RESEARCH ARTICLE

Cognition in Patients with Dementia: Ambulation vs Affective Disorders

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Abstract

Background: It is known that physical disabilities, and affective disorders affect the progression of dementia, cognitive decline, and therefore influence medication regimen and therapeutic interventions. According to Bennett et al the relationship between depression and dementia is complex and still not well understood [1]. Per Magdalena et al a decline in cognition is associated with a decline in mobility [2]. The aim of this research is to characterize depression / anxiety and mobility as they influence cognitive decline in dementia, in the assisted living environment. Therefore, leading to identifying patient risk and development of potential treatment interventions and appropriate therapies.

Objectives: To analyze the relationships between dementia, depression/anxiety and ambulation to determine their relative roles in cognitive performance and suggest treatment strategies.

Methods: This IRB approved study recruited residents from 3 memory care facilities with established diagnosis of mild, moderate, or severe dementia. Diagnosis was confirmed by patient exam, chart review and Mini2 Mental State Exam (MMSE) score. There were 81, power of attorney, consented participants. This sample size (N=81) included 47 females and 34 males, with an age range from 58 to 98 years. After analyzing 34 clinical data points (i.e. medications, number of falls, smoking history and others) ANOVA and Kruskal-Wallis analysis found a relationship between lack of ambulation, affective disorder and cognitive performance, leading to a comparison between these data to determine which has a greater impact on cognitive performance.

Results: Wheelchair-bound patients with dementia averaged a lower MMSE score (9.78) than ambulatory participants (14.4) with a statistical significance of p=0.03. Wheelchair-bound participants with depression or anxiety averaged the lowest MMSE score (8.77) than ambulatory participants with the same affective disorders (14.9) with a statistical significance of p=0.01.

Conclusion: Dementia patients, who are ambulatory regardless of affective comorbidity score higher on MMSE while those that were wheelchair-bound, appear to have worse cognitive status. Wheelchair-bound patients, who are concomitantly suffering from depression or anxiety, may be specifically at higher risk for detrimental cognitive effects in their dementia progress. Presenting the opportunity for a more tailored therapeutic ambulatory intervention.

Keywords: Dementia, Depression, Anxiety, Affective Disorder, Wheelchair, Ambulatory.

1. Background

Dementia is a leading cause of disability among older adults, a loss of independence follows[1]. Losing the ability to maintain proper hygiene[2], remembering one's living situation[3], and even forgetting familial faces[3], are but a few cognitive symptoms observed as dementia progresses. Though initial symptoms present as a cognitive decline, motor deficits ensue[4]. Individuals report motor deficits in bladder control,

difficulty swallowing, and of particular interest for this study, a decline in ambulation[5-6], leading to a need for wheelchair use.Furthermore, it has been well reported that sustained signs and symptoms of depression are more common amoungst older individuals with dementia[14]. The temporal and contributory relationship between dementia, depression and ambulation is unclear. Therefore, this study aims to sort out potential significance between these factors.

For a significant number of individuals, a decline in ambulation begins with a decrease in balance and gait coordination[7]. Balance deficits can be observed in the early stages of dementia[7]. As deficits worsen, fall risk increases with 40-60% of patients falling each year[7-9]. Therefore identifying potential fall causes and prevention strategies are key. A common treatment for fall prevention is wheelchair use, providing a level of safety and mobility. However, prolonged wheel chair use can lead to pressure ulcers, delayed wound healing, and an increased level of dependence on caretakers[6]. As studies have shown, the loss of independence and the need for a wheelchair serves as a significant factor in how patients determine their quality of life[12]. Dementia association with a loss of ambulation lead to poorer quality of life outcomes[13]. Minimizing wheelchair use in patients with dementia can prove beneficial.

In addition, it has been reported that patients with dementia have a higher incidence for exhibiting signs of depression[14], with at least a three-fold incidence in the physically disabled[15-16]. Compared to cognitively-normal individuals, older adults with cognitive impairment tend to perform poorly on mobility tests and report higher levels of disabilityX. While current literature highlights the complex relationship between dementia and affective disorders as well as depression and disability, their relative impact is unclear. This study aims to look at the level of dementia, affective disorders and a lack of ambulation, in comparison to ambulatory counterparts.

