

Supplementary Material

Change in cognitive performance during seven-year follow-up in midlife is associated with sex, age, and education – The Cardiovascular Risk in Young Finns Study

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Online Resource 1 Cognitive performance in 2011 and in 2018.

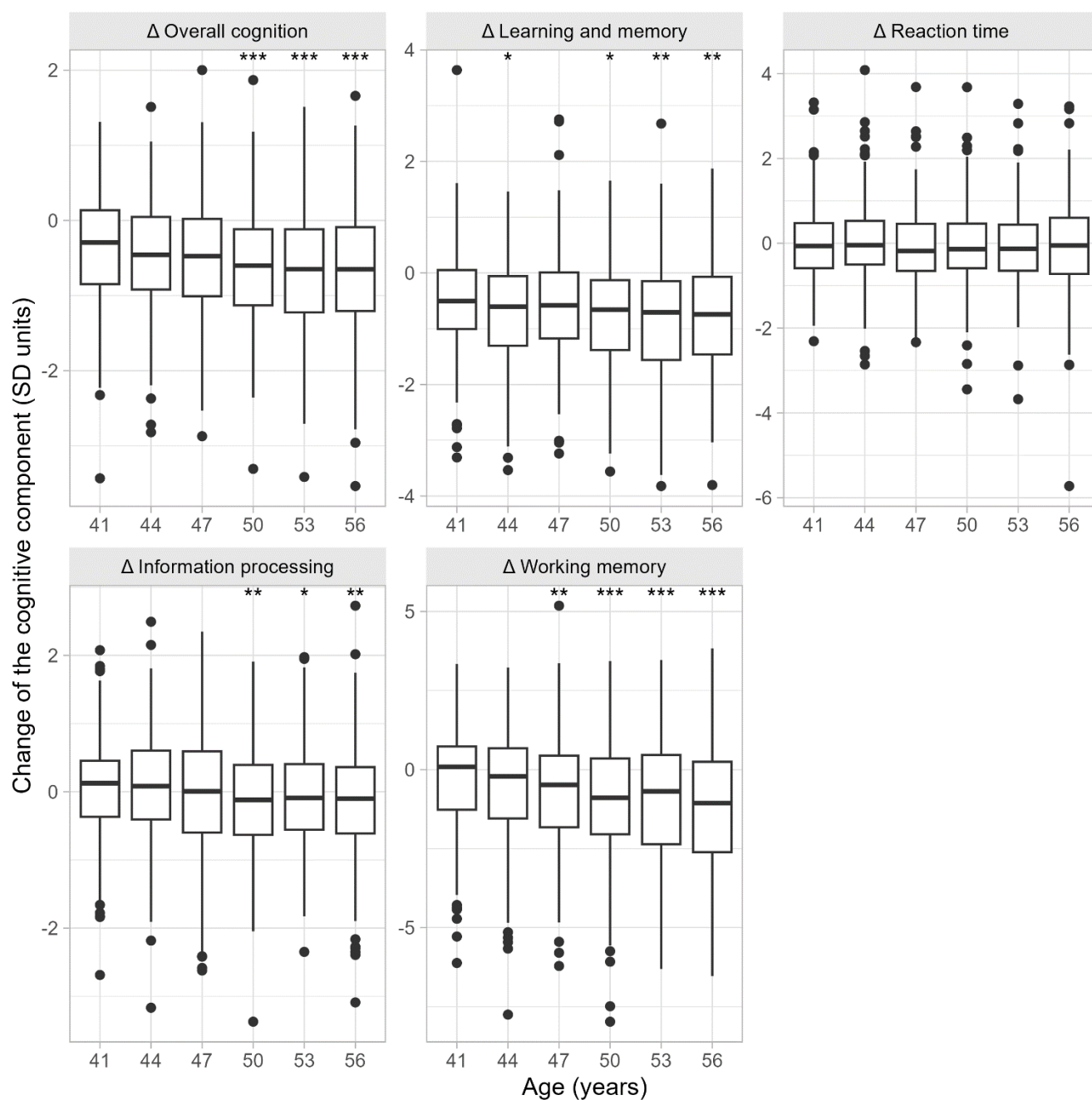
	2011	2018	<i>p</i> value 2011 vs. 2018
All subjects (n = 1671)			
<i>Overall cognition</i>			
Mean (SD)	0.00 (1.00)	-0.56 (1.19)	<0.001
Missing	169 (10.1%)	131 (7.8%)	
<i>Learning and memory</i>			
Mean (SD)	0.00 (1.00)	-0.70 (1.22)	<0.001
Missing	145 (8.7%)	65 (3.9%)	
<i>Reaction time</i>			
Mean (SD)	0.00 (1.00)	-0.06 (0.85)	0.019
Missing	165 (9.9%)	10 (0.6%)	
<i>Information processing</i>			
Mean (SD)	0.00 (1.00)	-0.03 (1.14)	0.016
Missing	23 (1.4%)	76 (4.5%)	
<i>Working memory</i>			
Mean (SD)	0.00 (1.00)	-0.81 (2.11)	<0.001
Missing	4 (0.2%)	6 (0.4%)	
Males (n = 740)			
<i>Overall cognition</i>			
Mean (SD)	0.02 (1.04)	-0.55 (1.24)	<0.001
Missing	69 (9.3%)	38 (5.1%)	
<i>Learning and memory</i>			
Mean (SD)	-0.06 (1.01)	-0.80 (1.23)	<0.001
Missing	61 (8.2%)	20 (2.7%)	
<i>Reaction time</i>			
Mean (SD)	0.14 (1.02)	-0.03 (0.88)	<0.001
Missing	69 (9.3%)	4 (0.5%)	
<i>Information processing</i>			
Mean (SD)	0.07 (1.01)	0.05 (1.16)	0.34
Missing	7 (0.9%)	21 (2.8%)	
<i>Working memory</i>			
Mean (SD)	0.21 (0.99)	-0.39 (2.10)	<0.001
Missing	3 (0.4%)	3 (0.4%)	
Females (n = 931)			
<i>Overall cognition</i>			
Mean (SD)	-0.02 (0.97)	-0.58 (1.15)	<0.001
Missing	100 (10.7%)	93 (10.0%)	
<i>Learning and memory</i>			
Mean (SD)	0.05 (0.99)	-0.62 (1.20)	<0.001
Missing	84 (9.0%)	45 (4.8%)	
<i>Reaction time</i>			
Mean (SD)	-0.11 (0.97)	-0.09 (0.81)	0.42
Missing	96 (10.3%)	6 (0.6%)	
<i>Information processing</i>			
Mean (SD)	-0.06 (0.99)	-0.10 (1.12)	0.017
Missing	16 (1.7%)	55 (5.9%)	
<i>Working memory</i>			
Mean (SD)	-0.16 (0.98)	-1.13 (2.06)	<0.001
Missing	1 (0.1%)	3 (0.3%)	

