

Divergent Network Trajectories in MCI: Converters vs. Non-Converters to Alzheimer's Disease

Daniele Romano, Giorgia Tosi, for the Alzheimer's Disease Neuroimaging Initiative

Supplementary Materials

The present file shows:

- Group comparison for all neuropsychological tests
- Edge weight and bootstrap results for each group
- Cross-lagged in-prediction and cross-lagged out-prediction for each group

Group comparison

Table MS1. Groups comparison. The left part of the table shows the results of the mixed (within-between) ANOVAs assessing the influence of group (HP, stabMCI, and convMCI) and time (baseline, 12th month, 24th month) on each test score. The right part of the table shows the results of the mixed (within-between) ANOVAs assessing the influence of group (stabMCI, and convMCI) and time (baseline, 12th month, 24th month) on each test score. DF_n = numerator degrees of freedom; DF_d = denominator degrees of freedom, ges = generalized eta squared; BNT=Boston Naming Test; CDTcopy=Clock Drawing Test (copy); CDTdraw=Clock Drawing Test (draw); IMEMimm=Logical Memory Test – immediate recall; IMEMdel=Logical Memory Test – delayed recall; MMSE=Mini Mental State Examination; RAVLTrec=Rey Auditory Verbal Learning Test - recognition; RAVLdel=Rey Auditory Verbal Learning Test - delayed recall; SEMfAN=Semantic Fluency test (animal); TMTa=Trials making Test – a; TMTb=Trials making Test – b.

Test	Effect	ANOVA 3(group)x3(time)						ANOVA 2(group)x3(time)					
		DF _n	DF _d	F	p	p<.05	ges	DF _n	DF _d	F	p	p<.05	ges
BNT	group	2.00	877.00	38.57	0.000	*	0.067	1.00	516.00	3.81	0.052		0.010
	time	1.91	1673.64	4.59	0.011	*	0.0001	1.92	992.67	1.45	0.236		0.000
	group: time	3.82	1673.64	4.92	0.001	*	0.002	1.92	992.67	6.35	0.002	*	0.000
CDTcopy	group	2.00	877.00	11.91	0.000	*	0.014	1.00	516.00	0.41	0.523		0.000
	time	1.76	1546.33	5.93	0.004	*	0.003	1.68	866.29	3.12	0.053		0.000
	group: time	3.53	1546.33	0.65	0.608		0.001	1.68	866.29	0.15	0.822		0.000
CDTdraw	group	2.00	877.00	16.39	0.000	*	0.021	1.00	516.00	0.04	0.834		0.000
	time	1.92	1684.52	1.84	0.161		0.001	1.87	963.03	2.48	0.088		0.000
	group: time	3.84	1684.52	1.92	0.108		0.002	1.87	963.03	1.80	0.169		0.000
IMEMdel	group	2.00	877.00	420.02	0.000	*	0.416	1.00	516.00	55.25	0.000	*	0.080
	time	1.82	1597.23	19.91	0.000	*	0.006	1.72	887.99	11.14	0.000	*	0.010
	group: time	3.64	1597.23	10.70	0.000	*	0.006	1.72	887.99	17.14	0.000	*	0.010
IMEMimm	group	2.00	877.00	320.51	0.000	*	0.347	1.00	516.00	30.22	0.000	*	0.040
	time	1.84	1617.30	26.74	0.000	*	0.008	1.80	928.58	8.73	0.000	*	0.000
	group: time	3.69	1617.30	5.36	0.000	*	0.003	1.80	928.58	9.00	0.000	*	0.010
MMSE	group	2.00	877.00	100.28	0.000	*	0.130	1.00	516.00	10.72	0.001	*	0.010
	time	1.80	1576.47	19.63	0.000	*	0.008	1.70	878.52	17.62	0.000	*	0.010
	group: time	3.60	1576.47	6.43	0.000	*	0.005	1.70	878.52	2.45	0.096		0.000
RAVLTrec	group	2.00	877.00	110.14	0.000	*	0.150	1.00	516.00	32.44	0.000	*	0.040
	time	1.82	1600.39	8.48	0.000	*	0.003	1.86	959.35	12.83	0.000	*	0.010
	group:	3.65	1600.39	9.76	0.000	*	0.007	1.86	959.35	12.67	0.000	*	0.010

	time												
<i>RAVLTdel</i>	group	2.00	877.00	145.91	0.000	*	0.207	1.00	516.00	32.06	0.000	*	0.050
	time	1.86	1631.90	1.74	0.179		0.000	1.87	966.89	8.76	0.000	*	0.000
	group: time	3.72	1631.90	7.18	0.000	*	0.004	1.87	966.89	1.90	0.153		0.000
<i>SEMfAN</i>	group	2.00	877.00	62.27	0.000	*	0.099	1.00	516.00	5.10	0.024	*	0.010
	time	1.85	1618.58	3.76	0.027	*	0.001	1.83	941.80	5.52	0.005	*	0.000
	group: time	3.69	1618.58	2.43	0.051		0.001	1.83	941.80	1.80	0.170		0.000
<i>TMTa</i>	group	2.00	877.00	18.65	0.000	*	0.028	1.00	516.00	0.18	0.672		0.000
	time	1.97	1731.25	0.38	0.678		0.000	1.66	855.00	0.79	0.434		0.000
	group: time c	3.95	1731.25	2.68	0.031	*	0.002	1.66	855.00	0.28	0.717		0.000
<i>TMTb</i>	group	2.00	877.00	32.94	0.000	*	0.055	1.00	516.00	0.75	0.387		0.000
	time	1.79	1572.00	1.95	0.147		0.001	1.75	904.84	2.41	0.098		0.000
	group: time	3.58	1572.00	1.69	0.156		0.001	1.75	904.84	1.96	0.148		0.000