2. Methods

This IRB approved study recruited residents, from three assisted living memory care communities, with established clinical diagnosis of mild, moderate, or severe dementia. Diagnosis was confirmed by patient clinical exam, chart review, and Mini-Mental State Exam (MMSE). There were 81, power of attorney, consented participants. This sample size (N=81) included 47 females and 34 males (gender is described as binary), with an age range of 58 to 98 years. Exclusion criteria included: Subjects who were

unable to complete MMSE, unable to or declined participation, no established dementia diagnosis, had acute medical issues, below age 55 or above 100. Likewise, clinical affective disorder diagnosis was confirmed by presenting signs and symptoms, history, chart review, and patient exam. Given the sample size a binary affective disorder definition was used. Although the MMSE is a screening tool, it can be used to categorize dementia into mild (20-30), moderate (10 - 19) and severe (0 - 9). The ease of MMSE administration makes it a very good tool in the assisted living memory care communities.

To evaluate the current level of dementia, each participant was given a one-time administration of the MMSE. The study did not distinguish amongst different types of dementia. Ambulation status (walking with or without the use of a cane) and the presence of affective disorder (depression and/or anxiety) were analyzed with respect to MMSE score. ANOVA single factor was used to assess statistical significance. To account for any discrepancy in variances, Kruskal–Wallis testing was further applied.

Participant data was organized into 3 cohorts. Cohort 1 included wheelchair bound versus ambulatory participants. Cohort 2 included participants suffering affective disorders versus their otherwise psychiatrically healthy counterparts. Cohort 3 included participants with both an affective disorder and wheelchair use versus participants with an affective disorder and no wheelchair use. For each cohort, the difference in mean MMSE was calculated and tested by Kruskall–Wallis against the null hypothesis.

3. Results

When analyzing the MMSE scores for wheelchair-bound participants and their ambulatory counterparts, wheelchair-bound participants exhibited significantly lower MMSE scores (Figure 1). In comparing MMSE scores based on the presence or absence of depression and/or anxiety, MMSE scores were not significantly different (Figure 2). Participants who were both wheelchairbound and diagnosed with depression and/or anxiety exhibited significantly lower MMSE scores than their ambulatory counterparts with affective disorders (Figure 3).

Figure 4 is a subset of Figure 1, showing distribution by gender (15 wheelchair-bound males, 19 ambulatory males, 17 wheelchair-bound females, 30 ambulatory females). The relationship between wheelchair use and MMSE score is similar for males and females. Likewise there are similar MMSE scores for ambulatory males and females. The Lower

MMSE scores were shared equally among wheelchair bound males and females suffering depression and/or anxiety. Gender was not a confounding variable for the results shown in this work.
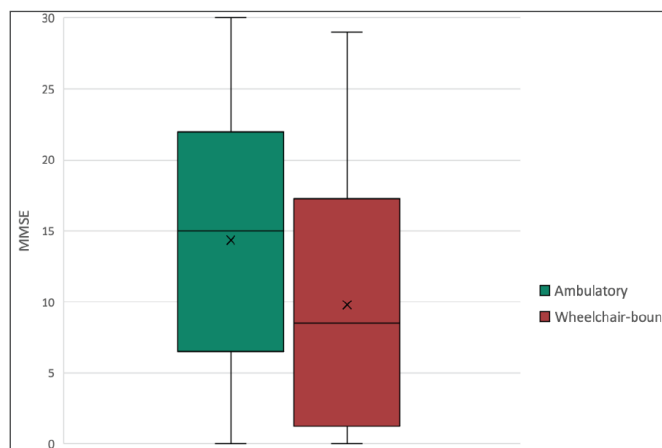

