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EXAMINING THE RELATIONSHIP BETWEEN ALZHEIMER'S DISEASE, DEPRESSION, AND SOCIAL SUPPORT

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EXAMINING THE RELATIONSHIP BETWEEN ALZHEIMER'S DISEASE, DEPRESSION, AND SOCIAL SUPPORT

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ABSTRACT

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This study examined the relationship between Alzheimer's Disease and depression to determine whether a correlation existed and whether depression led to greater outcomes of Alzheimer's Disease. Depression-Alzheimer's relations have been mixed in previous research. Data from an existing data set of visitors to the Alzheimer's Disease Centers with three or more visits (N= 19, 652) was used to test correlations between depression and Alzheimer's, later odds of developing Alzheimer's, and possible moderating effects of social support. A positive correlation was found between depression and Alzheimer's Disease. Patients with depression were found to be more likely to have Alzheimer's. There was also greater chance of Alzheimer's in those living with others (the indicator of social support). An interaction between depression and living situation also found increased odds but not as great as both items on their own. Results were consistent with hypothesis that a relationship between depression and Alzheimer's existed and that depressed individuals had greater odds of having Alzheimer's.

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INTRODUCTION

Dementia is a clinical syndrome defined by progressive decline in two or more cognitive domains such as memory, language, executive and visuospatial function, personality, and behavior, which causes loss of abilities to perform instrumental and/or basic activities of daily living (Weller and Budson, 2018). Five to 10 percent of the US population aged over 65 years suffers from a dementing disorder with the incidence doubling every five years after the age of 65 (Polidori et al., 2001).

AD, defined by its key feature of memory disturbance, is the most common form of dementia, accounting for between 66% and 80% of dementia cases, and is a leading cause of disability in late life (Crous-Bou et al., 2017; Cummings & Benson, 1986; Polidori et al., 2001; Prince et al., 2013). Although the overall death rate from other causes, such as stroke and heart disease, is decreasing, the rate of death from AD has increased by 89% between 2000 and 2014 (Alzheimer's Association, 2017). Given the predicted increase in life expectancy, this mortality rate, due to AD, will likely increase (Rizz, Rosset, & Roriz-Cruz, 2014). In AD, behavioral changes have been present in up to 88% of patients (Hart et al., 2003). These behavioral syndromes have been categorized into three basic groups; one group is defined by a few behavioral abnormalities, another by prominent symptoms of psychosis, and a third by a prominent mood disorder (McKeith and Cummings, 2005). The most common mood disorder, affecting half of patients, is depression (Hart et al., 2003; Di Iulio et al., 2010).

In patients early in their AD diagnosis, complaints about depressive symptoms have been observed more frequently, as well as roughly half of them potentially fulfilling the criteria for major depression (Polidori et al., 2001). Often, depression, which has a prevalence rate that increases with advancing age, is undetected the elderly due to the assumption by family and care providers that depressive symptoms are a normal subject of aging. Depression has also been shown to manifest as persistent sadness, vegetative symptoms, or a tendency to cry that may be reflective of a reaction to perceived cognitive decline. Among the elderly who are hospitalized prevalence rates for depression has been seen to vary with some studies finding the rate to be over 20% (Burn et al., 1993; Hammond et al., 1993; O'Riordan et al., 1989). Other studies have found the prevalence rate for depression to be between 35-45% of the elderly who are hospitalized (Kitchell et al., 1982; Koenig et al., 1988; Rapp et al., 1988). Theoretical models of depression in late life propose several vulnerability factors that may interact, including a decline in health and function and early or midlife depression (Fiske et al., 2009). Another theory with increasing evidence suggests that the pathological mechanisms induced by chronic stress may be a key factor in predisposing individuals with chronic stress or stress-related psychiatric disease, such as depression, to long term neurodegenerative diseases such as AD (Ross et al., 2018).

Comorbid prevalence rates vary for depression and dementia with some research indicating an 8.7% rate (Chiu et al., 2017). This rate increases when focusing specifically on AD. Other studies found that the association between depressive dementia with subsequent degenerative dementia ranged from 38% to 50% for depressive dementia (Lee and Lykestsos, 2003; Linka et al., 2000). When looking at the severity of depression with

AD, the rate differs as well. Research has found the rate of Major Depressive Disorder (MDD) to be comorbid with AD 25% of the time while less severe minor depression has been found to be comorbid at a rate of 27.4% (Linka et al., 2000). The rate varies again when using different criteria to define MDD. When using DSM-IV criteria to define MDD, the rate of comorbidity was found to be 12.7% whereas criteria specific to AD found the rate to be 40% (American Psychiatric Association, 1994; Olin et al., 2002). Studies have found that a significant correlation between depression and cognitive impairment exists with greater cognitive deterioration in individuals with depression (Sadavoy et al., 1990; Rovner et al., 1989).