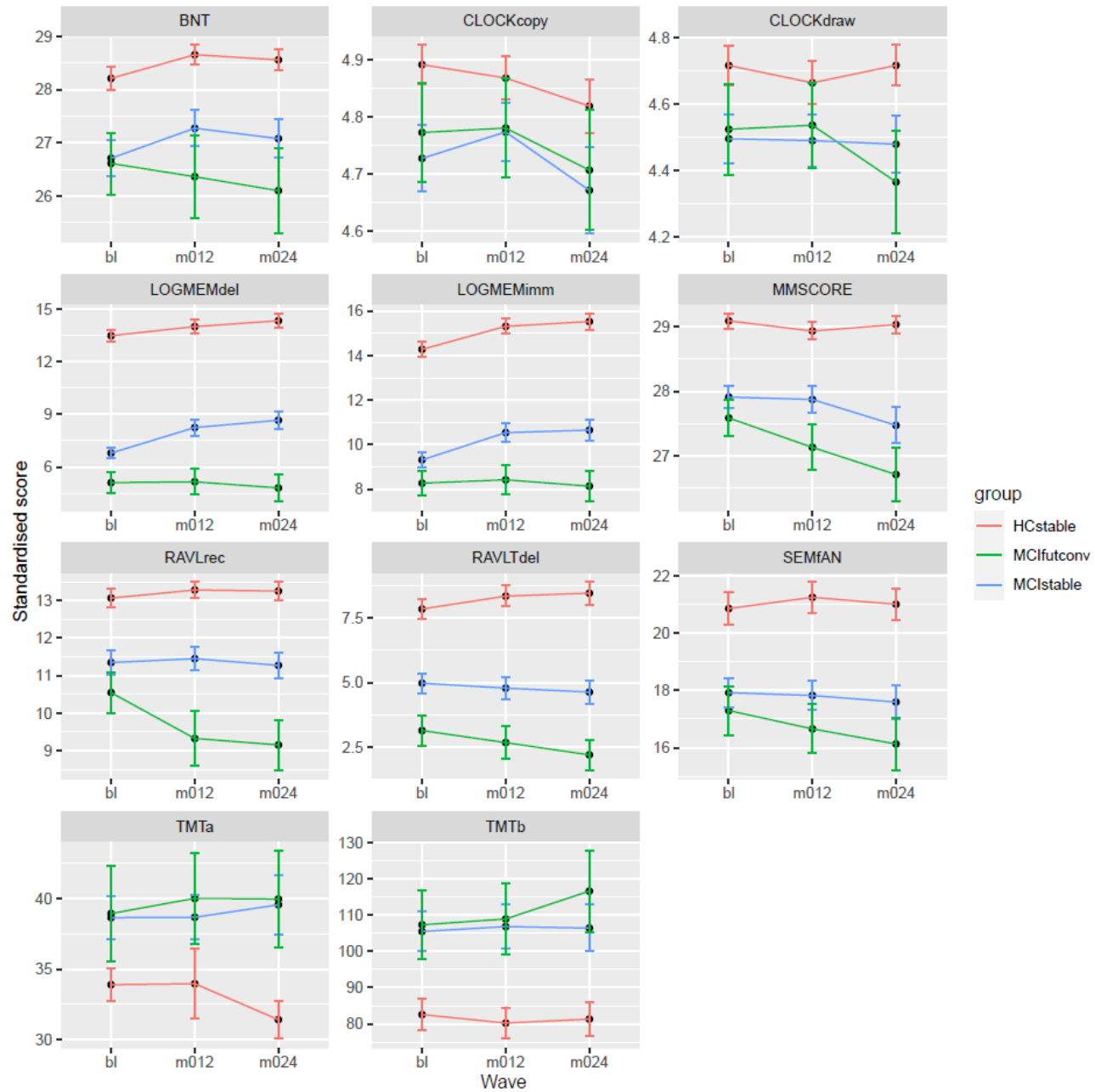


Figure SM1. *Time trajectories.* The figure shows time trajectories across time for each test in each group. BNT=Boston Naming Test; CDTcopy=Clock Drawing Test (copy); CDTdraw=Clock Drawing Test (draw); IMEMimm=Logical Memory Test – immediate recall; IMEMdel=Logical Memory Test – delayed recall; MMSE=Mini Mental State Examination; RAVLTrec=Rey Auditory Verbal Learning Test - recognition; RAVLTdel=Rey Auditory Verbal Learning Test - delayed recall; SEMfAN=Semantic Fluency test (animal); TMTa=Trail making Test – a; TMTb=Trail making Test – b.

Edge weight and bootstrap results

Healthy participants

Table SM2. HP stable edges. The diagonal shows the autoregressive patterns, the upper part of the table shows the cross-lagged prediction from the baseline (rows) to the 12th month (columns), and the lower part of the table shows the cross-lagged prediction from the 12th month (columns) to the 24th month (rows). BNT=Boston Naming Test; CDTcopy=Clock Drawing Test (copy); CDTdraw=Clock Drawing Test (draw); IMEMimm=Logical Memory Test – immediate recall; IMEMdel=Logical Memory Test – delayed recall; MMSE=Mini Mental State Examination; RAVLTrec=Rey Auditory Verbal Learning Test - recognition; RAVLTdel=Rey Auditory Verbal Learning Test - delayed recall; SEMfAN=Semantic Fluency test (animal); TMTa=Trials making Test – a; TMTb=Trials making Test – b.

