his moments of guilt, while he was still showing

significant apathy and cognitive disturbance, he told us about some prior episodes of hyper sexuality and indiscrete behaviors that he had not shared with anyone before. His wife also mentioned to us he had a liking for “good things” in life, including “fancy cars and younger women,” and despite his indiscreet behaviors, she had always remained very devoted to him. Even though he had never been treated or officially diagnosed with a psychiatric disorder, these symptoms suggested a lifelong undiagnosed bipolar disorder (with possible hypomanic episodes in the past) or a possible late life onset bipolar disorder most recent episode mixed versus depressed with psychotic features.

BASELINE LABORATORY INVESTIGATIONS

Routine chemistries done at the previous hospital were found to be within normal limits. Although our main differential diagnosis was an affective illness, a broad range of lab tests were ordered by us to evaluate the patient’s complex cognitive and psychiatric condition. Some of the conditions we ruled out included common and uncommon causes of cognitive impairments in the elderly such as HIV, neurosyphilis, vitamin B12 and folate deficiency, Porphyrias, hyperparathyroidism, neoplastic and paraneoplastic syndromes, etc. Patient’s liver function tests, serum protein electrophoresis, cerebrospinal fluid analysis, serum heavy metals, HIV, RPR, porphyrins, urine electrolytes, ceruloplasmin, folate, vitamin B12, methylmalonic acid levels, thyroid stimulating hormone, and anti-nuclear cytoplasmic antibody were also normal. Patient’s serum ionized calcium at admission was 1.42mmol/l and was 1.41mmol/l at discharge (normal range = 1.10-1.30mmol/l). However patient’s parathyroid hormone (PTH), parathyroid hormone-related protein (PTHrp), vitamin D 25, OH and 1, 25 Di Hydroxy, and vitamin D were normal. Anti-nuclear antibody was positive with speckled appearance, titer 1:80 of non-significance. C-Reactive Protein (CRP), a non-specific inflammatory marker, was elevated at 25.2mg/l. The patient’s erythrocyte sedimentation rate

(ESR) was mildly elevated to 20mm/hr. The patient’s routine EEG obtained in awake and drowsy states was normal.

BASELINE NEUROPSYCHOLOGICAL TESTING

Patient had shown a great deal of fluctuation in his MMSE at the previous hospital. It was notable that this fluctuation on MMSE was not specific to orientation in time, place, or person, which would have been indicative of a delirious process. The fluctuations rather seemed to be related to being unmotivated to finish testing or being paranoid at times. We decided to consult for neuropsychology testing to get a better picture of patient’s cognitive deficits. Cognitive tests including the RBANS (Repeatable Battery for the Assessment of Neuropsychological Status) and Trail Making Test were administered given the patient’s perplexing clinical presentation and history. RBANS is a brief neurocognitive battery measuring immediate and delayed memory, attention, language, and visuospatial skills. It was developed for two main applications: as a standalone battery for the detection and neurocognitive characterization of dementia and as a brief neurocognitive battery for the detection and tracking of neurocognitive deficits in a variety of disorders [3].

Results of the first testing (Table 1) showed a significant impairment in attention span, memory, and executive function, suggesting a possible neuro-degenerative condition such as dementia.

NEUROIMAGING STUDIES

MRI scan of the head was normal. Given the lack of a high resolution functional imager such as a PET (Positron Emission Tomography) scan at our hospital, a Single Photon Emission Computed Tomography (SPECT) was ordered after the MRI to evaluate regional cerebral blood flow and to look for patterns consistent with neurodegenerative disorders. The SPECT scan showed moderate hypoperfusion within the left parietal lobe/temporoparietal cortex. There was

Table 1. Neuropsychological Testing Results.

	November 2006	December 2006	August 2010
WTAR(SM=100, SD=15)	116	na	120
WMS Orientation (Maximum Score=14)	6	13	13
RBANS INDEX SCORES (SM = 100, SD =15 for all Indexes)			
Total Score	59	86	103
Immediate Memory	57	90	97
Visuospatial	78	84	126
Language	82	105	95
Attention	64	100	100
Delayed Memory	56	71	98
TMT			
Part A (SM=47.2, SD=17.9 for ages 75-79)	57	43	39
Part B (SM=119.2, SD=50.4 for ages 75-79)	360	75	108
GDS (0-9= Normal; 10-19= Mildly Depressed; 20-30= Severely Depressed)	15	6	5

WTAR = Wechsler Test of Adult Reading, WMS = Wechsler Memory Scale, TMT = Trail Making Test,

also mild hypoperfusion within the right parietal lobe/posterior temporoparietal and the frontal lobe, more evident within the left frontal lobe relative to the right. There were no findings compatible with a cerebral vascular accident. Perfusion within the thalamus, the cerebellum, the occipital lobe cortex, and visual cortex were within normal limits.

