Affective Change by Age Following Alzheimer's Disease (AD) Biomarker Disclosure

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Abstract

Dementia, characterized by cognitive decline affecting the ability to do everyday activities, poses a significant health challenge. Alzheimer's disease (AD), the most common cause of dementia, involves the accumulation of abnormal amyloid and tau proteins, which are measured using positron emission tomography (PET) scans. Elevated amyloid is the key indicator that AD brain changes are present. Early detection of this disease provides individuals with the opportunity to plan for the future and make informed decisions. Although prior research has found that most participants do not experience new or worsening mood or anxiety disorders following biomarker disclosure, few studies have examined predictive factors for positive or negative emotional reactions, such as patient characteristics like age at biomarker disclosure. This study aims to investigate emotional reactions after learning positive PET amyloid biomarker status among 49 participants 55 years of age and older with Mild Cognitive Impairment (MCI) or Dementia Alzheimer's Type (DAT) as a function of age. Emotional reactions were assessed using the Positive and Negative Affect Scale - Short Form (PANAS-SF) and and Impact of Neuroimaging in Alzheimer's Disease (INI-AD) given at baseline (before disclosure), immediately post-disclosure, and 6-week post-disclosure. PANAS and INI-AD scores will be compared across 2 age groups: 55-70 years and 71+, utilizing the assessments for amyloid-positive participants. Analysis focused on data collected immediately following disclosure and at 1-week post-disclosure. We hypothesize that participants within the ages of 55-70 will display a more negative affect than their older counterparts of 71+. Contrary to the initial hypothesis, the data did not support the notion that younger participants exhibit higher distress levels. The analysis revealed no significant overall difference in psychological reactions for both immediate ($F_{4,36}$ = 0.622, p =.650) and 1-week ($F_{4,35}$ = 1.050, p =.396) post disclosure, however, there was an overall medium effect size between groups (immediate: η_p^2=.065; 1-week: η_p^2=.107). In summary, there were small, non-significant effects of age for both measures of PANAS and INI-AD. Despite the absence of significant effects of age on psychological measures, these findings emphasize the importance of further research replication with larger sample sizes and diverse study populations. Such endeavors can provide insights into who may be more likely to have negative reactions after learning positive AD biomarker results, allowing for clinicians completing disclosure to better prepare and support these patients. By understanding participants' reactions and the age at which disclosure occurs, this research has the potential to enhance patient care and contribute to the broader understanding of the impact of biomarker disclosure.

Introduction

Dementia, characterized by cognitive decline affecting the ability to do everyday activities, poses a significant health challenge. Alzheimer's disease (AD), the most common cause of dementia, involves the accumulation of abnormal amyloid and tau proteins, quantifiable through positron emission tomography (PET) scans. These biomarkers, specifically elevated amyloid levels, serve as a key indicator that AD brain changes are present; elevated amyloid and elevated tau confirms a diagnosis of AD. Understanding emotional reactions to biomarker disclosure is critical, to ensure the safety of patients and protect against the possibility of adverse emotional reactions. Although prior research[1] has found that most participants do not experience new or worsening mood or anxiety disorders following biomarker disclosure, few studies have examined factors that may influence one's reaction to disclosure. The role of participant age at time of disclosure is one factor that could allow us to predict whether positive or negative emotional reactions are exhibited after learning one's PET biomarker results. By considering various age-groups within this population, this study aims to investigate whether a factor of age influences emotional reactions after learning positive PET amyloid biomarker status, aiming to fill this gap and recognize the diversity in emotional responses among individuals facing the challenges of Alzheimer's disease.

[1] Erickson CM, Clark LR, Ketchum FB, Chin NA, Gleason CE, Largent EA. Implications of preclinical Alzheimer's disease biomarker disclosure for US policy and society. *Alzheimer's Dement*. 2022; 14:e12339. https://doi.org/10.1002/dad2.12339

Methods

Participants: The overarching biomarker disclosure study included 65 participants aged 55 years and older with a research diagnosis of Mild Cognitive Impairment (MCI; *n*=33) or Dementia Alzheimer's Type (DAT; *n*=32). Given our focus on reactions to learning about positive AD biomarker results, we selected a subset of participants who had elevated amyloid on PET imaging (*n*=49; 53.1% female; 95.9% White, 4.1% Black; mean age = 71.06 ± 6.88 years; mean education = 16.16 ± 2.37 years). Exclusion criteria included moderate or severe depression or anxiety, or other significant neurological conditions.

Methods: Participants had previously completed an amyloid (PiB) PET scan as part of a separate neuromodulation clinical trial. An elevated (positive) scan was defined as 20 centiloids or higher; 75.7% of the sample exhibited positive results. Following a 1:1 education session with a trained study staff member, participants with decisional capacity for biomarker disclosure were offered the opportunity to learn their results. The disclosure session was also led by a trained study team clinician, who met with the participant and their loved ones to share the PET scan results, meaning of the results, and review relevant resources. Immediately following disclosure and at 1- and 6-week follow-up, participants completed brief measures of psychological reactions to disclosure.

Measures: Emotional responses were measured using the Positive and Negative Affect Scale Short Form (PANAS-SF; Watson et al., 1988) and Impact of Neuroimaging in Alzheimer's Disease (INI-AD; Chung et al., 2009) measures. The PANAS-SF measures positive and negative affect using a 20-item subscale on a 5-point Likert-style scale (1=very slightly, not all; 5= extremely). Scores can range from 10 to 50 for both the Positive and Negative Affect, higher scores representing higher levels of positive and negative emotions, respectively. The INI-AD measures distress (range 0-55; higher scores indicate higher distress) and positive emotions (range 0-20; higher scores indicate higher positive emotions) related to receiving AD-specific neuroimaging results. It is adapted from a similar measure used to assess reactions to AD genetic testing results.

