BALNEO RESEARCH Balneo and PRM Research Journal
English Edition
e ISSN 2734 - 8458 p ISSN 2734 - 844X ROMANIAN ASSOCIATION OF BALNEOLOGY

Research article

Medical management of organic psychomotor agitation and neurorehabilitation after revascularized vertebrobasilar stroke

Antonia Ioana Vasile [1,2,*], Cristina Nica [2] and Cristina Tiu [1,2]

Citation: Vasile A.I., Nica C., Tiu C. - Medical management of organic psychomotor agitation and neuro-reabilitation after revascularised vertebrobasilar stroke
Balneo and PRM Research Journal ***2024****, 15(4): 762*

Academic Editor(s):
Constantin Munteanu

Reviewer Officer:
Viorela Bembea

Production Officer:
Camil Filimon

Received: 28.11.2024
Published: 23.12.2024

Reviewers:
Mihai Hoteteu
Bistriceanu Roxana

Publisher's Note: Balneo and PRM Research Journal stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

1 Carol Davila University of Medicine and Pharmacy, Bucharest, Romania;
2 University Emergency Hospital of Bucharest, Bucharest, Romania;

* Correspondence: Antonia Ioana Vasile, antoniaioana97.vasile@gmail.com

Abstract: Psychomotor agitation is a behavioral and emotional symptom frequently seen in dementia patients. Vascular dementia has few options for treating non-cognitive symptoms such as agitation and psychotic symptoms. We present the case of a 71-year-old male who presented in the revascularisation window for confusional syndrome and tetrameric ataxia. The examination revealed: psychomotor agitation, dyscromatopsia, selfdisorientation, temporal and spatial disorientation, complex visual hallucinations with Capgras syndrome, facial agnosia, and akinetopsia. Brain CT revealed top of the basilar artery thrombosis which was treated with mechanical thrombectomy and intraarterial thrombosis. Brain imaging revealed constitutive lesions in the occipital lobe, parahippocampal, the lingual gyrus, in the paramedian pontine level, and a cerebellar lesion. The patient developed strategic infarct dementia with severe psychomotor agitation. As a therapeutic approach, the heroic combination that diminished the agitation was: Olanzapine and Levomepromazine (two sedative neuroleptics), Valproate (thymostabiliser), and Diazepam. We emphasize the need for heroic treatment options for severe psychomotor agitation and psychotic agitation in patients with cardiovascular risks such as stroke. In this case, we present our beneficial results with Olanzapine and Levomepromazine. We highlight the need for extensive treatment guidelines for severe cases of psychomotor agitation.

Keywords: strategic infarct dementia; Levomepromazine; akinetopsia; complex visual hallucinations; sedative neuroleptics; midbrain ischemia; extensive guidelines

1. Introduction

Psychomotor agitation is a behavioral and emotional symptom frequently seen in patients with cognitive decline, present in about 40% of the patients with vascular dementia [1, 2].

Dementia is characterized by psychic, psychological, and behavioral symptoms. Gnostic functions that are afected frecquently are: memory, learning, attention, orientation, speech, and reason. Psychiatric symptoms that may appear are: apathy, depression, psychotic symptoms, or behavioral symptoms.

We presented a case of vascular dementia by strategic infarct. From a vascular point of view, vascular dementia has two forms. The first form is often caused by multiple small strokes and is defined as multi-infarct dementia. The second form is called strategic infarct dementia and is caused by a small, single infarct localized in specific brain regions [3]. The sites for strategic infarcts are: profound regions (caudate nuclei, thalami, left capsular genu), frontal lobe, and left angular gyrus [3, 4]. They are caused by infarcts in the Papez circuit (medial limbic circuit) or Yakovlev circuit (ventrolateral limbic circuit) [5]. The Papez circuit involves: the hippocampus,

mamillary body, anterior nucleus of the thalamus, and posterior cingulate gyrus; while the Yakovlev circuit includes other structures such as the amygdala, anterior cingulate gyrus, and the dorsomedial nucleus of the thalamus [6]. Another clinical difference between the two is that multi-infarct dementia has a progressive cognitive impairment, in progressive steps, while a sudden cognitive impairment characterizes strategic infarct dementia.