		12 th month										
		<i>CDTdraw</i>	<i>CDTcopy</i>	<i>IMEMimm</i>	<i>IMEMdel</i>	<i>SEMfAN</i>	<i>TMTa</i>	<i>TMTb</i>	<i>BNT</i>	<i>RAVLTdel</i>	<i>RAVLTrec</i>	<i>MMSE</i>
Baseline	<i>CDTdraw</i>	0.21	0.03	0.00	0.00	0.04	0.00	-0.09	0.00	0.00	0.00	-0.01
	<i>CDTcopy</i>	0.18	0.29	-0.07	-0.01	0.00	0.00	-0.04	0.02	0.00	-0.03	0.02
	<i>IMEMimm</i>	0.00	0.07	0.44	0.24	0.00	0.00	0.00	0.04	0.04	0.04	0.00
	<i>IMEMdel</i>	0.10	0.03	0.17	0.40	0.00	-0.15	0.00	0.00	0.06	0.03	0.00
	<i>SEMf</i>	0.00	-0.04	0.07	0.08	0.58	0.00	-0.03	0.08	0.08	0.05	0.00
	<i>TMTa</i>	-0.06	-0.11	0.00	0.00	-0.06	0.29	0.24	0.07	-0.06	-0.05	0.00
	<i>TMTb</i>	-0.05	0.00	-0.05	-0.05	-0.08	0.42	0.49	-0.08	-0.03	0.04	-0.11
	<i>BNT</i>	0.01	0.00	0.02	0.01	0.10	-0.04	-0.07	0.59	-0.03	0.00	0.00
	<i>RAVLTdel</i>	0.00	0.10	0.07	0.08	0.06	0.00	0.00	0.05	0.53	0.19	0.02
	<i>RAVLTrec</i>	0.00	0.00	0.05	0.12	0.00	0.00	-0.11	-0.07	0.09	0.22	0.14
<i>MMSE</i>	0.00	0.03	0.06	0.07	0.00	0.00	-0.05	0.02	-0.03	0.00	0.35	
24 th month	<i>CDTdraw</i>	0.37	0.07	0.00	-0.03	0.00	0.05	-0.04	0.11	0.00	0.00	0.00
	<i>CDTcopy</i>	-0.02	0.44	0.19	-0.19	0.07	0.02	0.00	0.12	-0.02	0.00	0.02
	<i>IMEMimm</i>	0.00	0.04	0.49	0.15	0.08	0.00	0.00	0.04	0.08	0.07	0.05
	<i>IMEMdel</i>	0.00	0.12	0.15	0.49	0.05	0.00	0.02	0.10	0.13	0.05	0.03
	<i>SEMf</i>	0.00	0.00	0.00	0.00	0.67	-0.01	-0.05	0.04	0.11	0.00	0.00
	<i>TMTa</i>	0.00	0.00	0.00	0.01	0.00	0.12	0.32	0.00	0.00	0.00	0.00
	<i>TMTb</i>	-0.05	-0.06	0.00	0.00	-0.08	0.03	0.63	0.01	0.00	0.01	0.00
	<i>BNT</i>	0.00	0.04	-0.01	0.00	-0.02	0.00	-0.07	0.81	-0.02	0.06	-0.02
	<i>RAVLTdel</i>	0.00	0.00	-0.04	0.08	0.01	-0.07	-0.05	0.05	0.73	-0.05	0.04
	<i>RAVLTrec</i>	0.00	-0.09	0.23	-0.13	-0.03	-0.11	-0.05	0.00	0.15	0.56	0.00
<i>MMSE</i>	0.08	0.05	0.00	0.00	0.00	0.00	-0.21	0.00	0.12	-0.05	0.34	

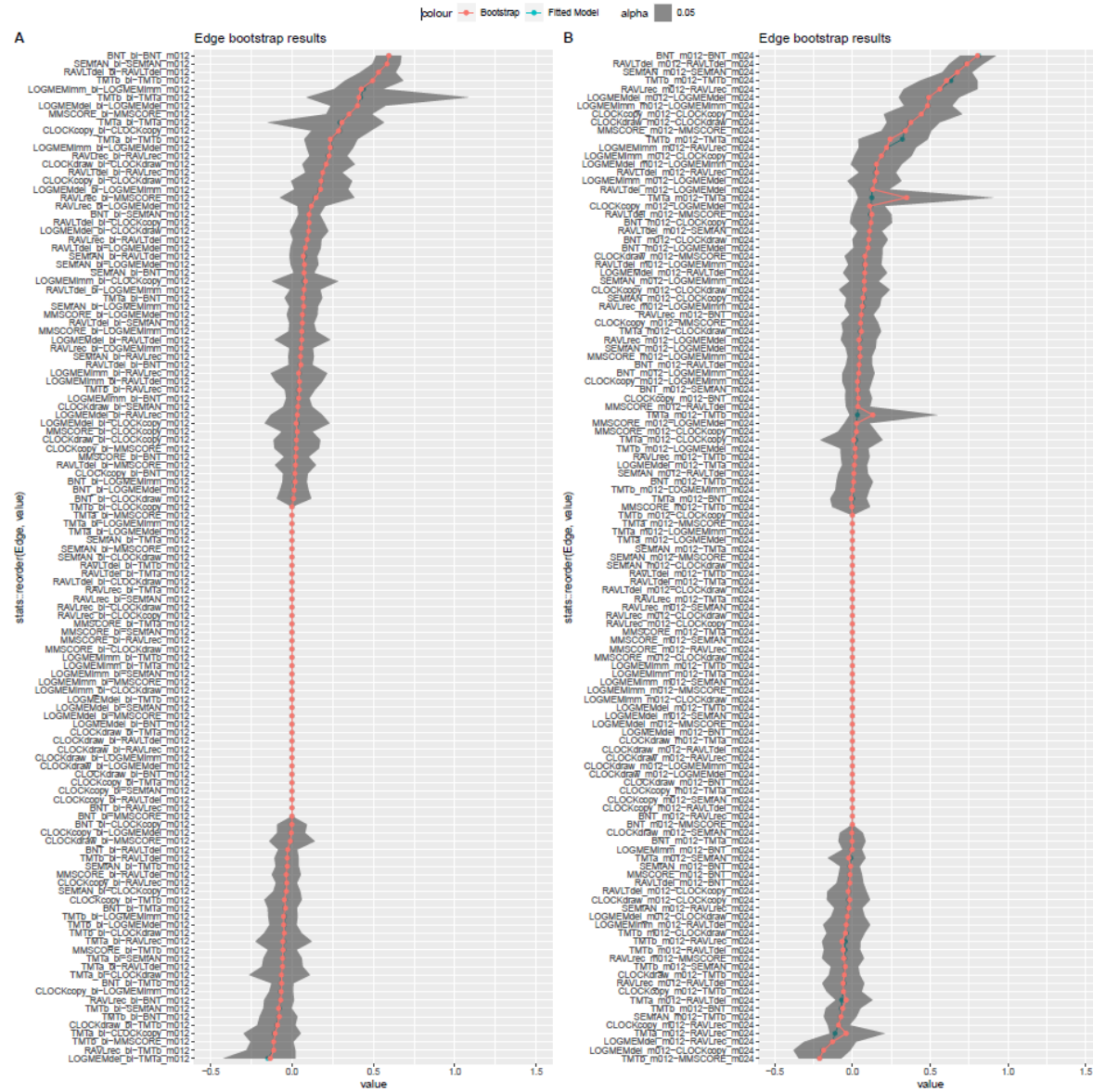


Figure SM2. Bootstrapped confidence intervals of estimated edge weights in healthy participants. The figure shows the 95% bootstrapped CIs of edge weights in the first (on the left) and the second (on the right) year. The orange line indicates the bootstrapped mean values of the confidence interval, the green line indicates the sample values and the grey area indicates the 95% confidence intervals.

