

Sex, caregiver status and amyloid positivity predict increased anxiety and depression during the COVID-19-related confinement

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Abstract

Background: Anxiety and depression are more prevalent in women and caregivers and are associated with increased Alzheimer's disease (AD) risk. We investigated multimodal predictors of increased anxiety/depression during the Covid19-related confinement in cognitively unimpaired (CU) older adults with an increased risk for AD with a special focus on sex/gender.

Method: We included 921 CU participants from the ALFA study (Table 1). Anxiety and depression (Hospital Depression and Anxiety Scale, HADS), perceived stress (Perceived Stress Scale, PSS) and stress resilience (Brief Resilience Scale, BRS) were measured during Covid19-related confinement. A subgroup completed the HADS (n=767) and underwent [¹⁸F]flutemetamol-PET imaging and sMRI (n=254) 2.4±0.8 years before confinement. Cross-sectional anxiety/depression measurements and change in anxiety/depression (delta score) from baseline to confinement were our primary outcomes of interest. We considered amyloid status (+/-) and cortical thickness (Cth) from the AD signature regions as imaging biomarkers. First, we investigated sex differences in the variables assessed during confinement. Second, we ran regression models to predict (i) cross-sectional anxiety/depression scores during confinement and (ii) change in anxiety/depression from baseline to confinement. Age, sex, education, APOE-ε4 status, caregiver status, stress related-variables and imaging biomarkers were considered as predictors.

Result: Fifteen percent of the participants were caregivers, 69% of which were women. Women showed increased stress perception relative to men (p<0.001) – notably, when they were caregivers (p=0.01). There were no sex-differences in stress resilience (p=0.5). In cross-sectional models, sex (women) and higher stress perception were independent predictors of greater anxiety/depression during confinement (Table 2a). Being a caregiver additionally predicted increase in anxiety/depressive symptomatology.

ogy from baseline (Table 3a). Finally, in the subsample with biomarkers, amyloid positivity - but not Cth in the AD signature - contributed to predict anxiety/depression both cross-sectionally (Table 2b) and longitudinally (Table 3b) along with sex (women), caregiver status and stress perception.

Conclusion: Our results showed sex differences in caregiver status and stress perception during the Covid19-related confinement. Further, women, caregivers and those with higher self-perceived stress showed an increase in anxiety/depressive symptomatology. Amyloid pathology prior to confinement was associated with greater levels of anxiety/depression suggesting a role of amyloid pathology in anxiety/depressive symptomatology.

TABLE 1

TABLE 1 Demographic, biological, imaging and clinical characteristics of the study participants

Variable	All Participants N= 921	Participants with Biomarkers N= 254
Age (yrs)	57.39 (6.81)	61.03 (4.73)
Time from Baseline to Confinement (yrs)	2.41 (0.76)	2.37 (0.77)
Female, n(%)	568 (61.7%)	154 (60.6%)
Education, y	13.8 (3.41)	13.4 (3.49)
APOE ε4 Carrier, n(%) ^a	342 (37.1%)	146 (57.5%)
Caregiver, n(%) ^b	134 (14.5%)	39 (15.4%)
Amyloid Positivity (>12CL), n(%) ^c	-	26 (10.2%)
AD Signature (Cth, mm) ^d	-	2.42 (0.096)
Baseline HADS Scores ^e	7.59 (5.14)	6.57 (4.81)
Confinement HADS Scores	8.91 (6.23)	8.07 (5.98)
Perceived Stress (PSS) Scores ^f	16.9 (8.65)	16.0 (8.68)
Stress Resilience (BRS) Scores ^g	3.15 (0.375)	3.16 (0.398)

Data are presented as mean (standard deviation) unless otherwise indicated.

