

Poor sleep Amplifies Depression - Plasma GFAP Association in Spousal Caregivers of Individuals with Cognitive Decline

#Monday - 1280

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INTRODUCTION																																																																																																																																																								
Background - Spousal caregivers(SCGs) of individuals with cognitive decline experience chronic stress, which is a known risk factor for accelerated neurodegeneration. - GFAP is sensitive to stress-induced brain changes. - The glymphatic system clears neurotoxic proteins primarily during sleep; thus, sleep disturbance - common among caregivers - may impair this mechanism and elevate plasma GFAP. Objective - To investigate whether modifiable lifestyle factors, such as sleep quality, moderate the impact of caregiving burden on Alzheimer’s disease biomarkers. Hypothesis - Poor sleep quality amplifies the association between caregiver depression and plasma GFAP																																																																																																																																																								
Statistical Analysis - Moderated regression analyses were conducted using the PROCESS macro for SPSS (Hayes, 2017). - Bootstrapping with 5,000 resamples and 95% bias-corrected confidence intervals was used to test the significance of main effects and interaction effects. - Adjusted for age, sex, APOE4 positivity, and clinical diagnosis of care-recipients. Caregiving Related Factors - GDS of SCGs - MMSE, NPI_total of care-recipients AD biomarkers - p-Tau 217, GFAP, NfL Modifiable Lifestyle Factors - Sleep Quality (PSQI) - Physical Activity (IPAQ) - Simple slope analyses were conducted only when interactions reached statistical significance (p<0.05)																																																																																																																																																								
METHODS																																																																																																																																																								
Subjects (Total N=151) - Recruited from a geriatric neuropsychiatric clinic from May 2020 - November 2024. - Spousal caregivers of individuals with cognitive decline who did not have dementia or MCI. Clinical assessments - Spousal caregivers - Geriatric Depression Scale (GDS): caregiving-related depression - Pittsburgh Sleep Quality Index (PSQI): quality of sleep - International Physical Activity Questionnaire (IPAQ): physical activity - Care-recipients - Mini-Mental State Examination (MMSE): global cognitive function - Neuropsychiatric Inventory (NPI): neuropsychiatric symptoms Measurement of plasma biomarkers - Neurobiological biomarkers known to be related to Alzheimer’s Disease were measured using Simoa technology. - p-Tau 217: a biomarker of amyloid pathology - Glial Fibrillary Acidic Protein (GFAP): a biomarker of neuroinflammation - Neurofilament Light chain (NfL): a biomarker of neurodegeneration																																																																																																																																																								
RESULTS																																																																																																																																																								
Table 1. The demographic and clinical characteristics of participants <table><tr><th>Variables</th><th>All participants (n=151)</th></tr><tr><td colspan="2">Spousal Care Giver factors</td></tr><tr><td colspan="2">Demographic variables</td></tr><tr><td>Age (years)</td><td>72.9 ± 6.8</td></tr><tr><td>Female sex, n (%)</td><td>93 (61.6%)</td></tr><tr><td>Education years</td><td>9.3 ± 4.5</td></tr><tr><td colspan="2">Clinical variables</td></tr><tr><td>*APOE4 carrier, n (%)</td><td>30 (21.1%)</td></tr><tr><td>GDS</td><td>13.4 ± 6.9</td></tr><tr><td>PSQI</td><td>8.2 ± 3.2</td></tr><tr><td>IPAQ (MET – min./week)</td><td>2243.6 ± 2314.1</td></tr><tr><td colspan="2">Plasma biomarker</td></tr><tr><td>p-Tau 217 (pg/mL)</td><td>0.07 ± 0.04</td></tr><tr><td>GFAP (pg/mL)</td><td>124.16 ± 66.21</td></tr><tr><td>NfL (pg/mL)</td><td>21.70 ± 16.88</td></tr><tr><td colspan="2">Care recipient factors</td></tr><tr><td>MMSE</td><td>18.9 ± 6.1</td></tr><tr><td>NPI</td><td>21.1 ± 16.9</td></tr><tr><td>Clinical Diagnosis</td><td></td></tr><tr><td>CN</td><td>16 (10.7%)</td></tr><tr><td>MCI</td><td>42 (28.0%)</td></tr><tr><td>Dementia</td><td>92 (61.3%)</td></tr></table> Notes: Data are presented as mean ± SD or n(%). *APOE = apolipoprotein E.		Variables	All participants (n=151)	Spousal Care Giver factors		Demographic variables		Age (years)	72.9 ± 6.8	Female sex, n (%)	93 (61.6%)	Education years	9.3 ± 4.5	Clinical variables		*APOE4 carrier, n (%)	30 (21.1%)	GDS	13.4 ± 6.9	PSQI	8.2 ± 3.2	IPAQ (MET – min./week)	2243.6 ± 2314.1	Plasma biomarker		p-Tau 217 (pg/mL)	0.07 ± 0.04	GFAP (pg/mL)	124.16 ± 66.21	NfL (pg/mL)	21.70 ± 16.88	Care recipient factors		MMSE	18.9 ± 6.1	NPI	21.1 ± 16.9	Clinical Diagnosis		CN	16 (10.7%)	MCI	42 (28.0%)	Dementia	92 (61.3%)																																																																																																											