In terms of treating dementia, the Romanian guideline discusses treating cognitive symptoms and treating non-cognitive symptoms (Burns & De Deyn, 2006). For treating the cognitive deficits from vascular dementia, the first line of treatment is cholinesterase inhibitors (Donepezil, Rivastigmine, and Galantamine), while the second line of treatment is an NMDA receptor antagonist (Memantine). In terms of the psychomotor agitation of dementia, the first line of treatment includes Trazodone [7]. The second line treatment is Valproate [8] and Carbamazepine [9]. The benzodiazepines that are recommended are Lorazepam and Oxazepam, because Diazepam may lead to confusional syndrome and disinhibition which can accentuate the psychomotor agitation. For psychotic symptoms (such as delusions and hallucinations), the recommended antipsychotics are: as the first line Risperidone [10]; as the second line Quetiapine, Ziprasidone and Clozapine [11]. Haloperidol should be used as a second-line treatment to atypical antipsychotics because of the cardiovascular and extrapyramidal adverse reactions.

The present study aims to present the medical guidelines for psychomotor agitation and its limits. There are cases where the guideline protocol is overruled and new medical options should be explored. We present the case of organic psychomotor agitation in a patient who presented in the revascularisation window for vertebrobasilar stroke. The results section presents the medical intervention and the heroic therapies that were used in severe cases of psychomotor agitation.

2. Materials and Methods

We present the case of a 71-year-old patient who presented to the Emergency Room for singultus, moderate dysarthria, and tetrameric ataxia (on the right side worse than on the left side). The debut was sudden, and presented to the hospital within 4.5 hours.

As per their personal history, the patient had atrial fibrillation which was recently diagnosed, so they had no anticoagulant treatment at presentation. Other cardiovascular risk factors were Dyslipidemia, Hypertension, and chronic smoking. However, he and the caregivers deny alcohol consumption.

The first brain computer tomography (CT) with contrast revealed: a spontaneous hyperdense appearance of the distal segment of the basilar artery, while post-contrast CT noted the stop of the contrast substance at this level, without any cranial lesions (Figure 1). Because the patient was eligible for revascularisation treatment, mechanical thrombectomy was decided. During the cerebral angiography procedure, contrast is injected on the left vertebral artery and a subocclusive thrombus is revealed on the top of the basilar artery (Figure 1). The thrombus was oriented towards the left posterior cerebral artery (PCA) (Figure 2). At the end of the mechanical thrombectomy, intraarterial thrombolysis is performed and posterior circulation is restored.