Figure 1. *MMSE Distribution Based on Ambulatory Status*

Comparison between ambulatory vs non-ambulatory groups. Both groups have a dementia diagnosis. Wheelchair bound groups exhibited lower MMSE scores (Avg. MMSE = 9.78) than their ambulatory counterparts (Avg. MMSE = 14.43) ($p = 0.03$).
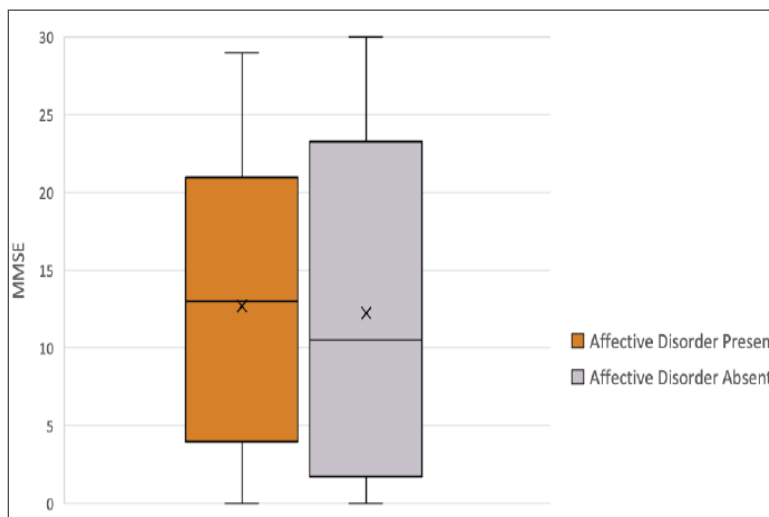

Figure 2. *MMSE Distribution Based on Presence/Absence of Affective Disorder*

Groups with affective disorder exhibited similar MMSE scores (Avg. MMSE = 12.73) to groups without affective disorder (Avg. MMSE = 12.23) ($p = 0.71$).
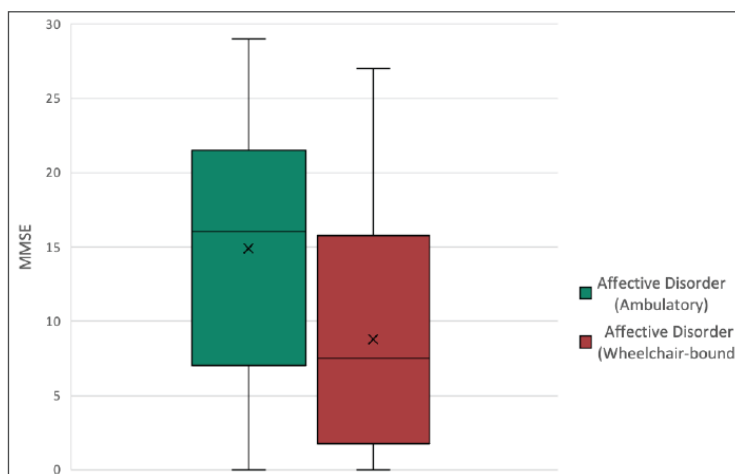

Figure 3. *Distribution of Wheelchair-bound and Ambulatory*

Participants with Affective Disorder Wheelchair-bound participants suffering from affective disorder exhibited lower MMSE scores (Avg. MMSE = 8.77) than their ambulatory counterparts (Avg. MMSE = 14.87) ($p = 0.01$).

Figure 4 is a subset of Figure 1, showing distribution by gender (15 wheelchair-bound males, 19 ambulatory males, 17 wheelchair-bound females, 30 ambulatory females). The relationship between wheelchair use and MMSE score is similar for males and females. Likewise there are similar MMSE scores for ambulatory males and females. The Lower MMSE scores were shared equally among wheelchair bound males and females suffering depression and/or anxiety. Gender was not a confounding variable for the results shown in this work.
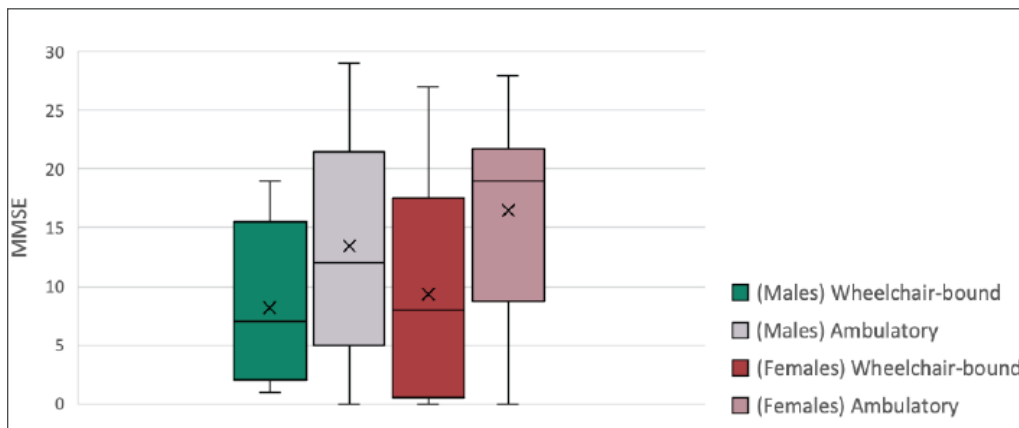