While research indicates a correlation between AD and depression, research is mixed on the direction in which the correlation runs. Some studies have found Depression to be a risk factor for AD in several case and cohort studies (Cooper and Holmes, 1998; Green et al., 2003; DalForno et al., 2005; Kessing and Nilson, 2003; Saczynski et al., 2010; Dotson et al., 2010; Byers and Yaffie, 2011). Supporting these findings are a number of meta-analysis that confirmed the association in general and finding that depression approximately doubles the risk of AD (Jorm, 2001; Ownby et al., 2006; Silva et al., 2013). Further studies have found that depressive symptoms in the elderly has been associated with clinical AD in cross sectional studies and longitudinal studies found that a risk of cognitive decline and dementia exists in those with depressive symptoms (Green et al., 2003, Wilson et al., 2003, Ownby et al., 2006). Chen et al (1999) found that patients developed AD within four years of presenting with depressive symptoms. In a co-twin control analysis, which controlled for genetic and early

environmental risk factors shared by the twins, twins with a history of depression were three times more likely to have AD than their co-twin (Brommelhoff et al., 2009).

Despite the evidence suggesting that depression may be a risk factor for AD, there exists evidence that the relationship may be more complicated than presented. Several studies have found that a higher risk of dementia only for depressive episodes that developed for the first time in closer proximity to dementia onset (Berger et al., 1999; Chen et al., 1999; Wetherell et al., 1999; Yaffe et al., 1999). The authors theorized that depression may be a prodromal feature of dementia, rather than a risk factor, and that depression may manifest as an early symptom. Further evidence comes from a meta-analysis conducted by Ownby and colleagues (2006) using 13 studies to analyze the relationship of interval length between diagnosis of depression and AD. The meta-analysis found a positive association between length of interval between diagnoses and increased risk of AD later in life. It should be noted that of the 13 studies used, only two showed that a diagnosis of depression 10 years prior to AD onset was associated with a higher risk of developing AD and this was only found to be true among individuals with a lower level of education (Ownby et al., 2006). Other studies have found that greater cognitive impairment and past psychiatric disorder is predictive of depression in Alzheimer's (Steck et al., 2018).

Another possibility is that a third factor may moderate the relationship between the two. Single studies have found that younger age, lower education level, being within closer onset to dementia, having a family history of psychiatric disorder, neuroticism, functional decline, presence of sleep disturbance and aggression and increased cardiovascular risk may result in greater risk of comorbid depression with AD (Steck et

al., 2018). Another possible factor is the heterogeneity of depression. Some studies have shown an inconsistent relationship between more severe depression (expressed by a higher frequency, duration, and severity of depressive episodes) and higher risk of dementia (Kessing and Andersen, 2004; Geerlings et al., 2008; Kessing, 2012; Silva et al., 2013).

The aim of this study was to determine whether a diagnosis of depression would result in greater likelihood of AD. The study focused on observing and determining the direction of the correlation between depression and AD presentation, as well as determine the likelihood a diagnosis of depression would have on a diagnosis of AD. It was predicted that there would be a correlation between depression and AD would exist. It was further hypothesized that a diagnosis of depression would be positively correlated with a diagnosis of AD such that a depression diagnosis would result in a greater likelihood for a diagnosis of AD.

A secondary aim of the study was to determine whether some other factor moderates the relationship between AD and depression. It was hypothesized that social support, characterized by living with others, would moderate the relationship between depression and AD. It is expected that increased social support, when combined with depression, would result in decreased presentation of AD.

STATEMENT OF PURPOSE

The first purpose of this project is to conduct a bivariate correlational analysis between diagnosis of depression and diagnosis of Alzheimer's Dementia (AD). Research has shown a relationship between depression and AD but has been mixed as to the exact relationship between the two (Simones do Couto et al., 2016). The second purpose is to conduct a logistic regression in order to determine the odds of an individual with depression being diagnosed with AD as well. Research has indicated that depression could be a risk factor of AD later in life (Cooper and Holmes, 1998; Green et al., 2003; DalForno et al., 2005; Kessing and Nilson, 2003; Saczynski et al., 2010; Dotson et al., 2010; Byers and Yaffie, 2011). The final purpose of the study is to determine whether an outside factor, in this case social support, moderates the relationship between depression and AD.