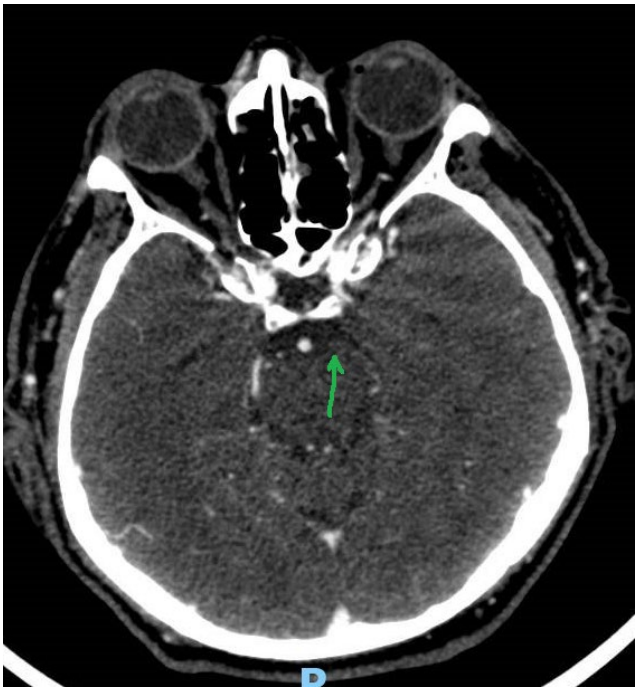


Figure 1. Top of basilar artery thrombosis

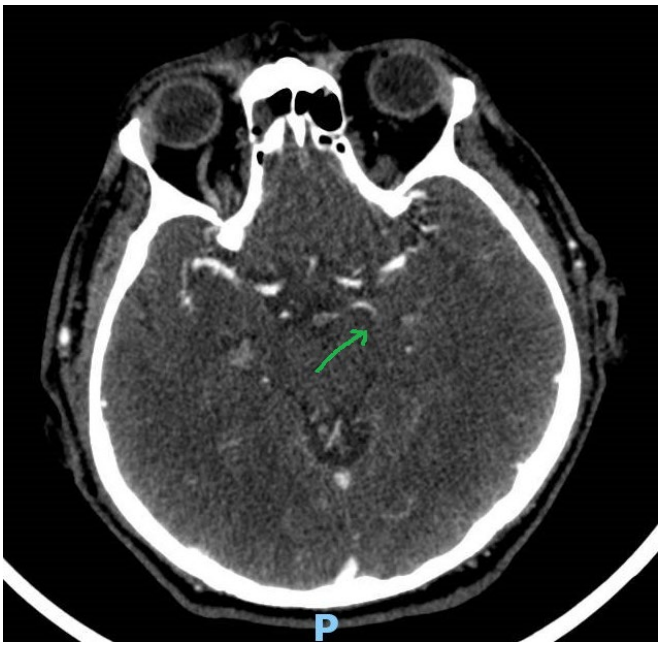


Figure 2. Posterior cerebral artery thrombosis

At 24 hours after admission, the neurological and psychiatric examination revealed: moderate psychomotor agitation, and a qualitative altered state of consciousness: the patient constantly stayed with their eyes closed, but opened them at verbal stimulation, named objects inconstantly, dyschromatopsia, was self-disoriented (fails to say their name, says that they are not married), temporal and spatial disoriented, complex visual hallucinations with Capgras syndrome (the delusion of doubles) (tells to the examiner that we are at their rented apartment, does not recognize the medical personnel and messes the medical personnel with known people from their past), unpermitted familiarity towards the medical personnel, sexual disinhibition, facial agnosia (does not recognize his family), akinetopsia (motor blindness), agraphia, facial symmetry, no motor deficit, no sensitivity disorder, tetrameric ataxia (left side more than the right side).

The general examination revealed that the patient was cardiac stable but had rales lung sounds, so we decided to do a thoracic CT scan along with the 24-hour control brain CT. The brain CT revealed: left occipital and parahippocampal edematous hypodensities bulging the intergyral sulci and impinging on the posterior horn of the left lateral ventricle (Figure 3). The thoracic CT revealed: basal bilateral pneumonia.

