The Longitudinal Assessment of Neuropsychiatric Symptoms in Mild Cognitive Impairment and Alzheimer's Disease and Their Association With White Matter Hyperintensities in the National Alzheimer's Coordinating Center's Uniform Data Set

SUPPLEMENTAL INFORMATION

Supplementary Table S1. MMSE sub-domain sub-scores and total scores at baseline.

	MCI-AD	AD
MMSE Orientation-Time (mean ± SD)	4.22 ± 1.07	3.07 ± 1.65
MMSE Orientation-Place (mean ± SD)	4.44 ±0.86	3.43 ±1.40
MMSE Pentagon (mean ± SD)	0.85 ± 0.36	0.62 ± 0.49
Total MMSE Score (mean ± SD)	26.34 ± 7.39	21.66 ± 4.76

Supplementary Table S2. The time frame (in years) between the baseline MRI and clinic visits, as well as the time frame (in years) between consecutive clinic visits (years).

	Visit 1 (N=252)	Visit 2 (N=247)	Visit 3 (N=184)	Visit 4 (N=117)	Visit 5 (N=55)	Visit 6 (N=30)
Average time between clinic visit and baseline MRI (years)	0.06±0.1	1.06±0.3	2.23±0.5	3.26±0.5	4.37±0.8	5.61±1.0
Average time between consecutive clinic visits (years)		1.11±0.0	1.19±0.4	1.14±0.3	1.15±0.6	1.08±0.3

Supplementary Table S3. Baseline mixed-effect model

Delusions Severity Score				
	Estimate	SE	tStat	pValue
Age	0.029	0.056	0.524	0.601
Sex	0.113	0.105	1.074	0.284
Education	-0.084	0.051	-1.642	0.102
WMH	0.022	0.055	0.393	0.694
Hallucinations Severity Score				
	Estimate	SE	tStat	pValue
Age	-0.045	0.032	-1.382	0.168
Sex	0.055	0.061	0.900	0.369
Education	0.170	0.030	5.714	0.000**
WMH	0.009	0.032	0.289	0.773

Agitation Severity Score			
	Estimate	SE	tStat	pValue
Age	-0.001	0.068	-0.009	0.993
Sex	0.107	0.128	0.835	0.405
Education	-0.102	0.063	-1.638	0.103
WMH	-0.051	0.067	-0.756	0.450

Depression Severity Score			
	Estimate	SE	tStat	pValue
Age	-0.141	0.063	-2.222	0.027
Sex	0.199	0.119	1.665	0.097
Education	-0.082	0.058	-1.401	0.163
WMH	0.087	0.062	1.385	0.167

Anxiety Severity Score			
	Estimate	SE	tStat	pValue
Age	-0.112	0.068	-1.649	0.101
Sex	0.140	0.127	1.099	0.273
Education	-0.034	0.062	-0.546	0.586
WMH	-0.020	0.067	-0.295	0.769

Elation Severity Score			
	Estimate	SE	tStat	pValue
Age	-0.035	0.053	-0.656	0.513
Sex	-0.049	0.100	-0.484	0.629
Education	-0.030	0.049	-0.619	0.537
WMH	-0.059	0.053	-1.133	0.259

Apathy Severity Score			
	Estimate	SE	tStat	pValue
Age	-0.029	0.063	-0.454	0.650
Sex	-0.097	0.119	-0.816	0.415
Education	-0.024	0.058	-0.415	0.679
WMH	-0.035	0.062	-0.563	0.574

Disinhibition Severity Score			
	Estimate	SE	tStat	pValue
Age	-0.026	0.064	-0.411	0.681
Sex	-0.046	0.120	-0.385	0.701
Education	-0.060	0.059	-1.021	0.308
WMH	0.064	0.063	1.020	0.309

Irritability Severity Score			
	Estimate	SE	tStat	pValue
Age	-0.057	0.066	-0.860	0.391

Sex	-0.180	0.125	-1.443	0.150
Education	-0.109	0.061	-1.782	0.076
WMH	-0.024	0.065	-0.360	0.719
Aberrant Motor Behaviour Severity Score				
	Estimate	SE	tStat	pValue
Age	0.005	0.062	0.076	0.939
Sex	0.138	0.116	1.186	0.237
Education	-0.021	0.057	-0.376	0.707
WMH	0.034	0.061	0.550	0.583
Night-time Behaviour Severity Score				
	Estimate	SE	tStat	pValue
Age	0.068	0.072	0.951	0.342
Sex	0.116	0.135	0.863	0.389
Education	-0.088	0.066	-1.338	0.182
WMH	0.055	0.071	0.777	0.438
Appetite Severity Score				
	Estimate	SE	tStat	pValue
Age	-0.057	0.061	-0.936	0.350
Sex	-0.056	0.115	-0.486	0.628
Education	-0.006	0.056	-0.111	0.912
WMH	-0.001	0.060	-0.020	0.984

Supplementary Table S4. Longitudinal Mixed-Effect Models of Annualized Change in NPI sub-scores explained by age, time (between baseline and clinical exam date), sex, education, whole brain WMH load and NPS severity scores, and interaction between time and WMH.