A two-sample paired Student's t test was used to study the difference between years 2011 and 2018. Statistically significant results are bolded.

Online Resource 2 Coefficients of the CANTAB test variables on the first principal components for cognitive performance.

	Overall cognition	Learning and memory	Reaction time	Information processing	Working memory
Variance explained by the first principal component (%)	24.9	59.4	36.7	64.5	33.2
PAL - First attempt memory score	0.339	0.474			
PAL - Mean errors to success	-0.272	-0.343			
PAL - Number of patterns reached	0.067	0.142			
PAL - Total errors (6 patterns, adjusted)	-0.237	-0.358			
PAL - Total errors (8 patterns, adjusted)	-0.262	-0.382			
PAL - Total errors (adjusted)	-0.297	-0.427			
PAL - Total attempts	-0.353	-0.426			
RTI - Error score	0.008		-0.018		
RTI - Mean movement time	-0.090		-0.826		
RTI - Mean reaction time	-0.087		-0.563		
RVP - Mean response latency	-0.168			-0.257	
RVP - A' (sensitivity to target sequence)	0.385			0.602	
RVP - Probability of false alarm	-0.093			-0.105	
RVP - Probability of hit	0.379			0.611	
RVP - Total false alarms	-0.045			-0.052	
RVP - Total hits	0.157			0.250	
RVP - Total misses	-0.214			-0.349	
SWM - Between errors (4 boxes)	-0.058				-0.281
SWM - Between errors (total)	-0.172				-0.655
SWM - Double errors (4 boxes)	-0.007				-0.027
SWM - Double errors (total)	-0.027				-0.193
SWM - Strategy (6-8 boxes)	-0.137				-0.643
SWM - Within errors (4 boxes)	-0.010				-0.021
SWM - Within errors (total)	-0.027				-0.198

PAL: Learning and memory; RTI: Reaction Time; RVP: Information Processing; SWM: Working Memory test. The cell colors visualize the loadings within each cognitive domain so that the values greater than zero are shown in red and smaller than zero in blue.



Online Resource 3 Association between the change in the cognitive performance and age. The asterisks indicate the statistical significance of the pairwise comparisons between each age cohort and the reference at age cohort of 41 years. *** $p < 0.001$; ** $p < 0.01$; * $p < 0.05$.

Online Resource 4 Association between change in cognitive performance, age, education, and menopause adjusted for year 2011 result for the respective cognitive domains in female subjects. The effect of menopause on females was tested only for information processing and working memory as these cognitive domains were decreased more in females compared to males (Table 2).

	β estimate	95% confidence interval	p value	R^2
Δ Information processing				0.10
(Intercept)	-0.11	-0.80, 0.59	0.760	
Age, years	-0.01	-0.02, 0.00	0.213	
Education, years	0.03	0.02, 0.05	<0.001	
Menopause, peri	0.03	-0.12, 0.17	0.714	
Menopause, post	-0.19	-0.35, -0.03	0.022	
Information processing 2011	-0.23	-0.29, -0.18	<0.001	
Δ Working memory				0.025
(Intercept)	0.81	-0.78, 2.40	0.317	
Age, years	-0.05	-0.08, -0.02	0.002	
Education, years	0.04	0.00, 0.07	0.036	
Menopause, peri	0.13	-0.20, 0.45	0.454	
Menopause, post	0.04	-0.34, 0.41	0.841	
Working memory 2011	-0.11	-0.24, 0.03	0.112	

Δ : Delta change of cognitive performance between years 2018-2020 and 2011.

