## Psychological stress, cognitive decline and the development of dementia in amnestic mild cognitive impairment

Rebecca Sussams<sup>1, 2</sup>, Wolff Schlotz<sup>3</sup>, Zoe Clough<sup>1,2</sup>, Jay Amin<sup>1, 2</sup>, Sharon Simpson<sup>4</sup>, Amelia Abbott<sup>1, 2</sup>, Rebecca Beardmore<sup>1, 2</sup>, Richard Sharples<sup>2</sup>, Rachel Raybould<sup>5</sup>, Keeley Brookes<sup>6</sup>, Kevin Morgan<sup>6</sup>, David Culliford<sup>7</sup>, Clive Holmes<sup>1, 2\*</sup>

Supplemental Table 1. Between- and within-subject effects of stress and covariates on S1 cortisol measures (immediately after awakening, Box-Cox transformed – original in units of nmol/L). Group interactions represent differences between comparison and aMCI group.

	Model 1							Model 2						
Variable	Univariat	e		Multivariate			Univariate			Multivariate				
	В	95% CI	Р	В	95% CI	Р	В	95% CI	Р	В	95% CI	Р		
Within-subjects			11			11			11					
PSS	0.0001	-0.01,0.01	.99	-0.003	-0.015,0.009	.61	-0.007	-0.026,0.011	.44	-0.005	-0.025,0.015	.64		
RLCQ	0.0004	-0.0001,0.001	.13	0.001	-0.0001,0.001	.12	-0.0004	-0.001,0.0004	.37	-0.0003	-0.001,0.001	.52		
Group x PSS							0.012	-0.012,0.037	.31	0.007	-0.019,0.032	.61		
Group x RLCQ							0.002	0.0004,0.003	.007	0.002	0.000,0.003	.017		
Between-subject	S													
PSS	0.016	0.003,0.028	.013	0.018	0.005,0.031	.007	0.002	-0.017,0.020	.87	-0.003	-0.023,0.018	.81		
RLCQ	0.0002	-0.001,0.001	.62	-0.0002	-0.001,0.001	.61	0.0002	-0.001,0.002	.76	0.001	-0.001,0.002	.71		
Group x PSS							0.022	-0.003,0.047	.084	0.025	-0.003,0.051	.077		
Group x RLCQ							0.0002	-0.002,0.002	.84	-0.001	-0.003,0.001	.49		
Age (years)	-0.003	-0.01,0.01	.47	-0.006	-0.014,0.003	.17	0.009	-0.003,0.022	.16	0.010	-0.002,0.023	.11		
Gender (Female)	-0.15	-0.30,0.001	.052	-0.179	-0.329,-0.028	.020	-0.148	-0.409,0.114	.27	-0.144	-0.284,0.097	.24		
Group x age							-0.034	-0.052,-0.017	< .001	-0.035	-0.053,-0.017	< .001		
Group x gender							0.044	-0.286,0.374	.80	-0.001	-0.309,0.308	.99		

Model 1 Model 2 Univariate Multivariate Univariate Multivariate Variable 95% CI 95% CI 95% CI 95% CI В Ρ В Ρ В Ρ В Ρ Within-subjects -0.007,0.018 PSS 0.001 .36 0.008 -0.005,0.020 .21 0.009 -0.010,0.028 .34 0.005 -0.015,0.026 .61 -0.001,0.0004 -0.001,0.0004 -0.0003,0.001 -0.0004,0.001 RLCQ -0.0001 .67 -0.0002 .57 0.001 .18 0.0005 .27 Group x PSS -0.031,0.018 -0.025,0.027 -0.006 .61 0.001 .96 Group x RLCQ -0.002,-.023 -0.001 -0.002,-0.000 .045 -0.001 0.0002 Between-subjects -0.026,-0.005 PSS -0.015 .004 -0.017 -0.027,-0.006 .002 -0.011 -0.026,0.005 .18 -0.010 -0.028,0.008 .27 RLCQ -0.0002 -0.002,0.001 -0.001 -0.001,0.0001 .099 -0.001,0.001 .68 -0.001 .38 -0.001,0.001 .77 -0.0002 Group x PSS -0.006 -0.027,0.015 .58 -0.006 -0.028,0.017 .63 Group x RLCQ -0.002,0.001 .58 -0.002,0.001 .69 -0.0004 -0.0003 -0.013,0.009 Age (years) 0.002 -0.005,0.009 .61 0.004 -0.003,0.011 .24 -0.002 .68 -0.002 -0.013,0.008 .68 Gender 0.045,0.299 0.185 0.021,0.457 0.046,0.450 0.172 .008 0.061,0.309 .004 0.239 .031 0.248 .016 (Female) Group x age 0.017 0.001,0.032 .033 0.017 0.002,0.032 .031 Group x gender -0.142 -0.418,0.134 .31 -0.150 -0.412,0.112 .26

Supplemental Table 2. Between- and within-subject effects of stress and covariates on CAR measures (increase after awakening, Box-Cox transformed – original in units of nmol/L). Group interactions represent differences between comparison and aMCI group.

Supplemental Table 3. Between- and within-subject effects of stress and covariates on AUC measures (diurnal cortisol area under the curve, Box-Cox transformed – original in units of nmol/L). Group interactions represent differences between comparison and aMCI group.

	Model 1							Model 2					
Variable	Univaria	te		Multivariate			Univariate			Multivariate			
	В	95% CI	Р	В	95% CI	Р	В	95% CI	Р	В	95% CI	Р	
Within-subjects													
PSS	-0.354	-1.61,0.91	.58	-0.587	-1.89,0.72	.38	-0.27	-2.20,1.66	.78	0.38	-1.73,2.49	.73	
RLCQ	0.035	-0.025,0.095	.25	0.042	-0.019,0.103	.18	-0.07	-0.15,0.02	.12	-0.08	-0.17,0.02	.11	
Group x PSS							-0.15	-2.71,2.40	.91	-0.96	-3.66,1.73	.49	
Group x RLCQ							0.20	0.08,0.32	.001	0.21	0.09,0.34	.001	
Between-subject	:S		1										
PSS	1.40	0.19,2.60	.023	1.40	0.16,2.64	.026	0.31	-1.49,2.10	.74	0.25	-1.77,2.28	.81	
RLCQ	-0.005	-0.09,0.08	.91	-0.02	-0.11,0.07	.62	-0.009	-0.131,0.114	.89	0.006	-0.135,0.147	.93	
Group x PSS							1.53	-0.90,3.96	.22	1.30	-1.33,3.92	.33	
Group x RLCQ							0.026	-0.143,0.194	.77	-0.006	-0.186,0.174	.95	
Age (years)	0.62	-0.21,1.45	.14	0.40	-0.43,1.23	.35	1.18	-0.08,2.43	.066	1.14	-0.12,2.39	.075	
Gender (Female)	-8.75	-23.67,6.17	.25	-9.56	-24.15,5.02	.20	-18.63	-43.78,6.53	.15	-17.55	-41.25,6.15	.15	
Group x age							-2.06	-3.88,-0.23	.027	-1.77	-3.60,0.07	.059	
Group x gender							25.08	-6.93,57.10	.13	18.01	-12.59,48.61	.25	