Figure 4. *Distribution by Ambulation Status and Gender*

Both wheelchair-bound males and females exhibited similar cognitive performance. Wheelchair-bound males revealed lower MMSE scores (Avg. MMSE = 8.22) than ambulatory males (Avg. MMSE = 13.41) (p = 0.18).Wheelchair-bound females revealed lower MMSE scores (Avg. MMSE = 9.33) than ambulatory females (Avg. MMSE = 16.44) (p = 0.07).

There appears to be a relationship between greater MMSE scores and ambulation regardless of whether the subjects have affective disorder or not (Table 1), with wheelchair-bound subjects scoring lower.

Table 1. Above is representation of all subjects (N=81), showing mean MMSE scores for the following categories ambulatory status versus affective disorder. Row 1 is demonstrative of figure 1 and row 2 is demonstrative of figure 3.

Table 1. *Ambulatory status versus affective disorder.*

	Ambulatory (column 1)	Wheelchair-bound (column 2)
Affective Disorder Absent (row1)	14.43	9.78
Affective Disorder Present (row 2)	14.87	8.77

4. Discussion

Note the similarities between the data in figure 1 and figure 3, possibly signifying that ambulation seems to play a greater positive significant role in the level of dementia. In figure 1, the mean MMSE values for ambulatory without affective disorder is 14.43 and in Figure 3 the mean MMSE for ambulatory with affective disorder is 14.87. Not taking into account the presence of affective disorder, the MMSE remains similar. Whether this relationship is causative or reactive is yet to be determined. If causative, it could potentially be beneficial to maintain ambulation as much as possible.

The lack of ambulation regardless of affective disorder shows a lower mean MMSE (Table 1 Column 2). Although subjects without affective disorder score slightly greater on mean MMSE 9.78 compared to 8.77 (those with affective disorder). Therefore, clinically affective disorder should not be the only factor assessed in regards to lack of ambulation.

Amongst those not suffering from affective disorder a lack of ambulation significantly contributed to a lower mean MMSE (Table 1, Row 1) and in those suffering from affective disorder, a similar pattern is seen (Table 1, Row 2). As the data suggests, the ability to maintain ambulation may show the benefit of being categorized in the moderate level as opposed to the severe level of dementia. This has consequences on how the patient is viewed, medically treated, potential for therapies and unforeseen burden on caregivers and family members. Depression and dementia, while two separate entities, have a rather complex relationship. While today's literature agrees that

depression is a risk factor, rather than a prodrome, for dementia, it has yet to be determined whether or not increased dementia risk is due to early or late onset of depression; it is known that timing of depression plays a large role[23-27]. Our study indicates that the presence or absence of affective 11 disorder does not have a bearing on the severity of dementia in ambulatory patients. Therefore, it is suggested that treating affective disorders appropriately could lead to improved ambulation. This study suggests a relationship between mobility and a greater MMSE score, however it has certain limitations. Given the small sample size (N=81) dementia was not separated into different types. The data is clinical in nature and future studies can utilize proven scales to determine level of affective disorder and separate into depression and anxiety. MMSE is an established method of categorizing dementia levels in the assisted living population; future studies can use neuropsychological testing and include controls.

As clinicians, we look to categorize patients correctly and identify potential treatment strategies and therapeutic interventions. This study suggests that ambulation may be beneficial in the cognitive level of patients with dementia. Therefore, providing appropriate physical therapy and ambulatory strategies may prove beneficial.