MCI patients – non-converter group

Table MS3. *MCI non-converter edges.* The diagonal shows the autoregressive patterns, the upper part of the table shows the cross-lagged prediction from the baseline (rows) to the 12th month (columns), and the lower part of the table shows the cross-lagged prediction from the 12th month (columns) to the 24th month (rows). BNT=Boston Naming Test; CDTcopy=Clock Drawing Test (copy); CDTdraw=Clock Drawing Test (draw); IMEMimm=Logical Memory Test – immediate recall; IMEMdel=Logical Memory Test – delayed recall; MMSE=Mini Mental State Examination; RAVLTrec=Rey Auditory Verbal Learning Test - recognition; RAVLTDel=Rey Auditory Verbal Learning Test - delayed recall; SEMfAN=Semantic Fluency test (animal); TMTa=Trials making Test – a; TMTb=Trials making Test – b.

		<i>12th month</i>										
		<i>CDTdraw</i>	<i>CDTcopy</i>	<i>IMEMimm</i>	<i>IMEMdel</i>	<i>SEMfAN</i>	<i>TMTa</i>	<i>TMTb</i>	<i>BNT</i>	<i>RAVLTdel</i>	<i>RAVLTrec</i>	<i>MMSE</i>
<i>Baseline</i>	<i>CDTdraw</i>	0.12	0.08	0.00	0.02	0.00	-0.06	0.03	0.01	0.06	0.00	-0.08
	<i>CDTcopy</i>	0.15	0.17	0.04	0.06	0.00	-0.01	-0.05	0.06	0.00	0.00	0.16
	<i>IMEMimm</i>	0.00	0.00	0.44	0.24	-0.04	0.00	0.00	0.03	0.12	0.14	0.10
	<i>IMEMdel</i>	0.21	0.17	0.18	0.46	0.11	-0.03	-0.02	0.12	0.00	0.03	0.03
	<i>SEMf</i>	0.10	0.01	0.03	-0.02	0.52	-0.05	-0.02	0.14	0.04	0.00	0.09
	<i>TMTa</i>	-0.15	-0.13	-0.02	-0.09	-0.09	0.58	0.24	-0.01	-0.11	0.06	0.00
	<i>TMTb</i>	-0.07	-0.04	-0.06	0.00	-0.01	0.19	0.57	-0.04	0.00	0.04	-0.09
	<i>BNT</i>	0.07	0.06	0.07	0.03	0.13	-0.02	-0.10	0.60	0.00	0.00	0.06
	<i>RAVLTdel</i>	0.05	0.00	0.31	0.37	0.19	-0.04	-0.04	0.09	0.71	0.26	0.20
	<i>RAVLTrec</i>	0.09	0.07	0.03	0.02	-0.07	0.00	0.00	-0.12	0.06	0.48	0.00
	<i>MMSE</i>	0.09	0.03	0.04	0.14	0.05	-0.02	-0.10	0.03	0.01	0.01	0.34
<i>24th month</i>	<i>CDTdraw</i>	0.55	0.1	0	0.07	0.01	0.01	-0.09	0.08	-0.06	0.04	0.03
	<i>CDTcopy</i>	0.03	0.92	0	0.07	-0.07	-0.15	0.09	0.06	0	-0.03	0.08
	<i>IMEMimm</i>	0	-0.02	0.56	0.2	0.08	0	-0.01	0.02	-0.01	0.07	0.11
	<i>IMEMdel</i>	-0.03	0.05	0.07	0.72	0.07	0.01	0	0	0.03	0.09	0.11
	<i>SEMf</i>	0.04	0	0.09	0.09	0.73	0	-0.05	0.05	-0.03	0.03	0.05
	<i>TMTa</i>	0	-0.1	0	0.05	-0.01	0.78	0.25	-0.03	0.02	0	-0.07
	<i>TMTb</i>	-0.02	-0.01	0	-0.05	-0.02	0.06	0.75	-0.03	0.02	0	-0.09
	<i>BNT</i>	0.09	-0.02	-0.05	0.06	0.06	0.06	-0.05	0.81	-0.01	0	0.08
	<i>RAVLTdel</i>	0.01	0	-0.03	0.14	0.03	-0.06	0	0	0.65	0.06	0.07
	<i>RAVLTrec</i>	0.05	0	-0.01	0.1	0	0.04	0.03	0	0.08	0.65	0.1
	<i>MMSE</i>	-0.02	0.01	0.05	0.01	-0.01	-0.11	0	0.08	0.07	0	0.9