MATERIALS AND METHODS

Data Source

This study used the Uniform Data Set (UDS) collected by the National Alzheimer's Coordinating Center. Data was collected from Alzhiemer's Disease Centers (ADC) from 2005 to 2019. The UDS consisted of data contributed using prospective, standardized, and longitudinal clinical evaluation of subjects in the National Institute on Aging's ADC program. Data was collected by clinicians, neuropsychologists, and other ADC research personnel, using up to 18 standardized forms at each visit. Some forms had Spanish language and telephone versions. These forms included topics on sociodemographics, family history, dementia history, neurological exam findings, functional status, neuropsycholigical test results, clinical diagnosis, imaging availability, and APOE genotype. The UDS had experienced two expansions over time. The first, implemented in 2012, was done in order to collect detailed clinical information related to frontotemporal lobar degeneration. The second expansion, implemented in 2015, was done to collect information on Lewy Body Disease. Both expansions were completed by ADCs on a voluntary basis and were not expected to have any impact on those diagnosed with AD

Participants

A total of 42,022 were enrolled in the data collection between 2005 to early 2019 when the data set was obtained. Of those enrolled, 19,652 were retained through three or more visits to the ADC.

Measures

Diagnosis of depression was determined based on clinical observation of the patient. Depression was scored using a binary scoring system in which the only responses

were if the participant was diagnosed with depression or whether diagnosis was not observed or diagnosed.

Diagnosis of AD was determined in a similar manner in which clinical observation of the patient was conducted and diagnosis based on this observation. AD was scored using three responses

Raters

Data was gathered by clinical research staff at the NACC ADCs following training in the UDS data gathering procedure.

Demographics

Included in the UDS were questions to characterize the sample in terms of age, sex, ethnicity, race, marital status, level of education, employment status, and household income.

RESULTS

Table 1. Case Summary

	Valid Cases	Cases Missing	Total
Year	n (%)	n (%)	N(%)
2005	1177 (6.0%)	18475 (94.0%)	19652 (100.00%)
2006	5631 (28.7%)	14021 (71.3%)	19652 (100.00%)
2007	7607 (38.7%)	12045 (61.3%)	19652 (100.00%)
2008	8924 (45.4%)	10728 (54.6%)	19652 (100.00%)
2009	9610 (48.9%)	10042 (51.1%)	19652 (100.00%)
2010	9807 (49.9%)	9845 (50.1%)	19652 (100.00%)
2011	9450 (48.1%)	10202 (51.9%)	19652 (100.00%)
2012	9885 (50.3%)	9767 (49.7%)	19652 (100.00%)
2013	9743 (49.6%)	9909 (50.4%)	19652 (100.00%)
2014	9331 (47.5%)	10321 (52.5%)	19652 (100.00%)
2015	8564 (43.6%)	11088 (56.4%)	19652 (100.00%)
2016	7866 (40.0%)	11786 (60.0%)	19652 (100.00%)
2017	6591 (33.5%)	13061 (66.5%)	19652 (100.00%)
2018	4901 (24.9%)	14751 (75.1%)	19652 (100.00%)
2019	135 (.07%)	19517 (99.93%)	19652 (100.00%)

Table 1 summarizes the number of cases and percent that were valid each year. As shown in Table 1, the number of participants varied per year and increased as the study progressed, until 2012 when it gradually started to decline again. The low number of valid cases in 2019 is a function of the data being obtained early in the year before data collection was completed.

Table 2. Correlation Between Depression and AD

Year	Pearson's R	Approximate Significance ($p<.001$)
2006	.126	.000
2007	.140	.000
2008	.179	.000
2009	.172	.000
2010	.189	.000
2011	.178	.000
2012	.180	.000
2013	.177	.000
2014	.188	.000
2015	.175	.000
2016	.192	.000
2017	.199	.000
2018	.174	.000
2019	.133	.143

Table 2 displays the results of the correlation analysis determining the relationship between depression and AD. For the depression variable, a binary scoring system was used in which a value of one indicated depression was diagnosed and a value of zero indicated that no depression was found to be diagnosed. For the AD variable, data was coded such that a value of one indicated AD was diagnosed and a value of zero indicated that AD was not diagnosed, and no cognitive impairment was found. In each of the years listed, a significant positive correlation between AD and depression was observed. The exception to this was the final year, 2019, where a positive correlation was observed but not found to be statistically significant.

Table 3. Logistic regression predicting diagnosis of depression to diagnosis of AD

Year	OR	95% CI	Approximate Significance (p<.001)
2006	2.25	1.41-3.56	.000
2007	2.27	1.64-3.16	.000
2008	2.73	2.14-3.51	.000
2009	2.81	2.24-3.55	.000
2010	2.65	2.13-3.30	.000
2011	2.40	1.93-3.00	.000
2012	2.48	1.98-3.09	.000
2013	3.15	2.51-3.98	.000
2014	2.89	2.27-3.69	.000
2015	3.34	2.54-4.39	.000
2016	2.53	2.20-2.89	.000
2017	3.48	2.49-4.76	.000
2018	2.69	1.82-3.97	.000
2019	1.29*	.21-7.80	.785

Table 3 displays the results of logistic regression models predicting the likelihood of being diagnosed with AD when diagnosed with depression. For this analysis, the binary outcome variables remained the same. Results indicated that depression was significantly predictive of AD for each year. The exception to this was 2019 which was found to be predictive but not statistically significant.