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Main effects - Among the main effects of caregiving related factors on plasma p-Tau 217, GFAP, NfL in SCGs, only the association between NPI and p-Tau 217 was statistically significant (Table 2). Table 2. The main effect of care-recipient NPI on plasma p-Tau217 among SCGs <table><tr><th rowspan="2"></th><th colspan="4">model 1</th><th colspan="4">model 2</th></tr><tr><th>β</th><th>SE</th><th>t</th><th>p</th><th>β</th><th>SE</th><th>t</th><th>p</th></tr><tr><td>NPI</td><td>0.0005</td><td>0.0002</td><td>2.278</td><td>0.025</td><td>0.0003</td><td>0.0002</td><td>1.302</td><td>0.196</td></tr></table> Model 1: adjusted for age, sex of SCGs Model 2: adjusted for age, sex, APOE4 positivity of SCGs and clinical diagnosis of care-recipients Moderation effects - The moderating effects of sleep quality and physical activity on the associations between Caregiving-related factors and plasma p-Tau 217, GFAP, NfL were examined in SCGs (Table 3). - Sleep quality significantly moderated the association between GDS and GFAP of SCGs - Physical activity significantly moderated the association between NPI of care-recipients and p-Tau 217 of SCGs Table 3. The moderating effect of PSQI, IPAQ on the associations between caregiving related factors and plasma GFAP, p-Tau217 among SCGs <table><tr><th rowspan="2"></th><th colspan="4">model 1</th><th colspan="4">model 2</th></tr><tr><th>B</th><th>SE</th><th>t</th><th>P</th><th>B</th><th>SE</th><th>t</th><th>p</th></tr><tr><td colspan="9">GFAP</td></tr><tr><td>GDS</td><td>-0.539</td><td>0.792</td><td>-0.680</td><td>0.497</td><td>-0.674</td><td>0.882</td><td>-0.765</td><td>0.446</td></tr><tr><td>PSQI</td><td>1.586</td><td>1.746</td><td>0.909</td><td>0.365</td><td>1.222</td><td>1.774</td><td>0.689</td><td>0.492</td></tr><tr><td>GDS x PSQI</td><td>0.882</td><td>0.249</td><td>3.549</td><td><0.001</td><td>0.880</td><td>0.253</td><td>3.475</td><td><0.001</td></tr><tr><td>R²</td><td colspan="4">0.185</td><td colspan="4">0.213</td></tr><tr><td>R² change</td><td colspan="4">0.078</td><td colspan="4">0.079</td></tr><tr><td colspan="9">p-Tau 217</td></tr><tr><td>NPI_total</td><td>0.001</td><td><0.001</td><td>2.707</td><td>0.008</td><td><0.001</td><td><0.001</td><td>1.692</td><td>0.094</td></tr><tr><td>IPAQ</td><td><0.001</td><td><0.001</td><td>0.829</td><td>0.409</td><td><0.001</td><td><0.001</td><td>0.528</td><td>0.599</td></tr><tr><td>NPI x IPAQ</td><td><0.001</td><td><0.001</td><td>-2.339</td><td>0.021</td><td><0.001</td><td><0.001</td><td>-1.917</td><td>0.058</td></tr><tr><td>R²</td><td colspan="4">0.234</td><td colspan="4">0.276</td></tr><tr><td>R² change</td><td colspan="4">0.035</td><td colspan="4">0.025</td></tr></table> Model 1: adjusted for age, sex of SCGs Model 2: adjusted for age, sex, APOE4 positivity of SCGs and clinical diagnosis of care-recipients - Simple slope analyses were performed for the two statistically significant interactions (Figure 1). a) GDS × PSQI → GFAP b) NPI_total × IPAQ → pTau217 Figure 1. The Moderating effect of (a) PSQI, (b) IPAQ on associations between Caregiving-related Factors and Plasma GFAP, p-Tau 217 among SCGs			model 1				model 2				β	SE	t	p	β	SE	t	p	NPI	0.0005	0.0002	2.278	0.025	0.0003	0.0002	1.302	0.196		model 1				model 2				B	SE	t	P	B	SE	t	p	GFAP									GDS	-0.539	0.792	-0.680	0.497	-0.674	0.882	-0.765	0.446	PSQI	1.586	1.746	0.909	0.365	1.222	1.774	0.689	0.492	GDS x PSQI	0.882	0.249	3.549	<0.001	0.880	0.253	3.475	<0.001	R ²	0.185				0.213				R ² change	0.078				0.079				p-Tau 217									NPI_total	0.001	<0.001	2.707	0.008	<0.001	<0.001	1.692	0.094	IPAQ	<0.001	<0.001	0.829	0.409	<0.001	<0.001	0.528	0.599	NPI x IPAQ	<0.001	<0.001	-2.339	0.021	<0.001	<0.001	-1.917	0.058	R ²	0.234				0.276				R ² change	0.035				0.025			
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- Our findings suggest the need to integrate sleep hygiene interventions and exercise prescriptions into dementia caregiver support programs to reduce both subjective distress and objectively measurable neurobiological risk of Alzheimer’s Disease. - Such interventions can better protect caregivers’ health and help them foster a more positive caregiving experience with their spouses.																																																																																																																																																								
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