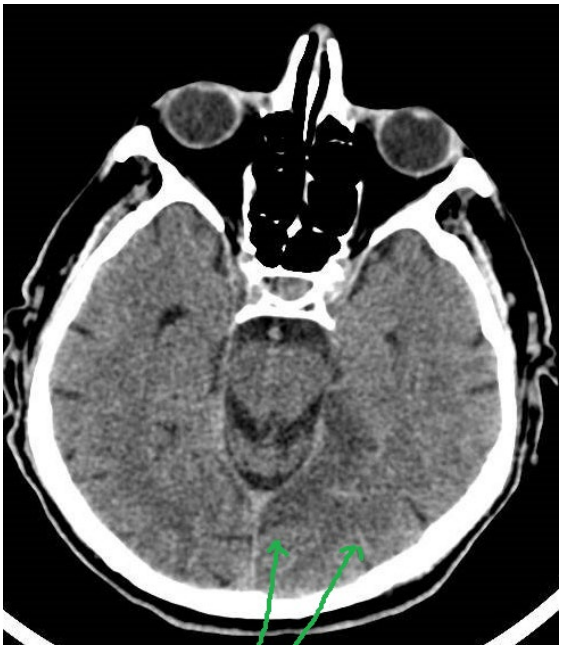


Figure 3. Occipital and parahippocampal ischemic stroke

For pneumonia, we decided to administer intravenous Meropenem and after one dose, the patient developed generalized maculopapular exanthema and the mild psychomotor agitation intensified. Because of the glottic edema risk, the allergist prescribed corticosteroid treatment with intravenous Dexamethasone which reduced general inflammation and cerebral edema. However, corticoid treatment exacerbated their psychomotor agitation.

During hospitalization, we did a cerebral MRI examination with sedation, which revealed: lesions in the lingual gyrus and left parahippocampal gyrus (with bright DWI and increased ADC), a lesion in the right paramedian pontine level next to the pontomedullary junction (with bright DWI and decreased ADC), and a left cerebellar millimeter lesion (with almost normalized ADC) (Figure 4 and Figure 5).

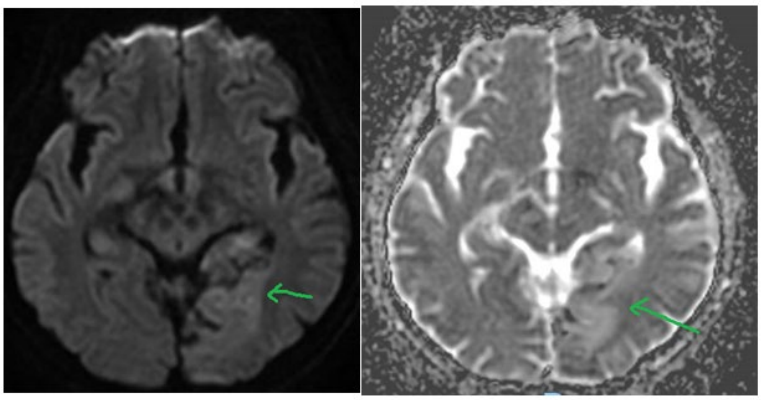
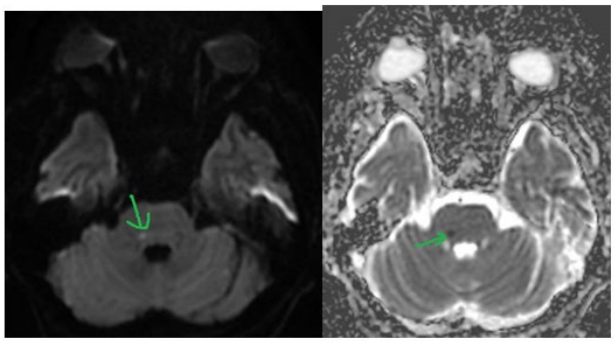
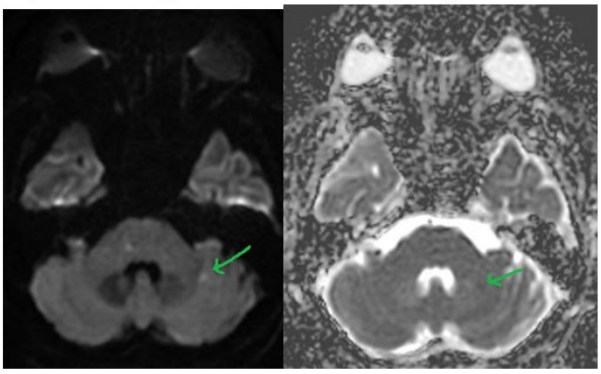


Figure 4. Lesions in the lingual gyrus and left parahippocampal gyrus



A lesion in the right paramedian pontine level next to the pontomedullary junction



A left cerebellar millimeter lesion

Figure 5. Lesions in the pons and cerebellum

3. Results

The results section explains the series of medical interventions and the medical treatment of this patient.