DIAGNOSIS, TREATMENT, AND HOSPITAL COURSE

Once the initial workup was complete and other medical illness was ruled out, the patient was diagnosed with bipolar illness most recent episode mixed versus depressed with psychotic features. His medications were

gradually cross tapered from risperidone 2mg BID to aripiprazole, which was eventually titrated to 30 mg once a day. Aripiprazole was chosen as it is an FDA-approved agent for treatment of mania and mixed episodes in bipolar illness in adults. It is also an FDA-approved medication for augmentation agent for major depressive disorder in adults. It was also chosen as it is one of the less sedating atypical antipsychotic agents with a lower anticholinergic profile, hence a lower propensity to cause confusion and hypotensive effects compared with other atypical antipsychotics [4].

The patient's family had reported worsening of depression with sertraline 150mg, so it was gradually cross-tapered to a com-

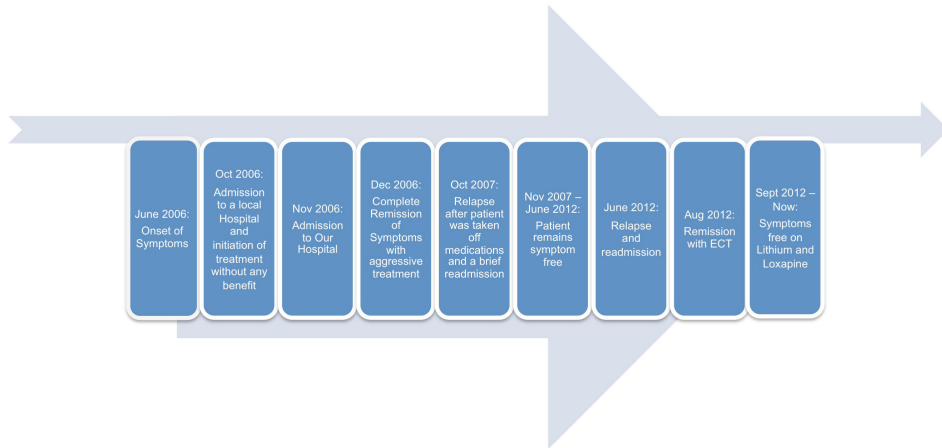


Figure 1. Timeline of events.

bination of venlafaxine extended release (gradually increased to 300mg once a day) and mirtazapine (eventually increased to 45mg at bed time). Venlafaxine was chosen as it is a dual, serotonergic, and noradrenergic reuptake inhibitor [5]. Mirtazapine was also chosen as it has a positive effect on sleep and appetite as well as depression and anxiety [6]. While we were significantly concerned about polypharmacy in a 76-year-old man, the combination of two antidepressants along with aripiprazole was chosen because of the severity of his depression and rapidly deteriorating status. Patient's family was not agreeable to trying other potentially effective agents such as lithium or ECT to alleviate his depression and psychotic symptoms. Later, the patient was also started on galantamine 4mg 2 times a day to address cognitive impairment. Gradually, 10 to 12 days after starting the new medication regimen, the patient started to show improvement in his psychomotor retardation, appetite, sleep, thought process, and paranoia. With the improvement in his condition, a diagnosis of dementia was less likely so we tapered off the galantamine. Had the patient's symptoms not improved and his diagnosis remained dementia, we would have possibly increased the dose of galantamine rather than discontinuing it. Atypical antipsychotics are commonly used to treat aggression and psychotic symptoms in dementia. However, the FDA has issued a black box warning that elderly patients

with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. If patient had true dementia, we would have very been cautious about using a high dose of aripiprazole. We would have possibly continued mirtazapine to help patient with sleep and appetite. A bigger challenge would have been to discuss a future course of action, including suitable placement for the patient in a nursing home. Fortunately, the patient had a complete remission of symptoms as his diagnosis indeed turned out to be a bipolar illness.