Abbreviations: CL = Centiloid, AD = Alzheimer's Disease, Cth= Cortical thickness, HADS = Hospital Anxiety Depression Scale, PSS = Perceived Stress Scale, BRS = Brief Resilience Scale.

a: Overall N= 913; b: Overall N= 834, Biomarker Subsample N= 238; c: Biomarker Subsample N= 206; d: Biomarker Subsample N= 246; e: Overall N= 767, Biomarker Subsample N= 253; f: Overall N= 895, Biomarker Subsample N= 242; g: Overall N= 904, Biomarker Subsample N= 252.

TABLE 2

TABLE 2 Results from cross-sectional analyses with HADS score as the dependent variable

Predictor	a. All Participants		b. Participants with Biomarkers	
	B Value (95% CI)	p Value	B Value (95% CI)	p Value
Age	-0.009 (-0.052 to 0.034)	0.681	-0.179 (-0.3 to -0.058)	0.004
Sex	-1.094 (-1.634 to -0.553)	< 0.001	-1.617 (-2.703 to -0.531)	0.004
Education (yrs)	-0.051 (-0.128 to 0.026)	0.194	-0.118 (-0.271 to 0.034)	0.128
APOEε4 Status	-0.074 (-0.612 to 0.465)	0.788	-0.891 (-1.967 to 0.185)	0.104
Caregiver Status	-0.244 (-0.966 to 0.478)	0.507	-1.839 (-3.298 to -0.381)	0.014
Perceived Stress (PSS)	0.558 (0.527 to 0.589)	< 0.001	0.529 (0.467 to 0.591)	< 0.001
Stress Resilience (BRS)	-0.411 (-1.105 to 0.283)	0.245	-	-
Amyloid Positivity (CL>12)	-	-	1.972 (0.323 to 3.621)	0.019
AD Signature (Cth)	-	-	-4.636 (-10.395 to 1.123)	0.114

Abbreviations: HADS = Hospital Anxiety and Depression Scale, CI = Confidence Interval, CL = Centiloid, Cth = Cortical Thickness, PSS = Perceived Stress Scale, BRS = Brief Resilience Scale, AD = Alzheimer's Disease.

The unstandardized B represents the variation in HADS scores with 1-unit variation in the given predictors.

TABLE 3

TABLE 3 Results from the analyses with change in HADS (delta) score as the dependent variable

Predictor	a. All Participants		b. Participants with Biomarkers	
	B Value (95% CI)	p Value	B Value (95% CI)	p Value
Age	-0.033 (-0.075 to 0.008)	0.116	-0.186 (-0.307 to -0.064)	0.003
Sex	-1.032 (-1.604 to -0.46)	< 0.001	-1.523 (-2.635 to -0.411)	0.008
Education (yrs)	-0.041 (-0.123 to 0.041)	0.328	-0.126 (-0.28 to 0.028)	0.109
APOEε4 Status	-0.127 (-0.688 to 0.439)	0.657	-0.845 (-1.917 to 0.226)	0.121
Caregiver Status	-0.845 (-1.608 to -0.082)	0.030	-1.935 (-3.415 to -0.454)	0.011
Perceived Stress (PSS)	0.489 (0.452 to 0.527)	< 0.001	0.518 (0.451 to 0.585)	< 0.001
Stress Resilience (BRS)	-0.046 (-0.784 to 0.693)	0.904	-	-
Amyloid Positivity (CL>12)	-	-	1.86 (0.196 to 3.524)	0.029
AD Signature (Cth)	-	-	-4.404 (-10.16 to 1.352)	0.133
Baseline HADS	-0.766 (-0.83 to -0.701)	< 0.001	-0.947 (-1.071 to -0.823)	< 0.001

Abbreviations: HADS = Hospital Anxiety and Depression Scale, CI = Confidence Interval, PSS = Perceived Stress Scale, BRS = Brief Resilience Scale, AD = Alzheimer's Disease, CL = Centiloid, Cth = Cortical Thickness.

The unstandardized B represents the variation in HADS scores with 1-unit variation in the given predictors.