Change in Delusions Severity Score				
	Estimate	SE	tStat	pValue
Age	0.029	0.040	0.729	0.466
Time (between baseline and clinical exam date)	0.091	0.024	3.710	0.000**
Sex	0.202	0.074	2.742	0.006**
Education	0.065	0.034	1.915	0.056**
WMH	-0.003	0.050	-0.061	0.952
Delusions baseline severity score	0.458	0.037	12.512	0.000**
Interaction between Time and WMH	0.056	0.024	2.282	**0.023**

Change in Hallucinations Severity Score				
	Estimate	SE	tStat	pValue
Age	0.016	0.044	0.366	0.715
Time (between baseline and clinical exam date)	0.112	0.026	4.252	0.000**
Sex	0.023	0.081	0.281	0.779
Education	-0.048	0.041	-1.175	0.240
WMH	-0.035	0.055	-0.633	0.527
Hallucinations baseline severity score	0.299	0.045	6.722	0.000**
Interaction between Time and WMH	0.054	0.026	2.060	**0.040**
Change in Agitation Severity Score				
	Estimate	SE	tStat	pValue
Age	0.004	0.034	0.108	0.914
Time (between baseline and clinical exam date)	0.045	0.023	2.007	0.045**
Sex	0.094	0.063	1.483	0.139
Education	0.036	0.029	1.246	0.213
WMH	0.017	0.045	0.387	0.699
Agitation baseline severity score	0.635	0.032	19.990	0.000**
Interaction between Time and WMH	0.038	0.023	1.681	**0.093**
Change in Depression Severity Score				
	Estimate	SE	tStat	pValue
Age	-0.085	0.037	-2.318	0.021**
Time (between baseline and clinical exam date)	0.022	0.024	0.917	0.359
Sex	0.159	0.067	2.388	0.017**
Education	-0.007	0.030	-0.239	0.811
WMH	-0.027	0.048	-0.573	0.567
Depression baseline severity score	0.505	0.033	15.308	0.000**
Interaction between Time and WMH	0.058	0.024	2.382	**0.017**
Change in Anxiety Severity Score				
	Estimate	SE	tStat	pValue
Age	-0.077	0.037	-2.095	0.036**
Time (between baseline and clinical exam date)	0.034	0.026	1.318	0.188
Sex	0.029	0.067	0.435	0.664
Education	-0.016	0.030	-0.525	0.600

WMH	-0.012	0.049	-0.253	0.801
Anxiety baseline severity score	0.455	0.033	13.868	0.000**
Interaction between Time and WMH	0.028	0.026	1.085	0.278

Change in Elation Severity Score

	Estimate	SE	tStat	pValue
Age	-0.056	0.034	-1.665	0.096**
Time (between baseline and clinical exam date)	0.026	0.024	1.106	0.269
Sex	-0.013	0.062	-0.211	0.833
Education	-0.004	0.028	-0.159	0.874
WMH	0.053	0.045	1.162	0.246
Elation baseline severity score	0.648	0.034	19.311	0.000**
Interaction between Time and WMH	0.008	0.024	0.357	0.721

Change in Apathy Severity Score

	Estimate	SE	tStat	pValue
Age	-0.038	0.038	-1.003	0.316
Time (between baseline and clinical exam date)	0.098	0.023	4.320	1.76E-05**
Sex	-0.114	0.069	-1.649	0.100
Education	0.039	0.032	1.207	0.228
WMH	-0.010	0.047	-0.218	0.828
Apathy baseline severity score	0.565	0.034	16.830	1.57E-54**
Interaction between Time and WMH	0.027	0.023	1.1784	0.239

Change in Disinhibition Severity Score

	Estimate	SE	tStat	pValue
Age	0.017	0.039	0.430	0.667
Time (between baseline and clinical exam date)	0.039	0.024	1.652	0.099**
Sex	0.069	0.072	0.959	0.338
Education	0.034	0.033	1.008	0.313
WMH	0.030	0.049	0.604	0.546
Disinhibition baseline severity score	0.543	0.036	14.889	2.35E-44**
Interaction between Time and WMH	0.024	0.024	1.028	0.304

Change in Irritability Severity Score

	Estimate	SE	tStat	pValue
Age	-0.010	0.038	-0.256	0.798

Time (between baseline and clinical exam date)	0.020	0.022	0.893	0.372
Sex	0.018	0.070	0.261	0.794
Education	0.034	0.032	1.056	0.291
WMH	0.008	0.046	0.169	0.866
Irritability baseline severity score	0.611	0.034	17.777	0.000**
Interaction between Time and WMH	0.069	0.022	3.151	**0.002****
Change in Aberrant Motor Behaviour Severity Score				
	Estimate	SE	tStat	pValue
Age	-0.001	0.038	-0.034	0.970
Time (between baseline and clinical exam date)	0.075	0.025	3.005	0.000**
Sex	0.079	0.070	1.121	0.260
Education	-0.026	0.032	-0.825	0.410
WMH	0.019	0.050	0.379	0.700
Aberrant motor behaviour baseline severity score	0.463	0.034	13.719	0.000**
Interaction between Time and WMH	-0.021	0.025	-0.850	0.400
Change in Night-Time Behaviour Severity Score				
	Estimate	SE	tStat	pValue
Age	-0.031	0.038	-0.830	0.407
Time (between baseline and clinical exam date)	0.004	0.025	0.144	0.886
Sex	-0.105	0.069	-1.532	0.126
Education	0.020	0.032	0.629	0.529
WMH	0.044	0.049	0.910	0.363
Night-time behaviour baseline severity score	0.503	0.034	15.008	0.000**
Interaction between Time and WMH	0.004	0.025	0.147	0.883
Change in Appetite Severity Score				
	Estimate	SE	tStat	pValue
Age	-0.056	0.039	-1.411	0.159
Time (between baseline and clinical exam date)	0.053	0.027	2.005	0.045**
Sex	0.003	0.072	0.040	0.968
Education	0.002	0.033	0.073	0.942
WMH	0.034	0.052	0.658	0.511
Appetite baseline severity score	0.377	0.035	10.910	0.000**
Interaction between Time and WMH	0.022	0.027	0.814	0.416

** denotes statistical significance, ◊Denotes a trend; one-tailed test p<0.1