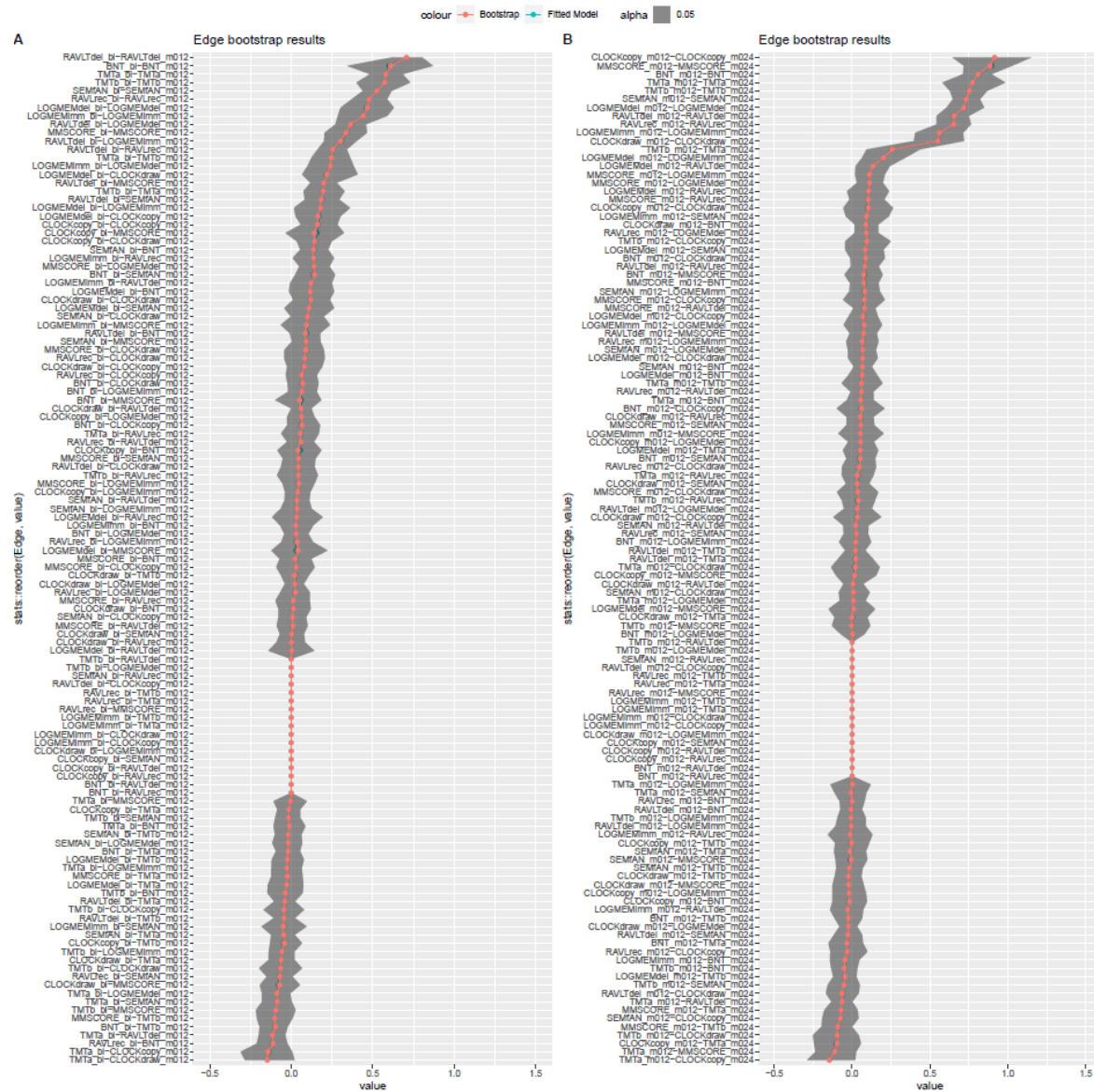


Figure SM3. Bootstrapped confidence intervals of estimated edge weights in MCI patients non-converter group. The figure shows the 95% bootstrapped CIs of edge weights in the first (on the left) and the second (on the right) year. The orange line indicates the bootstrapped mean values of the confidence interval, the green line indicates the sample values and the grey area indicates the 95% confidence intervals.

MCI patients – converter group

Table SM4. MCI converter edges. The diagonal shows the autoregressive patterns, the upper part of the table shows the cross-lagged prediction from the baseline (rows) to the 12th month (columns), and the lower part of the table shows the cross-lagged prediction from the 12th month (columns) to the 24th month (rows). BNT=Boston Naming Test; CDTcopy=Clock Drawing Test (copy); CDTdraw=Clock Drawing Test (draw); IMEMimm=Logical Memory Test – immediate recall; IMEMdel=Logical Memory Test – delayed recall; MMSE=Mini Mental State Examination; RAVLTrec=Rey Auditory Verbal Learning Test - recognition; RAVLTDel=Rey Auditory Verbal Learning Test - delayed recall; SEMfAN=Semantic Fluency test (animal); TMTa=Trials making Test – a; TMTb=Trials making Test – b.

		<i>12th month</i>										
		<i>CDTdraw</i>	<i>CDTcopy</i>	<i>IMEMimm</i>	<i>IMEMdel</i>	<i>SEMfAN</i>	<i>TMTa</i>	<i>TMTb</i>	<i>BNT</i>	<i>RAVLTdel</i>	<i>RAVLTrec</i>	<i>MMSE</i>
<i>Baseline</i>	<i>CDTdraw</i>	0.35	0.19	-0.08	-0.11	0.02	0.00	-0.03	0.00	0.00	-0.13	-0.08
	<i>CDTcopy</i>	0.00	0.04	-0.06	0.00	0.11	0.03	-0.03	0.11	0.00	0.00	-0.11
	<i>IMEMimm</i>	0.08	-0.10	0.27	-0.01	0.14	0.00	0.00	0.10	0.00	0.00	0.14
	<i>IMEMdel</i>	0.00	0.22	0.41	0.62	0.00	0.00	0.00	0.08	0.14	0.12	-0.03
	<i>SEMf</i>	0.02	-0.02	0.14	0.09	0.54	0.00	-0.03	-0.01	0.00	0.00	0.12
	<i>TMTa</i>	-0.09	-0.11	0.00	0.00	-0.19	0.47	0.07	0.00	0.00	0.00	0.02
	<i>TMTb</i>	-0.02	-0.20	0.05	0.10	0.16	0.29	0.73	0.00	0.00	-0.10	-0.15
	<i>BNT</i>	-0.05	0.00	0.09	0.06	0.03	-0.08	0.00	0.91	0.00	0.00	-0.12
	<i>RAVLTdel</i>	0.00	0.08	0.10	0.24	0.20	0.00	-0.07	0.00	0.68	0.25	0.20
	<i>RAVLTrec</i>	0.27	0.00	0.06	0.19	0.00	0.00	0.14	0.00	0.06	0.58	0.12
	<i>MMSE</i>	0.00	0.09	0.16	0.11	-0.07	0.00	0.00	0.11	0.02	0.00	0.53
<i>24th month</i>	<i>CDTdraw</i>	0.19	0.00	0.13	0.00	0.22	-0.23	-0.17	0.06	0.00	0.01	0.00
	<i>CDTcopy</i>	-0.02	0.26	0.11	0.08	0.08	-0.28	-0.01	0.00	-0.04	0.00	-0.12
	<i>IMEMimm</i>	0.04	0.12	0.33	0.44	-0.01	0.00	-0.04	0.09	0.12	0.04	-0.05
	<i>IMEMdel</i>	0.12	0.00	0.04	0.72	-0.04	0.00	0.04	0.07	0.19	0.01	-0.01
	<i>SEMf</i>	0.11	0.00	0.00	0.00	0.54	0.05	-0.21	0.18	0.11	0.00	0.07
	<i>TMTa</i>	0.00	-0.06	0.00	0.00	0.00	0.60	0.26	-0.15	0.00	0.00	0.00
	<i>TMTb</i>	-0.07	-0.11	0.00	0.00	-0.09	0.31	0.59	0.00	0.25	-0.12	0.00
	<i>BNT</i>	0.00	0.07	0.00	0.03	0.24	0.00	0.00	0.63	0.00	0.00	-0.17
	<i>RAVLTdel</i>	0.00	0.00	0.00	0.04	0.00	0.00	0.00	0.00	0.63	0.10	0.07
	<i>RAVLTrec</i>	0.11	0.00	0.00	0.20	0.00	0.00	0.10	0.00	0.22	0.40	0.00
	<i>MMSE</i>	0.21	0.21	0.03	0.05	0.02	0.07	0.07	0.14	0.19	-0.05	0.51