At the time of discharge, almost 1 month after admission, patient's CRP and ESR normalized. Studies have shown that in old age, depressed mood is associated with high levels of inflammatory markers, suggesting that depressed mood is causing and/or caused by systemic inflammation [7]. It is significant that in our case, CRP and ESR values came down to normal after successful treatment.

Repeat neuropsychological testing was obtained at the time of discharge and showed significant improvement compared with admission. As can be seen in Figure 1, his scores improved significantly relative to scores at admission and were now all in the average range except the Delayed Memory Index, which showed improvement and was now in the Borderline range. His Geriatric Depression Scale score improved to within normal limits (Table 1).

LONG-TERM FOLLOW-UP

Over the 2 months following his discharge from the hospital, we discontinued his antidepressants venlafaxine and mirtazapine as we thought his mixed-depressive symptoms were more on a bipolar spectrum rather than just a unipolar depressive disorder. We also changed aripiprazole to quetiapine 300 mg at bed time as patient was noted to have akathisia symptoms of fidgetiness and reported constant "inner restlessness." As mentioned above, we had discontinued the galantamine earlier, as patient had no evidence of residual cognitive impairment whatsoever. Six months after discharge from our hospital, the patient transferred his care to a community psychiatrist near his house who questioned the diagnosis of bipolar disorder and discontinued quetiapine as well. Soon thereafter, the patient experienced a relapse with a similar but milder episode, including cognitive symptoms as well as paranoia, sleep disturbance, and racing thoughts. He was briefly hospitalized to our facility again and was restabilized on quetiapine 300mg at bed time, lorazepam 0.5mg as needed, and zolpidem 6.25mg at bed time.

At 4-year follow-up, patient remained on quetiapine 300mg QHS, off and on lorazepam 0.5mg PRN, and zolpidem 6.25mg at bed time to help with anxiety and sleep, respectively. Although he had cut down on his professional work, he stayed very productive. Despite significant psychosocial stressors including a worsening economy, moving, and family problems, he did not have a relapse or required a further hospitalization for the last 4 years. His MMSE continued to be 30 on every subsequent visit, and he had no adverse effect from any of his medications. In August 2010, neuropsychological testing was again repeated and results are presented in Figure 1. Thus, at 4-year follow-up, all scores including Delayed Memory were in the average range, and the patient's depression score remained normal.

After doing well for more than 5 years, patient decompensated again in June 2012 after his wife was diagnosed with a neo-

plasm. His initial symptoms were again of confusion, paranoia, and sleep disturbance. We gradually increased the dose of quetiapine to up to 600mg a day in divided doses. However, he had to be hospitalized after a few weeks as his cognitive and affective symptoms worsened. He began to refuse food because of his paranoia and stopped doing his activities of daily living, including showering and shaving. Given a lack of response to an increased dose of quetiapine, the inpatient team switched him back to a combination of aripiprazole 30mg once a day, venlafaxine 225mg once a day, and mirtazapine 45mg at bed time, a combination he had responded well to previously. His cognitive and affective symptoms continued to stay somewhat impaired despite being on the new medication regimen for over 3 weeks. Since the patient's condition was not improving satisfactorily with medications alone and he did not have the capacity to give informed consent for Electro Convulsive Therapy (ECT) treatment, an ECT against will hearing was scheduled to achieve a faster alleviation his symptoms. A probate judge granted permission to start ECT, and he was started on Right Unilateral ECT, two times a week. After four ineffective treatments of Right Unilateral ECT, he was switched to Bi Frontal ECT. After two treatments with Bi Frontal ECT, his symptoms of cognitive, affective, and paranoia completely resolved. There were no adverse effects noticed or reported from ECT treatment. The patient continued with maintenance ECT treatment for 2 months. At the time of submission of this manuscript, the patient had stopped maintenance ECT treatment. He was tapered off aripiprazole and venlafaxine as he developed akathisia again. He was tapered off mirtazapine as he had a sleeping walking episode from it. We transferred his care to a psychiatrist near his house as commuting to us was becoming a problem. After discussions with us, his new psychiatrist switched him over to a combination of lithium 300mg once a day and loxapine 10mg once a day. Patient tolerated the changes very well without resurgence of mood symptoms, cognitive symptoms, or

Table 2. Symptoms of bipolar disorder that may present as symptoms of a dementia process.