During admission, the management of the psychomotor agitation was delicate. We faced an uncooperative patient with extreme organic psychomotor agitation which required physical restriction and aggressive medical treatment for the confusional syndrome. The psychiatric examination revealed: unpermitted familiarity towards the medical personnel, hypersexuality, sexual disinhibition, inadequate, hostile, and denigrating jokes that did not contaminate the entourage, and physical aggression toward the auxiliary personnel.

In a multidisciplinary team composed of the neurologist and psychiatrist, a series of medical treatment heroic combinations were administered. The **first** combination was *Quetiapine* (50 mg, 1-0-1) and *Valproate* (200 mg, 1-0-1). Subsequently, the **second** combination added Tiapride and Diazepam like this: *Quetiapine* (50 mg, 1-0-1), *Valproate* (200 mg, 1-1-1), *Tiapride* (100 mg, 1-1-1) and *intravenous Diazepam* (5mg/ml dissolved in 10ml physiological serum, 1-1-1). The patient developed a paradoxical reaction to intravenous Diazepam that intensified their agitation. With a combination of 4 drugs (two antipsychotics, a thymostabilizer, and an anxiolytic), the psychomotor agitation continues and the multidisciplinary team composed of a neurologist and an anesthesiologist, sedation with Propofol was suggested. The **third** combination changed Tiapride and Quetiapine to another antipsychotic, Olanzapine, like this: *Olanzapine* (10mg, 1-0-1), *Valproate* (200 mg, 1-1-1), and *oral Diazepam* (10 mg, 1-1-1) and the agitation diminished slowly. The **fourth** combination added other antipsychotics, Levomepromazine and Haloperidol like this: *Levomepromazine* (25 mg, ½-½-1), *Olanzapine* (10 mg, 1-0-1), *Valproate* (200 mg, 1-1-1), and *oral Diazepam* (10 mg, 1-1-1) with the possibility of adding up to 50 drops of *Haloperidol* (up to 5mg) per day in case the agitation progressed. In addition, the psychiatrist on call suggested adding

intravenous Lorazepam (½ vial) in case the agitation persisted, but it was hard to procure in a multidisciplinary hospital that did not have a psychiatry ward. The patient calmed down using the fourth treatment combination. By the end of their hospitalization, the need for sedation with benzodiazepine diminished, and they were discharged only with: *Levomepromazine* (25 mg, ½-½-1), *Olanzapine* (10 mg, 1-0-1) and *Valproate* (200 mg, 1-1-1). The series of treatment combinations compared to the guideline recommendations can be seen in Figure 6.

Chronologically	Thymostabilisers		Benzodiazepins		Incisive antipsychotics		Sedative neuroleptics				Antidepressant
					Neuroleptic	Atypical	Neuroleptic	Atypical	Atypical	Sedative neuroleptic	
	CBZ	**VAL**	**DIA**	**ANX**	**HALO**	**RISP**	**TIAPRIDAL**	**QUETIAPINE**	**OLAN**	**LEVO**	**TRAZODONE**
T1		X						X			
T2		X	X				X	X			
T3		X	X						X		
T4		X	X		X				X	X	
Guideline for psychomotor agitation	L2		acute								L1
Guideline for psychotic symptoms			acute		L3	L1		L2			
CBZ= carbamazepine; VAL= Valproate; DIA= Diazepam; ANX= Lorazepam; HALO= Haloperidole; RISP= Risperidone; OLAN= Olanzapine; LEVO= Levomepromazine											

Figure 6. Treatment combinations for psychomotor agitation

In terms of neurological treatment, the patient received secondary prevention of stroke with anticoagulant for their atrial fibrillation, antihypertensives, and gastric protection.

