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Abstract Title: History of Psychiatric Disease Inversely Correlates with Age of Onset in Alzheimer's Disease

Press Release Title: People with Depression, Anxiety May Develop Alzheimer's at Younger Age

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Objective: To investigate the impact of psychiatric disease on Alzheimer's Disease (AD).

Background: Depression has been established as a risk factor in AD that may accelerate the development and disease course. Less studied are the effects of other mood disorders, psychotic disorders, and post-traumatic stress disorder (PTSD) on AD.

Design/Methods: We screened 1,500 AD patients from the UCSF Memory and Aging Center for history of psychiatric disorders: depression, anxiety, bipolar disorder, schizophrenia and PTSD. We determined disease prevalence and investigated association with age at onset (AAO), demographics, typical AD risk factors (hypertension, hyperlipidemia, diabetes mellitus, education and *APOE4*) as well as novel AD-associated factors, previously detailed (non-right-handedness, learning disability, autoimmune disease and seizure history).

Results: 43.3% (650/1,500) had a history of depression, 32.3% (485/1,500) anxiety, 1.2% (18/1,500) bipolar disorder, 1% (15/1,500) PTSD and 0.4% (6/1,500) schizophrenia. Those with depression or anxiety were significantly younger at AAO (2.1 and 3.0 yrs, respectively; $p<0.001$). Further, AAO reductions doubled with each additional psychiatric diagnosis: the presence of only one psychiatric disorder was associated with a 1.5 yr younger AD AAO, history of two psychiatric conditions led to a 3.3 yr decrease in AAO, and three or more diagnoses produced a 7.3 yr reduction in AAO ($p<0.001$). Depression and anxiety cohorts were more female and possessed fewer amounts of typical AD risk factors. The depression cohort possessed a significantly higher amount of autoimmune disease ($p=0.01$), whereas the anxiety cohort possessed a greater frequency of seizures ($p=0.002$).

Conclusions: We find that diagnoses of depression and anxiety are inversely associated with AD AAO. Further, AAO differences compounded with increasing number of psychiatric diagnoses, suggesting each possess unique and additive effects on AD pathophysiology. We speculate that the presence of depression might reflect a greater burden of neuroinflammation and anxiety a greater degree of hyperexcitability, given associations with autoimmune disease and seizure.

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