Decreased need for sleep or a disrupted sleep process
Increased distractibility and impaired attention span
Irritability or aggression
Psychomotor agitation or retardation
Paranoia and other psychotic symptoms such as auditory hallucinations
Inappropriate guilt (which may be delusional)
Fatigue or loss of energy
Significant weight loss
Racing thoughts/ Impaired thought process
Diminished ability to think or concentrate
Sadness
Diminished interest and pleasure in activities

akathisia. Reportedly, he has resumed his work and all other activities as well. It is notable that during the last 3 years, two of the patient's children and grandchildren have also suffered from manic episodes and major depression with psychotic features, further confirming a strong genetic loading of mood disorder in his family. Figure 1 summarizes the patient's important clinical events and medication periods and helps frame the reader to the timeline of his disease onset and recovery.

DISCUSSION

Our case illustrates the challenges clinicians face in the evaluation and treatment of impaired cognitive functioning presenting in the elderly [8]. The patient's presentation included both depressive symptoms and cognitive difficulties, the latter being so pronounced that a comprehensive subacute dementia and an acute cerebrovascular workup were ordered. Our case shows that the distinction between "organic" cognitive symptoms (thought of as symptoms due to structural or neurodegenerative, irreversible conditions) and "functional" symptoms (thought of as symptoms due to reversible conditions, usually psychiatric in nature) can be challenging using our current diagnostic nosology. Table 2 further highlights the overlap between symptoms of bipolar disorder and pseudodementia, demonstrating the subtleties in the diagnosis. The patient's cognitive presentation and neuroimaging results

were consistent with a neurodegenerative condition such as Alzheimer's disease. Because of the mismatch of a dementia diagnosis with the time-course of symptoms, we hypothesized that the patient's disordered thought process (i.e., due to a primary mood or psychotic disorder) might be more central to his presentation. As a result of treatment for affective symptoms, the patient's cognitive symptoms and associated neuropsychological symptoms abnormalities reversed [9].

This supports two hypotheses: 1) that the distinction between "functional" and "organic" conditions may be impossible to make based on our current diagnostic tests, since the diagnosis of most "organic" conditions are made by autopsy; and/or 2) that different etiological conditions may present similarly based on the neural circuits they affect, circuits whose dysfunction can be observed clinically and via neuroimaging methods.

The question arises as to whether our patient's depression may represent a prodrome of a later dementing process [10]. Although this has not yet occurred over 6 years of follow-up, we cannot predict how our patient's affective symptoms will progress over time.

In recent literature, some authors conclude that reversible cognitive impairment in late life moderate to severe depression appears to be a strong predictor of later onset dementia [11]. Even when the cognitive impairment improves with the treatment of the depressive symptoms, patients are still at a substantially greater risk for dementia than demographically similar people without de-

pression. In a study of more than 1,000 individuals over 60 years of age living in a community, baseline depressed mood was associated with a moderately increased risk for incident dementia at follow-up examination [12]. Other authors have suggested that depression with reversible cognitive impairment may be an early phase of dementia rather than a risk factor for it. One hypothesis postulates that people with higher cognitive reserves are able to compensate enough at baseline so that their cognition stays marginal but out of the clinical arena [13]. Any additional insult to their brain, however (such as a physical illness or depression), overwhelms their already strained cognitive reserves and these people's cognition crosses the threshold of clinical impairment [14]. Should the physical illness, depression, or other brain insult improve, these patients' cognitive abilities may return but not to baseline [15]. Thus, brain insults such as depression obviate the patients' decreased cognitive reserves. Some authors recommend that patients with dementia of depression have a full dementia screening, comprehensive cognitive testing, and ongoing monitoring of their cognitive function [11,16,17].