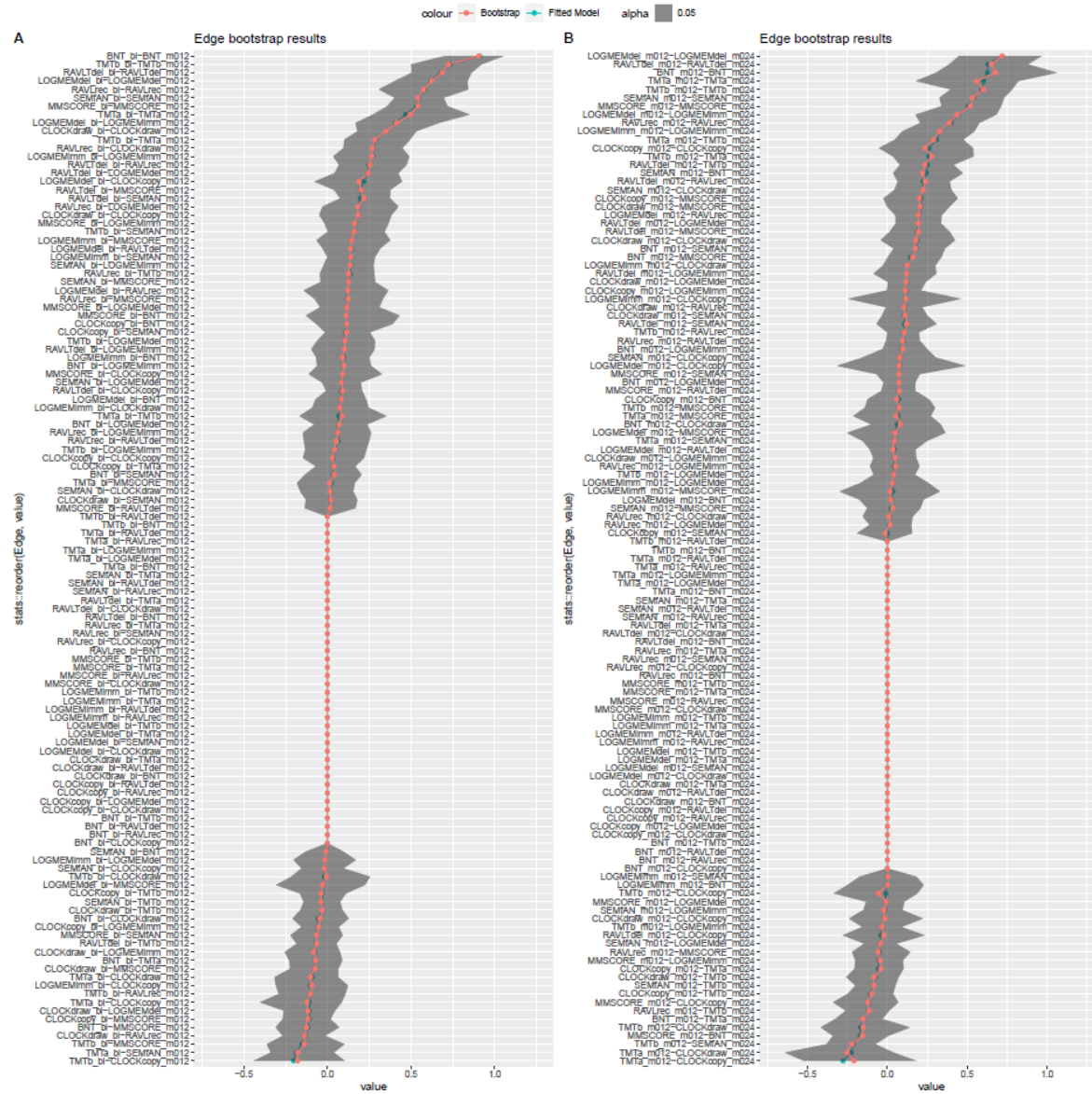


Figure SM4. Bootstrapped confidence intervals of estimated edge weights in MCI patients converter group. The figure shows the 95% bootstrapped CIs of edge weights in the first (on the left) and the second (on the right) year. The orange line indicates the bootstrapped mean values of the confidence interval, the green line indicates the sample values and the grey area indicates the 95% confidence intervals.

Cross-lagged in-prediction and cross-lagged out-prediction

Healthy participants

Table SM5. HP stable cross-lagged prediction. The table shows the cross-lagged in- and out-predictions (i.e., the extent to which each variable is predicted by or predicts other variables, excluding auto-regressive patterns). T1 = prediction from baseline (bl) to 12 months (m012); T2 = prediction from 12 months (m012) to 24 months (m024). BNT=Boston Naming Test; CDTcopy=Clock Drawing Test (copy); CDTdraw=Clock Drawing Test (draw); lMEMimm=Logical Memory Test – immediate recall; lMEMdel=Logical Memory Test – delayed recall; MMSE=Mini Mental State Examination; RAVLrec=Rey Auditory Verbal Learning Test - recognition; RAVLdel=Rey Auditory Verbal Learning Test - delayed recall; SEMfAN=Semantic Fluency test (animal); TMTa=Trials making Test – a; TMTb=Trials making Test – b.

Prediction index	Time	Variable	Fitted value	Bootstrap mean	Lower quantile	Upper quantile
In-prediction	T1	BNT_m012	0.03	0.04	0.01	0.07
In-prediction	T1	CLOCKcopy_m012	0.04	0.06	0.03	0.11
In-prediction	T1	CLOCKdraw_m012	0.04	0.06	0.01	0.13
In-prediction	T1	LOGMEMdel_m012	0.13	0.14	0.07	0.24
In-prediction	T1	LOGMEMimm_m012	0.07	0.09	0.04	0.18
In-prediction	T1	MMSCORE_m012	0.03	0.05	0.01	0.13
In-prediction	T1	RAVLrec_m012	0.06	0.08	0.04	0.13
In-prediction	T1	RAVLdel_m012	0.04	0.05	0.02	0.09
In-prediction	T1	SEMfAN_m012	0.04	0.05	0.02	0.09
In-prediction	T1	TMTa_m012	0.11	0.12	0.03	0.25
In-prediction	T1	TMTb_m012	0.10	0.12	0.05	0.21
Out-prediction	T1	BNT_bl	0.00	0.00	0.00	0.01
Out-prediction	T1	CLOCKcopy_bl	0.00	0.00	0.00	0.01
Out-prediction	T1	CLOCKdraw_bl	0.00	0.00	0.00	0.01
Out-prediction	T1	LOGMEMdel_bl	0.00	0.01	0.00	0.02
Out-prediction	T1	LOGMEMimm_bl	0.01	0.01	0.00	0.02
Out-prediction	T1	MMSCORE_bl	0.00	0.00	0.00	0.01
Out-prediction	T1	RAVLrec_bl	0.01	0.01	0.00	0.03
Out-prediction	T1	RAVLdel_bl	0.01	0.01	0.00	0.02
Out-prediction	T1	SEMfAN_bl	0.00	0.00	0.00	0.01
Out-prediction	T1	TMTa_bl	0.00	0.01	0.00	0.01
Out-prediction	T1	TMTb_bl	0.01	0.01	0.00	0.03
In-prediction	T2	BNT_m024	0.01	0.02	0.00	0.04