4. Discussion

We explained the therapeutic management of the neurological and psychiatric symptoms of a patient who presented for vertebrobasilar stroke that led to strategic infarct dementia. The patient presented for acute onset psychomotor agitation, confusion, and disorientation associated with tetrameric ataxia. His first brain CT with contrast revealed a *top of basilar artery thrombosis*. The cerebral angiography showed that the thrombus was until the left posterior cerebral artery. The following brain CT revealed lesions in the occipital and parahippocampal regions. The following brain MRI revealed lesions in the lingual gyrus, parahippocampal gyrus, paramedian pons, and cerebellum.

The PCA supplies posterior structures such as the midbrain, thalamus, occipital lobe, and regions of the internal capsule and temporal lobe [3]. Also, patients with *posterior infarcts* can present aggressive symptoms, anxiety, and frustration [3, 12].

Impairment of motion perception such as *akinetopsia* was described in multiple forms of dementia such as Alzheimer's disease, dementia from Parkinson's disease, dementia with Lewy body [13]. Capgras syndrome, or delusion of double, is characterized by the false belief that someone next to the patient (medical personnel, auxiliary personnel, caregivers) was replaced with an identical duplicate of someone significant from the patient's past [14]. Capgras syndrome can appear in several brain damage such as several types of dementia, epilepsy, or stroke [14].

On the other hand, visual hallucinations are formed in the inferior temporo-occipital visual association cortex. The main organic causes for formed visual hallucinations are: metabolic disorders, acute toxicities, focal seizures, complex migraine, Lewy body dementia, *midbrain ischemia* (peduncular hallucinosis) [15]. Lesions in the occipital lobe due to a PCA infarct cause homonymous hemianopsia with macular sparing because the macula is supplied also by the middle cerebral artery [16].

The particularity of the case came from the therapeutic approach to the severe psychomotor agitation. Chronologically, the patient presented with an altered state of consciousness with a mild level of agitation, because of the posterior cerebral infarct. Further, they received antibiotic treatment for pneumonia to which they were allergic, and the agitation was exacerbated. For treating the allergic reaction we prescribed them corticoid therapy which exacerbated further the agitation. Corticoids are used to treat cerebral edema, however, steroid-related toxicities include behavioral disorders [17].

Secondly, we want to emphasize the difference between the guideline recommendations and what the heroic combination for treating psychomotor agitation. The first guideline recommendation was Trazodone. However, indications for trazodone are mainly: major depressive disorder, the group of anxiety disorders, eating disorders, and substance use disorders [18–20]. So, in our patient presentation, giving an antidepressant could exacerbate the psychotic symptoms and further increase the psychomotor agitation. Our patient presented with complex visual hallucinations, so the need for an antipsychotic was understandable [21]. The second guideline recommendation was Valproate and Carbamazepine, which was also included in our first combination. However, high doses of Valproate did not diminish enough our patient's agitation. In terms of benzodiazepines we used intravenous Diazepam which increased the confusion, but the oral administration was more effective. As for the psychotic symptoms, the first guideline recommendation was Risperidone. However, Risperidone is an antipsychotic used usually for diminishing positive psychotic symptoms, such as delusions and hallucinations. Our patient needed a more sedative antipsychotic. Further, the first guideline recommendation was Quetiapine, which was also included in our first combination. In the guideline, it is also suggested to use Ziprasidone, which is hard to procure; and Clozapine, which has a high risk of adverse reactions for our patient. Clozapine has a great risk of developing agranulocytosis [22, 23]. Haloperidol, which is also included in the guideline, has a great risk of inducing extrapyramidal syndrome, aggravating tremors and rigidity [22].