5. References

1. Satizabal, C. L., Ph.D., Beiser, A. S., Ph.D., Chouraki, V., M.D., Chene, G., M.D., Dufouil, C., Ph.D., & Seshadri, S., M.D. (2016, February 11). Incidence of Dementia over Three Decades in the Framingham Heart Study: NEJM. Retrieved from https://www.nejm.org/doi/full/10.1056/NEJMoa1504327

2. Hamdy, R. C., MD, Kinser, A., PhD, Culp, J. E., BFA, Kendall-Wilson, T., RN, Depelteau, A., PhD, Copeland, R., MD, & Whalen, K., BA. (n.d.). Agnosia Interferes With Daily Hygiene in Patients With Dementia - R. C. Hamdy, A. Kinser, J.E. Culp, T. Kendall-Wilson, A. Depelteau, R. Copeland, K. Whalen, 2018. Retrieved from https://journals.sagepub.com/doi/full/10.1177/2333721418778419

3. Memory Loss and Confusion. (n.d.). Retrieved from https://www.alz.org/helpsupport/ caregiving/stages-behaviors/memory-loss-confusion

4. Boller, F., Verny, M., Hugonot-Diener, L., & Saxton, J. (2002, March 07). Clinical features and assessment of severe dementia. A review1. Retrieved from https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1468-1331.2002.00356.x

5. Mitchell, S. L., M.D., M.P.H. (2015, September 24). Advanced Dementia: NEJM. Retrieved from https://www.nejm.org/doi/full/10.1056/NEJMcp1412652

6. Mortenson, W., PhD, Oliffe, J., PhD, Miller, W., PhD, & Backman, C., PhD. (2012, March). Grey spaces: The wheeled fields of residential care. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4014430/

7. Gras, L., Kanaan, S., McDowd, J., Colgrove, Y., Burns, J., & Pohl, P. (2015). Balance and gait of adults with very mild Alzheimer disease. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4632639/

8. Fernando, E., MPT, Fraser, M., MPT, Hendriksen, J., MPT, Kim, C., MPT, & Muir-Hunter, S., PhD, PT. (2017). Risk Factors Associated with Falls in Older Adults with Dementia: A Systematic Review. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5435396/

9. Ganz, D. A., M.D., Ph. D, & Latham, N. K., P.T., Ph.D. (2020, June 25). Prevention of Falls in Community-Dwelling Older Adults: NEJM. Retrieved from https://www.nejm.org/doi/full/10.1056/NEJMcp1903252

10. Deal, PhD, J. A., Reed, AuD, N. S., Kravetz, PharmD, A. D., Weinreich, MD, MPH, H., Yeh, MD, C., Lin, MD, PhD, F. R., & Altan, PhD, A. (2019, January 01). Incident hearing loss and comorbidity. Retrieved from https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2714050

11. Deal, PhD, J. A., Reed, AuD, N. S., Kravetz, PharmD, A. D., Weinreich, MD, MPH, H., Yeh, MD, C., Lin, MD, PhD, F. R., & Altan, PhD, A. (2019, January 01). Incident hearing loss and comorbidity. Retrieved from https://jamanetwork.com/journals/jamaotolaryngology/fullarticle/2714050

12. Tolea, M. I., Ph.D., Morris, J. C., M.D., & Galvin, J. E., M.D., M.P.H. (2016). Trajectory of Mobility Decline by Type of Dementia. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4592781/

13. Van de Beek, M., Van Steenoven, I., Ramakers, I., Aalten, P., Koek, H., Olde Rikkert, M., . . Van der Flier, W. (2019). Trajectories and Determinants of Quality of Life in Dementia with Lewy Bodies and Alzheimer's Disease. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6839497/

14. Kitching, D. (2015, December). Depression in dementia. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4674029/

15. Noh, J., Kwon, Y., Park, J., Oh, I., & Kim, J. (2016, November 30). Relationship between Physical Disability and Depression by Gender: A Panel Regression Model. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5130183/

16. Shen, S., Huang, K., Kung, P., Chiu, L., & Tsai, W. (2017, March 31). Incidence, risk, and associated factors of depression in adults with physical and sensory disabilities: A nationwide population-based study. Retrieved 2020, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5376337/