CONCLUSION

This case brings to highlight the phenomenon of late life onset bipolar illness presenting as pseudodementia. New onset of bipolar disorder becomes less common with age, but late onset bipolar disorder may still constitute about 5 percent to 8 percent of all annual inpatient psychiatric admissions [18, 19]. Some studies have suggested that 6 percent to 8 percent of patients with bipolar illness may have a late life onset [20]. Some authors have defined this late onset of mixed affective and cognitive symptoms as bipolar type VI, a variant of the broader bipolar spectrum illness [21]. This presentation of bipolar illness seems to have a lower association with family history [22], and patients generally have a higher premorbid psychosocial functioning as compared to early onset illness before the age 65 years. Even euthymic elders with late onset bipolar ill-

ness when compared to age matched controls seem do worse in domains of cognition, language, and executive functioning [23,24,25]. Some older literature has described symptoms as mixed or agitated depressive states with overexpression of complaints, occasional hyper sexuality, irritability, and motor agitations often bordering pseudo-hysteria or histrionic personality disorder [26]. Mania in elderly often may be secondary to a physical illness. A truly frank manic picture may be mistaken for dementia or an organic brain disease even if it is indeed a primary affective illness [19,27]. Therefore, before beginning a specific treatment especially in the elderly, neuroimaging to rule out cerebrovascular organic disease is of paramount importance [28,29,30].

There are no clear guidelines available to treat late life onset bipolar illness presenting as pseudodementia. In addition to a thorough medical workup and psychiatric assessment, a firm understanding of baseline psychosocial functioning and timeline of events is very important. Besides affective symptoms, our patient also had paranoia, so we did not try a traditional mood stabilizer first and straight away tried an atypical antipsychotic. It is reported that mood stabilizers in the form of anticonvulsants are better tolerated in the elderly with bipolar illness than lithium [30]. However, recently this particular patient has now been switched to lithium and is tolerating it well. It is also suggested that acute mania responds well to valproate and atypical antipsychotics in the same population [29]. Pseudodementia associated with late onset bipolar illness, when treated with only antidepressants and or acetylcholinesterases, may worsen or aggravate symptoms by unmasking mania [2]. These challenges call for closer clinical follow up and monitoring [30]. Other forms of treatment such as ECT may be tried in refractory cases as evidenced by several mixed age studies. There is a serious dearth of literature on treatment of this condition and most available literature is currently extrapolated from case series [31,32] and mixed age population studies [21]. Further research and high quality longitudinal studies needed

to shed light on the various neuropsychiatric associations and management of late life onset bipolar illness and its associated complications such as pseudo-dementia [18].

Acknowledgments: We acknowledge Dr. John Vento MD, Assistant Professor, Department of Nuclear Medicine, for doing the SPECT scans.