The problem and the particularity of the case were here, in the moment when we used all the recommended drugs from the Romanian guideline for treating psychomotor agitation having in mind the risks of other antipsychotic drugs and our patient's comorbidities. The third heroic combination which was outside the guideline was replacing the tried antipsychotics (Tiapride and Quetiapine) with another antipsychotic: *Olanzapine*. Some of the adverse reactions of Olanzapine are dyslipidemia, endocrine dysfunction, insulin resistance, and hyperglycemia [22]. Our patient did not have diabetes, his lipid profile was under control. Moreover, he suffered from atrial fibrillation, so the probable mechanism for his vertebrobasilar stroke was cardioembolic, not atherosclerotic. Another benefit of Olanzapine was the administration, using the sublingual tablets which was beneficial for an agitated patient. However, we needed to augment the treatment combination with *Levomepromazine*. The main advantage of Levomepromazine was its sedative effect [23, 24].

5. Conclusions

The particularity of the case came from the therapeutic approach for treating some psychiatric symptoms in a neurological patient with strategic infarct dementia in the context of vertebrobasilar stroke that was revascularised with mechanical thrombectomy and intraarterial thrombolysis. In addition, we highlight the need for extensive treatment guidelines, for heroic therapies that can be used in severe cases of psychomotor agitation. Particularly, in our case, we highlight the benefits of Olanzapine and Levomepromazine as sedative antipsychotics for treating psychomotor agitation and psychotic symptoms in a stroke patient. We highlight the need for extensive treatment guidelines for severe cases of psychomotor agitation.

Author Contributions: Conceptualization, A.I.V., C.N., C.T.; methodology, A.I.V., C.N., C.T.; software, A.I.V., C.N., C.T.; validation, A.I.V., C.N., C.T.; formal analysis, A.I.V.; investigation, A.I.V., C.N., C.T.; resources, A.I.V., C.N., C.T.; data curation, A.I.V., C.N., C.T.; writing—original draft preparation, A.I.V.; writing—review and editing, A.I.V., C.N., C.T.; visualization, C.T.; supervision, C.T; project administration, C.T. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted in accordance with the Declaration of Helsinki, and approved by the Ethics Committee of Carol Davila University of Medicine and Pharmacy, Bucharest, Romania.

Informed Consent Statement: Written informed consent for participation in this study was provided by the patient for publication of any potentially identifiable images, personal history, personal details, or data included in this article. Written informed consent has been obtained from the patient to publish this paper.