17. Van Ooteghem, K., Musselman, K., Mansfield, A., Gold, D., Marcil, M., Keren, R., . . . Iaboni, A. (2019, August 31). Key factors for the assessment of mobility in advanced dementia: A consensus approach. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6726753/

18. Buchman, A., & Bennett, D. (2011, May). Loss of motor function in preclinical Alzheimer's disease. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3121966/

19. Burton, E., PhD, McKeith, I., MD, Burn, D., MD, & O'Brien, J., DM. (2005, August 22). Brain atrophy rates in Parkinson's disease with and without dementia using serial magnetic resonance imaging. Retrieved from https://onlinelibrary.wiley.com/doi/abs/10.1002/mds.20652

20. Peters, R. (2006, February). Ageing and the brain. Retrieved from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2596698/

21. Bocchetta, M., Gordon, E., Cardoso, M., Modat, M., Ourselin, S., Warren, J., & Rohrer, J. (2020, December 22). Thalamic atrophy in frontotemporal dementia - Not just a C9orf72 problem. Retrieved from https://www.sciencedirect.com/science/article/pii/S2213158218300536

22. Hornberger, M., Savage, S., Hsieh, S., Mioshi, E., Piguet, O., & Hodges, J. (2011, January 20). Orbitofrontal Dysfunction Discriminates Behavioral Variant Frontotemporal Dementia from Alzheimer's Disease. Retrieved from https://www.karger.com/Article/FullText/321670

23. Brommelhoff, J. A., Gatz, M., Johansson, B., McArdle, J. J., Fratiglioni, L., & Pedersen, N. L. (n.d.). Depression as a risk factor or prodromal feature for dementia? Findings in a population-based sample of Swedish twins. Retrieved from https://pubmed.ncbi.nlm.nih.gov/19485655/

24. Jorm, A. (2000, June 16). Is Depression a Risk Factor for Dementia or Cognitive Decline? Retrieved 2020, from https://www.karger.com/Article/Abstract/22163

25. Byers, A., & Yaffe, K. (2011, May 3). Depression and risk of developing dementia. Retrieved 2020, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3327554/

26. Li, G., MD, PhD, Wang, L. Y., MD, Shofer, J. B., MS, Thompson, M. L., PhD, Peskind, E. R., MD, McCormick, W., MD,MPH, . . . Larson, E. B., MD, MPH. (2011, September 01). Temporal Relationship Between Depression and Dementia. Retrieved 2020, from https://jamanetwork.com/journals/jamapsychiatry/fullarticle/1107276

27. Muliyala, K., & Varghese, M. (2010, December). The complex relationship between depression and dementia. Retrieved 2020, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3039168/

28. Buyukdura, J., McClintock, S., & Croarkin, P. (2011, March 30). Psychomotor retardation in depression: Biological underpinnings, measurement, and treatment. Retrieved 2020, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3646325/

29. Vitanova, K., Stringer, K., Benitez, D., Brenton, J., & Cummings, D. (2019, August 07). Dementia associated with disorders of the basal ganglia. Retrieved 2020, from https://onlinelibrary.wiley.com/doi/epdf/10.1002/jnr.24508

30. Ryu, S., Jung, H., Lee, K., Moon, S., Lee, D., Hong, N., . . . Lee, C. (2017, May). Incidence and Course of Depression in Patients with Alzheimer's Disease. Retrieved 2020, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5440429/

31. Chi, S., Yu, J., Tan, M., & Tan, L. (n.d.). Depression in Alzheimer's disease: Epidemiology, mechanisms, and management. Retrieved 2020, from https://pubmed.ncbi.nlm.nih.gov/24946876/

32. National Collaborating Centre for Mental Health (UK). (1970, January 01). THERAPEUTIC INTERVENTIONS FOR PEOPLE WITH DEMENTIA – COGNITIVE SYMPTOMS AND MAINTENANCE OF FUNCTIONING. Retrieved from https://www.ncbi.nlm.nih.gov/books/NBK55462/

33. Barnes, D., Mehling, W., Wu, E., Beristianos, M., Yaffe, K., Skultety, K., & Chesney, M. (2015, February 11). Preventing loss of independence through exercise (PLIÉ): A pilot clinical trial in older adults with dementia. Retrieved 2020, from https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4324943/