REFERENCES

- Caine ED. Pseudodementia. Current concepts and future directions. *Arch Gen Psychiatry*. 1981;38(12):1359-64.
- Ng B, Camacho A, Lara DR, Brunstein MG, Pinto OC, Akiskal HS. A case series on the hypothesized connection between dementia and bipolar spectrum disorders: Bipolar type VI? *J Affect Disord*. 2008;107(1-3):307-15.
- Randolph C, Tierney MC, Mohr E, Chase TN. The repeatable battery for the assessment of neuropsychological status (RBANS): Preliminary clinical validity. *J Clin Exp Neuropsychol*. 1998;20(3):310-9.
- Grunder G, Kungel M, Ebrecht M, Gorocs T, Modell S. Aripiprazole: Pharmacodynamics of a dopamine partial agonist for the treatment of schizophrenia. *Pharmacopsychiatry*. 2006;39(Suppl 1):S21-5.
- Papakostas GI, Thase ME, Fava M, Nelson JC, Shelton RC. Are antidepressant drugs that combine serotonergic and noradrenergic mechanisms of action more effective than the selective serotonin reuptake inhibitors in treating major depressive disorder? A meta-analysis of studies of newer agents. *Biol Psychiatry*. 2007;62(11):1217-27.
- Anttila SA, Leinonen EV. A review of the pharmacological and clinical profile of mirtazapine. *CNS Drug Rev*. 2001;7(3):249-64.
- Penninx BW, Kritchovsky SB, Yaffe K, Newman AB, Simonsick EM, Rubin S, et al. Inflammatory markers and depressed mood in older persons: Results from the health, aging and body composition study. *Biol Psychiatry*. 2003;54(5):566-72.
- Steffens DC. Separating mood disturbance from mild cognitive impairment in geriatric depression. *Int Rev Psychiatry*. 2008;20(4):374-81.
- Beats BC, Sahakian BJ, Levy R. Cognitive performance in tests sensitive to frontal lobe dysfunction in the elderly depressed. *Psychol Med*. 1996;26(3):591-603.
- Green RC, Cupples LA, Kurz A, Auerbach S, Go R, Sadovnick D, et al. Depression as a risk factor for alzheimer disease: The M1-RAGE study. *Arch Neurol*. 2003;60(5):753-9.
- Saez-Fonseca JA, Lee L, Walker Z. Long-term outcome of depressive pseudodementia in the elderly. *J Affect Disord*. 2007;101(1-3):123-9.
- Chen P, Ganguli M, Mulsant BH, DeKosky ST. The temporal relationship between depressive symptoms and dementia: A community-based prospective study. *Arch Gen Psychiatry*. 1999;56(3):261-6.
- Stern Y, Albert S, Tang MX, Tsai WY. Rate of memory decline in AD is related to education and occupation: Cognitive reserve? *Neurology*. 1999;53(9):1942-7.
- Krauthammer C, Klerman GL. Secondary mania: Manic syndromes associated with antecedent physical illness or drugs. *Arch Gen Psychiatry*. 1978;35(11):1333-9.
- Nebes RD, Pollock BG, Houck PR, Butters MA, Mulsant BH, Zmuda MD, et al. Persistence of cognitive impairment in geriatric patients following antidepressant treatment: A randomized, double-blind clinical trial with nortriptyline and paroxetine. *J Psychiatr Res*. 2003;37(2):99-108.
- Wilkins CH, Mathews J, Sheline YI. Late life depression with cognitive impairment: Evaluation and treatment. *Clin Interv Aging*. 2009;4:51-7.
- Alexopoulos GS, Meyers BS, Young RC, Mattis S, Kakuma T. The course of geriatric depression with "reversible dementia." A controlled study. *Am J Psychiatry*. 1993;150(11):1693-9.
- Depp CA, Jeste DV. Bipolar disorder in older adults: A critical review. *Bipolar Disord*. 2004;6(5):343-67.
- Yassa R, Nair NP, Iskandar H. Late-onset bipolar disorder. *Psychiatr Clin North Am*. 1988;11(1):117-31.
- Sajatovic M, Blow FC, Ignacio RV, Kales HC. New-onset bipolar disorder in later life. *Am J Geriatr Psychiatry*. 2005;13(4):282-9.
- Azarin JM, Kaladjian A, Adida M, Fakra E. Late-onset bipolar illness: The geriatric bipolar type VI. *CNS Neurosci Ther*. 2012;18(3):208-13.
- Moorhead SR, Young AH. Evidence for a late onset bipolar-I disorder sub-group from 50 years. *J Affect Disord*. 2003;73(3):271-7.
- Gildengers AG, Butters MA, Chisholm D, Rogers JC, Holm MB, Bhalla RK, et al. Cognitive functioning and instrumental activities of daily living in late-life bipolar disorder. *Am J Geriatr Psychiatry*. 2007;15(2):174-9.
- Martino DJ, Igoa A, Marengo E, Scapola M, Ais ED, Strejilevich SA. Cognitive and motor features in elderly people with bipolar disorder. *J Affect Disord*. 2008;105(1-3):291-5.
- Radanovic M, Nunes PV, Gattaz WF, Forlenza OV. Language impairment in euthymic, elderly patients with bipolar disorder but no dementia. *Int Psychogeriatr*. 2008;20(4):687-96.
- Garcia C, Sander HJ. Pseudohysterical behavior patterns in endogenous depressions. *Nervenarzt*. 1983;54(7):354-62.
- Fortin L. Manic disorder in the aged: A review of the literature. *Can J Psychiatry*. 1990;35(8):679-83.

28. Starkstein SE, Robinson RG. Mechanism of disinhibition after brain lesions. *J Nerv Ment Dis.* 1997;185(2):108-14.
29. Aziz R, Lorberg B, Tampi RR. Treatments for late-life bipolar disorder. *Am J Geriatr Pharmacother.* 2006;4(4):347-64.
30. Shulman KI, Herrmann N. Bipolar disorder in old age. *Can Fam Physician.* 1999;45:1229-37.
31. Casey DA, Fitzgerald BA. Mania and pseudodementia. *J Clin Psychiatry.* 1988;49(2):73-4.
32. Sachdev PS, Smith JS, Angus-Lepan H, Rodriguez P. Pseudodementia twelve years on. *J Neurol Neurosurg Psychiatry.* 1990;53(3):254-9.