In-prediction	T2	CLOCKcopy_m024	0.02	0.04	0.01	0.09
In-prediction	T2	CLOCKdraw_m024	0.02	0.03	0.01	0.09
In-prediction	T2	LOGMEMdel_m024	0.09	0.11	0.04	0.21
In-prediction	T2	LOGMEMimm_m024	0.08	0.09	0.04	0.18
In-prediction	T2	MMSCORE_m024	0.07	0.09	0.04	0.15
In-prediction	T2	RAVLrec_m024	0.08	0.09	0.03	0.18
In-prediction	T2	RAVLTdel_m024	0.03	0.04	0.01	0.09
In-prediction	T2	SEMfAN_m024	0.02	0.03	0.01	0.05
In-prediction	T2	TMTa_m024	0.16	0.13	0.00	0.33
In-prediction	T2	TMTb_m024	0.02	0.05	0.01	0.11
Out-prediction	T2	BNT_m012	0.00	0.00	0.00	0.01
Out-prediction	T2	CLOCKcopy_m012	0.00	0.00	0.00	0.01
Out-prediction	T2	CLOCKdraw_m012	0.00	0.00	0.00	0.01
Out-prediction	T2	LOGMEMdel_m012	0.01	0.01	0.00	0.02
Out-prediction	T2	LOGMEMimm_m012	0.01	0.01	0.00	0.02
Out-prediction	T2	MMSCORE_m012	0.00	0.00	0.00	0.00
Out-prediction	T2	RAVLrec_m012	0.00	0.00	0.00	0.01
Out-prediction	T2	RAVLTdel_m012	0.01	0.01	0.00	0.02
Out-prediction	T2	SEMfAN_m012	0.00	0.00	0.00	0.01
Out-prediction	T2	TMTa_m012	0.00	0.01	0.00	0.02
Out-prediction	T2	TMTb_m012	0.02	0.02	0.00	0.04

MCI patients – non-converter group

Table MS6. *MCI non-converter cross-lagged prediction.* The table shows the cross-lagged in- and out-predictions (i.e., the extent to which each variable is predicted by or predicts other variables, excluding auto-regressive patterns). T1 = prediction from baseline (bl) to 12 months (m012); T2 = prediction from 12 months (m012) to 24 months (m024). BNT=Boston Naming Test; CDTcopy=Clock Drawing Test (copy); CDTdraw=Clock Drawing Test (draw); lMEMimm=Logical Memory Test – immediate recall; lMEMdel=Logical Memory Test – delayed recall; MMSE=Mini Mental State Examination; RAVLTrec=Rey Auditory Verbal Learning Test - recognition; RAVLTdel=Rey Auditory Verbal Learning Test - delayed recall; SEMfAN=Semantic Fluency test (animal); TMTa=Trials making Test – a; TMTb=Trials making Test – b.

<i>Prediction index</i>	<i>Time</i>	<i>Variable</i>	<i>Fitted value</i>	<i>Bootstrap mean</i>	<i>Lower quantile</i>	<i>Upper quantile</i>
In-prediction	T1	BNT_m012	0.07	0.08	0.02	0.19
In-prediction	T1	CLOCKcopy_m012	0.12	0.15	0.08	0.24
In-prediction	T1	CLOCKdraw_m012	0.22	0.24	0.16	0.32

In-prediction	T1	LOGMEMdel_m012	0.27	0.28	0.20	0.37
In-prediction	T1	LOGMEMimm_m012	0.20	0.21	0.14	0.30
In-prediction	T1	MMSCORE_m012	0.18	0.20	0.12	0.30
In-prediction	T1	RAVLrec_m012	0.09	0.10	0.06	0.15
In-prediction	T1	RAVLTdel_m012	0.04	0.05	0.02	0.08
In-prediction	T1	SEMfAN_m012	0.09	0.10	0.05	0.15
In-prediction	T1	TMTa_m012	0.08	0.09	0.05	0.16
In-prediction	T1	TMTb_m012	0.10	0.11	0.05	0.19
Out-prediction	T1	BNT_bl	0.00	0.01	0.00	0.02
Out-prediction	T1	CLOCKcopy_bl	0.01	0.01	0.00	0.02
Out-prediction	T1	CLOCKdraw_bl	0.00	0.00	0.00	0.01
Out-prediction	T1	LOGMEMdel_bl	0.01	0.01	0.00	0.02
Out-prediction	T1	LOGMEMimm_bl	0.01	0.01	0.00	0.02
Out-prediction	T1	MMSCORE_bl	0.00	0.00	0.00	0.01
Out-prediction	T1	RAVLrec_bl	0.00	0.01	0.00	0.01
Out-prediction	T1	RAVLTdel_bl	0.03	0.03	0.02	0.05
Out-prediction	T1	SEMfAN_bl	0.00	0.01	0.00	0.01
Out-prediction	T1	TMTa_bl	0.01	0.01	0.01	0.02
Out-prediction	T1	TMTb_bl	0.01	0.01	0.00	0.02
In-prediction	T2	BNT_m024	0.03	0.04	0.02	0.07
In-prediction	T2	CLOCKcopy_m024	0.02	0.04	0.01	0.08
In-prediction	T2	CLOCKdraw_m024	0.04	0.06	0.02	0.12
In-prediction	T2	LOGMEMdel_m024	0.05	0.06	0.03	0.11
In-prediction	T2	LOGMEMimm_m024	0.10	0.11	0.05	0.20
In-prediction	T2	MMSCORE_m024	0.03	0.04	0.02	0.08
In-prediction	T2	RAVLrec_m024	0.05	0.06	0.03	0.10
In-prediction	T2	RAVLTdel_m024	0.05	0.06	0.02	0.10
In-prediction	T2	SEMfAN_m024	0.06	0.07	0.04	0.11
In-prediction	T2	TMTa_m024	0.07	0.08	0.03	0.16
In-prediction	T2	TMTb_m024	0.02	0.03	0.01	0.08
Out-prediction	T2	BNT_m012	0.00	0.00	0.00	0.01
Out-prediction	T2	CLOCKcopy_m012	0.00	0.00	0.00	0.01