Statistical Analysis: In order to compare responses in younger versus older participants, we divided the participant group by median age to create two age strata: 56 to 70 years and 71 years and above. We utilized a series of multivariate analysis of variance (MANOVA) tests to examine differences in positive affect (PANAS Positive subscale), negative affect (PANAS Negative subscale), positive impact of imaging (INI-AD Positive), and negative impact of imaging

(INI-AD Distress) by age, at each time point. Analysis focused on data collected immediately following disclosure and at 1-week post-disclosure.

PANAS: Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: the PANAS scales.Journal of personality and social psychology,54(6), 1063

INI-AD: Chung, W. W., Chen, C. A., Cupples, L. A., Roberts, J. S., Hiraki, S. C., Nair, A. K., Green, R. C., & Stern, R. A. (2009). A new scale measuring psychologic impact of genetic susceptibility testing for Alzheimer disease. Alzheimer disease and associated disorders, 23(1), 50–56. https://doi-org.proxy.lib.umich.edu/10.1097/wad.0b013e318188429e

Current or Expected Results

Results:

We conducted basic data screening to evaluate statistical assumptions and confirm the accuracy of the data. A MANOVA test was used to evaluate group differences in psychological outcome measures at the immediate post-disclosure time point. This analysis revealed no significant overall difference in psychological reactions ($F_{4,36} = 0.622$, $p = .650$); however, there was a medium effect of age group ($\eta_p^2 = .065$). Tests of between-subjects effects for each individual outcome demonstrated that there were small, non-significant effects of age on PANAS Positive subscale ($F_1 = 0.205$, $p = .653$, $\eta_p^2 = .005$), PANAS Negative subscale ($F_1 = 0.222$, $p = .640$, $\eta_p^2 = .006$), and the INI-AD Positive score ($F_1 = 0.029$, $p = .866$, $\eta_p^2 = .001$). Though not significant, older participants endorsed higher distress on the INI-AD Negative score with a medium effect ($F_1 = 2.341$, $p = .134$, $\eta_p^2 = .057$). Average scores on outcome measures are summarized in Table 1.

A second MANOVA test was used to evaluate group differences in psychological outcome measures at the 1-week post-disclosure time point. This analysis revealed no significant overall difference in psychological reactions ($F_{4,35} = 1.050$, $p = .396$); however, there was a medium effect of age group ($\eta_p^2 = .107$). Tests of between-subjects effects for each individual outcome (Table 1) demonstrated that there were small, non-significant effects of age on PANAS Positive subscale ($F_1 = 0.992$, $p = .325$, $\eta_p^2 = .025$), PANAS Negative subscale ($F_1 = 0.039$, $p = .845$, $\eta_p^2 = .001$), the INI-AD Positive score ($F_1 = 0.798$, $p = .377$, $\eta_p^2 = .021$), or the INI-AD Negative score ($F_1 = 0.125$, $p = .736$, $\eta_p^2 = .003$).

Table 1. Means and standard deviations for psychological outcome measures by age group and time point

	Immediate Post-Disclosure		1-Week Post-Disclosure	
	M (SD)		M (SD)	
	56-70 years (n=18)	71+ years (n=23)	56-70 years (*n*=17)	71+ years (*n*=23)
PANAS Positive	33.78 (5.81)	34.78 (7.88)	32.41 (8.76)	35.13 (8.36)
PANAS Negative	13.94 (3.61)	14.70 (5.95)	16.59 (6.26)	16.13 (7.96)
INI-AD Positive	12.11 (3.79)	12.30 (3.48)	11.76 (5.09)	10.52 (3.72)
INI-AD Distress	9.56 (9.49)	14.09 (9.35)	11.00 (11.60)	12.22 (10.13)

Note. PANAS = Positive and Negative Affect Scale (range 10-50; higher scores indicate higher positive or negative affect); INI-AD = Impact of Neuroimaging in Alzheimer's Disease ((range 0-55; higher scores indicate higher distress) and positive emotions (range 0-20; higher scores indicate higher positive emotions))

Discussion: Contrary to the initial hypothesis, the data did not support the notion that younger participants would exhibit higher distress levels. In fact, some preliminary evidence shows that older participants may have higher test-related distress immediately upon learning their amyloid positive results than younger participants. Although the difference was not statistically significant, the effect size suggests a potential relationship in which our sample size or other factors may have contributed to. The study also found relatively low scores on the PANAS negative and INI-AD distress scales, indicating that participants are not experiencing significant psychological concern following biomarker disclosure, aligning with previous research[2]. Conversely, there were no significant differences among our positive subscales.

Future Directions: Moving forward, there are several ways in which we can enhance future research. Although this study is ongoing and participant engagement is increasing, there is a need for larger sample sizes to further explore age-related differences in distress. Therefore, future studies should address these issues and implement strategies to overcome this challenge. Additionally, as biomarker tests become more accessible to a broader audience, including those who are likely to be younger such as middle-aged individuals or those without impairment, future studies should replicate these findings with participants of this demographic. Furthermore, future research should address limitations found within this study, such as the inclusion of participants who had already completed not only a clinical trial study for memory problems, but also completed a PET scan. These participants may possess more knowledge about AD and may be more motivated to learn their PET scan results, highlighting the need to examine the reactions of individuals who are less educated about AD.

[2] Masters, M. C., & Morris, J. C. (2015). Abstract thinking and memory in aging: The relationship with education. *Alzheimer's & Dementia*, 11(4), 370-377. https://doi.org/10.1016/j.jalz.2015.09.005