Data Availability Statement: Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Anor CJ, O'Connor S, Saund A, et al (2017) Neuropsychiatric Symptoms in Alzheimer Disease, Vascular Dementia, and Mixed Dementia. Neurodegener Dis 17:127–134. https://doi.org/10.1159/000455127
2. Carrarini C, Russo M, Dono F, et al (2021) Agitation and Dementia: Prevention and Treatment Strategies in Acute and Chronic Conditions. Front Neurol 12:644317. https://doi.org/10.3389/fneur.2021.644317
3. Sanker V, Mathew R, Pranala M, et al (2022) Cognitive Impairment in Strategic Infarct Dementia: A Report of Three Cases. Cureus 14:e30009. https://doi.org/10.7759/cureus.30009
4. Khan A, Kalaria RN, Corbett A, Ballard C (2016) Update on Vascular Dementia. J Geriatr Psychiatry Neurol 29:281–301. https://doi.org/10.1177/0891988716654987
5. Weininger J, Roman E, Tierney P, et al (2019) Papez's Forgotten Tract: 80 Years of Unreconciled Findings Concerning the Thalamocingulate Tract. Front Neuroanat 13:14. https://doi.org/10.3389/fnana.2019.00014
6. Maeshima S, Osawa A (2021) Memory Impairment Due to Stroke. In: Departments of Radiology and Neurology, New York University Langone Medical Center, New York, NY, USA, Dehkharghani S (eds) Stroke. Exon Publications, pp 111–120
7. Starkstein SE, Mizrahi R, Power BD (2008) Depression in Alzheimer's disease: Phenomenology, clinical correlates and treatment. International Review of Psychiatry 20:382–388. https://doi.org/10.1080/09540260802094480
8. Lonergan E, Luxenberg J (2004) Valproate preparations for agitation in dementia. In: The Cochrane Collaboration (ed) Cochrane Database of Systematic Reviews. John Wiley & Sons, Ltd, Chichester, UK, p CD003945.pub2
9. Olin JT, Fox LS, Pawluczyk S, et al (2001) A pilot randomized trial of carbamazepine for behavioral symptoms in treatment-resistant outpatients with Alzheimer disease. Am J Geriatr Psychiatry 9:400–405
10. Burns A, De Deyn PP (2006) Risperidone for the Treatment of Neuropsychiatric Features in Dementia: Drugs & Aging 23:887–896. https://doi.org/10.2165/00002512-200623110-00004
11. Lacasse H, Perreault MM, Williamson DR (2006) Systematic Review of Antipsychotics for the Treatment of Hospital-Associated Delirium in Medically or Surgically III Patients. Ann Pharmacother 40:1966–1973. https://doi.org/10.1345/aph.1H241
12. Kuybu O, Tadi P, Dossani RH (2024) Posterior Cerebral Artery Stroke. In: StatPearls. StatPearls Publishing, Treasure Island (FL)
13. Barton JJS (2021) Motion perception and its disorders. In: Handbook of Clinical Neurology. Elsevier, pp 257–275
14. Shah KP, Jain SB, Wadhwa R (2024) Capgras Syndrome. In: StatPearls. StatPearls Publishing, Treasure Island (FL)
15. Penney L, Galarneau D (2014) Peduncular hallucinosis: a case report. Ochsner J 14:450–452
16. Fraser JA, Newman NJ, Biousse V (2011) Disorders of the optic tract, radiation, and occipital lobe. In: Handbook of Clinical Neurology. Elsevier, pp 205–221
17. Lim-Fat MJ, Bi WL, Lo J, et al (2019) Letter: When Less is More: Dexamethasone Dosing for Brain Tumors. Neurosurgery 85:E607–E608. https://doi.org/10.1093/neuros/nyz186
18. Bossini L, Coluccia A, Casolaro I, et al (2015) Off-Label Trazodone Prescription: Evidence, Benefits and Risks. CPD 21:3343–3351. https://doi.org/10.2174/1381612821666150619092236

19. Carboni L, Rullo L, Caputi FF, et al (2022) Chronic Trazodone and Citalopram Treatments Increase Trophic Factor and Circadian Rhythm Gene Expression in Rat Brain Regions Relevant for Antidepressant Efficacy. IJMS 23:14041. https://doi.org/10.3390/ijms232214041
20. Goracci A, Forgione RN, De Giorgi R, et al (2016) Practical guidance for prescribing trazodone extended-release in major depression. Expert Opinion on Pharmacotherapy 17:433–441. https://doi.org/10.1517/14656566.2016.1133587
21. Trifu S, Gutt A (2015) Interpretative Process–From Utilization of Predominant to Psychotic Decompensation. Procedia - Social and Behavioral Sciences 187:429–433. https://doi.org/10.1016/j.sbspro.2015.03.080
22. Piłat P, Nikel K, Smolarczyk J, Piegza M (2024) The Use of Ascorbic Acid in Adjunctive Treatment for Schizophrenia—Current State of Knowledge. Life 14:828. https://doi.org/10.3390/life14070828
23. Trifu S, Trifu AD (2020). RECEPTOR PROFILES OF ATYPICAL ANTIPSYCHOTIC MOLECULES. U.P.B. Sci. Bull., Series B, vol 82, issue 1, 113-128
24. Richards CA (2020) Postfundoplication retching: Strategies for management. Journal of Pediatric Surgery 55:1779–1795. https://doi.org/10.1016/j.jpedsurg.2020.03.032