Out-prediction	T2	CLOCKdraw_m012	0.00	0.00	0.00	0.01
Out-prediction	T2	LOGMEMdel_m012	0.01	0.01	0.00	0.02
Out-prediction	T2	LOGMEMimm_m012	0.00	0.00	0.00	0.01
Out-prediction	T2	MMSCORE_m012	0.00	0.01	0.00	0.01
Out-prediction	T2	RAVLrec_m012	0.00	0.00	0.00	0.01
Out-prediction	T2	RAVLTdel_m012	0.00	0.00	0.00	0.01
Out-prediction	T2	SEMfAN_m012	0.00	0.00	0.00	0.01
Out-prediction	T2	TMTa_m012	0.00	0.00	0.00	0.02
Out-prediction	T2	TMTb_m012	0.01	0.01	0.00	0.04

MCI patients – converter group

Table SM7. MCI converter cross-lagged prediction. The table shows the cross-lagged in- and out-predictions (i.e., the extent to which each variable is predicted by or predicts other variables, excluding auto-regressive patterns). T1 = prediction from baseline (bl) to 12 months (m012); T2 = prediction from 12 months (m012) to 24 months (m024). BNT=Boston Naming Test; CDTcopy=Clock Drawing Test (copy); CDTdraw=Clock Drawing Test (draw); IMEMimm=Logical Memory Test – immediate recall; IMEMdel=Logical Memory Test – delayed recall; MMSE=Mini Mental State Examination; RAVLTrec=Rey Auditory Verbal Learning Test - recognition; RAVLTdel=Rey Auditory Verbal Learning Test - delayed recall; SEMfAN=Semantic Fluency test (animal); TMTa=Trials making Test – a; TMTb=Trials making Test – b.

<i>Prediction index</i>	<i>Time</i>	<i>Variable</i>	<i>Fitted value</i>	<i>Bootstrap mean</i>	<i>Lower quantile</i>	<i>Upper quantile</i>
In-prediction	T1	BNT_m012	0.04	0.06	0.01	0.15
In-prediction	T1	CLOCKcopy_m012	0.20	0.24	0.11	0.42
In-prediction	T1	CLOCKdraw_m012	0.09	0.12	0.05	0.22
In-prediction	T1	LOGMEMdel_m012	0.16	0.19	0.09	0.31
In-prediction	T1	LOGMEMimm_m012	0.28	0.32	0.15	0.53
In-prediction	T1	MMSCORE_m012	0.17	0.20	0.12	0.31
In-prediction	T1	RAVLrec_m012	0.08	0.11	0.03	0.22
In-prediction	T1	RAVLTdel_m012	0.02	0.03	0.00	0.09
In-prediction	T1	SEMfAN_m012	0.10	0.14	0.06	0.25
In-prediction	T1	TMTa_m012	0.09	0.10	0.02	0.23
In-prediction	T1	TMTb_m012	0.02	0.05	0.01	0.13
Out-prediction	T1	BNT_bl	0.00	0.01	0.00	0.01
Out-prediction	T1	CLOCKcopy_bl	0.00	0.01	0.00	0.01
Out-prediction	T1	CLOCKdraw_bl	0.01	0.01	0.00	0.03
Out-prediction	T1	LOGMEMdel_bl	0.02	0.02	0.01	0.04

Out-prediction	T1	LOGMEMimm_bl	0.01	0.01	0.00	0.02
Out-prediction	T1	MMSCORE_bl	0.00	0.01	0.00	0.02
Out-prediction	T1	RAVLrec_bl	0.01	0.01	0.00	0.03
Out-prediction	T1	RAVLTdel_bl	0.02	0.03	0.01	0.05
Out-prediction	T1	SEMfAN_bl	0.00	0.01	0.00	0.02
Out-prediction	T1	TMTa_bl	0.01	0.01	0.00	0.03
Out-prediction	T1	TMTb_bl	0.02	0.02	0.01	0.05
In-prediction	T2	BNT_m024	0.06	0.07	0.01	0.19
In-prediction	T2	CLOCKcopy_m024	0.09	0.15	0.05	0.32
In-prediction	T2	CLOCKdraw_m024	0.20	0.25	0.13	0.41
In-prediction	T2	LOGMEMdel_m024	0.05	0.08	0.02	0.20
In-prediction	T2	LOGMEMimm_m024	0.30	0.33	0.15	0.56
In-prediction	T2	MMSCORE_m024	0.16	0.20	0.11	0.31
In-prediction	T2	RAVLrec_m024	0.17	0.20	0.07	0.34
In-prediction	T2	RAVLTdel_m024	0.04	0.05	0.00	0.13
In-prediction	T2	SEMfAN_m024	0.11	0.15	0.06	0.27
In-prediction	T2	TMTa_m024	0.10	0.14	0.03	0.38
In-prediction	T2	TMTb_m024	0.16	0.17	0.06	0.32
Out-prediction	T2	BNT_m012	0.01	0.01	0.00	0.03
Out-prediction	T2	CLOCKcopy_m012	0.01	0.01	0.00	0.02
Out-prediction	T2	CLOCKdraw_m012	0.01	0.01	0.00	0.02
Out-prediction	T2	LOGMEMdel_m012	0.02	0.03	0.01	0.06
Out-prediction	T2	LOGMEMimm_m012	0.00	0.01	0.00	0.03
Out-prediction	T2	MMSCORE_m012	0.00	0.01	0.00	0.02
Out-prediction	T2	RAVLrec_m012	0.00	0.01	0.00	0.01
Out-prediction	T2	RAVLTdel_m012	0.02	0.03	0.01	0.05
Out-prediction	T2	SEMfAN_m012	0.01	0.01	0.00	0.03
Out-prediction	T2	TMTa_m012	0.02	0.02	0.00	0.05
Out-prediction	T2	TMTb_m012	0.01	0.02	0.01	0.05