Table 4. Logistic regression predicting living situation to diagnosis of AD

Year	OR	95% CI	Approximate Significance (p<.001)
2006	3.46	2.87-4.18	.000
2007	3.31	2.85-3.84	.000
2008	2.78	2.46-3.14	.000
2009	2.49	2.23-2.79	.000
2010	2.49	2.22-2.80	.000
2011	2.61	2.32-2.94	.000
2012	2.42	2.16-2.72	.000
2013	2.51	2.23-2.82	.000
2014	2.34	2.08-2.64	.000
2015	2.59	2.28-2.95	.000
2016	2.53	2.20-2.89	.000
2017	2.64	2.267-3.07	.000
2018	2.52	2.12-2.99	.000
2019	1.89*	.71-5.00	.202

Table 4 displays the results of logistic regression models predicting the likelihood of being diagnosed with AD based on living situation (the variable for social support). For this analysis, the binary outcome variables for AD remained the same. The outcomes for living situation were coded using a binary scoring system in which zero indicated living alone and one indicated living with others. For each year, living situation was significantly predictive of AD. The exception to this was 2019 where it was found to be predictive but not statistically significant.

Table 5. Logistic regression predicting interaction of living situation and depression diagnosis to diagnosis of AD

Year	OR	95% CI	Approximate Significance (p<.001)
2006	1.06	.63-1.79	.819
2007	1.13	.769-1.66	.536
2008	1.09	.81-1.48	.546
2009	.932	.706-1.23	.620
2010	1.19	.913-1.56	.196
2011	1.17	.89-1.53	.245
2012	1.20	.919-1.58	.179
2013	.87	.67-1.16	.357
2014	1.07	.80-1.43	.649
2015	.83	.60-1.15	.262
2016	1.14	.80-1.60	.470
2017	1.03	.71-1.51	.861
2018	1.18	.75-1.85	.472
2019	2.78	.29-26.17	.370

Table 5 displays the results of logistic regression models predicting the likelihood of being diagnosed with AD when using the interaction of living situation and depression. Results found that living situation did not significantly moderate the relationship between depression and AD at any point throughout the study.

DISCUSSION

This study examined the relations between depression and AD in a sample of individuals who were in the National Institute on Aging's ADC program. Results indicated that a significant positive correlation existed between depression and cognitive functioning: such that as depression was diagnosed, the likelihood of an AD diagnosis also increased. Individuals who had been diagnosed with AD were more likely to not live alone. Finally, results indicated that living situation did not moderate the relationship between depression and AD.

The difference between significance between variables and the interaction term is interesting. Although the variables of depression and living situation resulted in greater likelihood of developing AD, the interaction term was found to not have a significant effect on the likelihood of being diagnosed with AD. One possibility is that while both may be predictive of AD, they may not affect each other in a manner that provides more predictive ability than the initial observed effect.

Also, of interest is the relationship between living situation and AD diagnosis. Living situation was used as a variable to represent social support, in that those living with others had more social support than those who lived alone. The results indicate that living situation had a significant effect on the predictive ability of AD. It should be noted that there is a strong possibility that these results may be due to individuals with AD needing more care and thus live with others in order to receive that care. In this case, living with others would only identify those who may already have AD and need assistance. In order to control for this possibility, a different variable should be used to rate social support.

These results contribute to the research on the progression of AD. The data suggests that experiencing depression may result in greater chance to be diagnosed with AD. This may lead to increases in mortality (Sub et al., 2005), moving into care (Lyketsos and Olin, 2002), care giver burden and costs of care (Zhu and Sano, 2005). By providing treatment to depression, it may be possible to limit the impact and slow the progression of AD providing for better outcomes.

There are some important limitations to the current study, including the use living situation as a measure of social support that does not consider the relationship with co-habitors. Another limitation is the criteria of using individuals who had at least three visits that may have tainted the data by limiting the observation of the progression of both depression and AD in participants. The use of clinical judgement also limits the results, in that assessors may vary in their clinical judgement to diagnosis which may result in greater or fewer diagnosis of depression or AD. In addition, the large sample size may have resulted in greater possibility for significant results than may have been otherwise possible.

This study provided support for the hypothesis that a diagnosis of depression may result in greater risk for AD. The clinical significance and robustness of these correlations and variances is still not fully known, however. Greater understanding of depression-AD relations and other possible moderating or mediating factors may help researchers develop better ways to treat AD and mitigate the impact of the disease on patients. In this way, elucidating the relationship between depression and AD may lead to improved interventions for AD patients in the future.

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