Menopause was reported in three categories: pre-menopause (no symptoms; reference group), peri-menopause (symptoms including irregular menstruation or hot flushes or night sweats), and post-menopause (menstruation ceased at least one year ago). Statistically significant results are bolded.

Online Resource 5 Prevalence of illnesses in year 2018.

	<i>female</i> (<i>N</i> =931)	<i>male</i> (<i>N</i> =740)	<i>p-value</i> (<i>females vs. males</i>)
Cardiovascular disease ^{1,*}			
No	681 (73.1%)	513 (69.3%)	0.45
Yes	225 (24.2%)	186 (25.1%)	
Missing	25 (2.7%)	41 (5.5%)	
Brain disease ^{2,*}			
No	892 (95.8%)	687 (92.8%)	0.94
Yes	14 (1.5%)	12 (1.6%)	
Missing	25 (2.7%)	41 (5.5%)	
Type 2 diabetes*			
No	866 (93.0%)	660 (89.2%)	0.37
Yes	37 (4.0%)	36 (4.9%)	
Missing	28 (3.0%)	44 (5.9%)	
Cancer*			
No	883 (94.8%)	683 (92.3%)	0.65
Yes	21 (2.3%)	13 (1.8%)	
Missing	27 (2.9%)	44 (5.9%)	
Migraine*			
No	692 (74.3%)	646 (87.3%)	<0.001
Yes	212 (22.8%)	49 (6.6%)	
Missing	27 (2.9%)	45 (6.1%)	
Depression*			
No	808 (86.8%)	649 (87.7%)	0.009
Yes	96 (10.3%)	47 (6.4%)	
Missing	27 (2.9%)	44 (5.9%)	
Anxiety or other mental disorder ^{3,*}			
No	844 (90.7%)	655 (88.5%)	0.52
Yes	59 (6.3%)	39 (5.3%)	
Missing	28 (3.0%)	46 (6.2%)	
Obesity ⁴			
No	665 (71.4%)	536 (72.4%)	0.69
Yes	266 (28.6%)	204 (27.6%)	

¹Cardiac infarction, coronary heart disease, hypertension, insufficiency of heart, atrial fibrillation, other arrhythmia, valvular defect, congenital heart defect, dilation of aorta, constriction of carotid artery, and/or claudication.

²Cerebral thrombosis, cerebral hemorrhage, and/or cerebrovascular accident in the past.

³Anxiety or other mental disorder was asked as a one question in self-reported questionnaire. Therefore, this group includes individuals diagnosed with anxiety as well with other affective and non-affective psychotic disorders and personality disorders.

⁴If body mass index is greater than 30 m²/kg, participant is considered obese.

*Values are based on self-reported questionnaires of whether a medical doctor has diagnosed the given condition by the year 2018.

Online Resource 6 Association between change in cognitive performance, sex, age, and education adjusted for year 2011 result for the respective cognitive domains and illnesses.

	β estimate	95% confidence interval	p value	R^2
Δ Overall cognition				0.081
(Intercept)	0.22	-0.26, 0.70	0.372	
Sex, male	0.07	-0.02, 0.15	0.126	
Age, years	-0.03	-0.04, -0.02	<0.001	
Education, years	0.04	0.02, 0.05	<0.001	
Overall cognition 2011	-0.17	-0.21, -0.12	<0.001	
Cardiovascular disease ¹ , yes	-0.02	-0.12, 0.08	0.696	
Brain disease ² , yes	-0.08	-0.43, 0.26	0.630	
Type 2 diabetes, yes	-0.09	-0.31, 0.12	0.405	
Cancer, yes	0.19	-0.10, 0.48	0.201	
Migraine, yes	0.07	-0.05, 0.19	0.228	
Depression, yes	0.02	-0.14, 0.18	0.795	
Anxiety or other mental disorder ³ , yes	-0.14	-0.33, 0.05	0.138	
Obesity ⁴ , yes	-0.02	-0.12, 0.08	0.659	
Δ Learning and memory				0.095
(Intercept)	0.32	-0.25, 0.90	0.266	
Sex, male	-0.09	-0.19, 0.02	0.101	
Age, years	-0.03	-0.04, -0.02	<0.001	
Education, years	0.03	0.01, 0.04	<0.001	
Learning and memory 2011	-0.28	-0.33, -0.23	<0.001	
Cardiovascular disease ¹ , yes	0.00	-0.12, 0.12	0.969	
Brain disease ² , yes	-0.29	-0.68, 0.09	0.131	
Type 2 diabetes, yes	0.01	-0.23, 0.26	0.908	
Cancer, yes	0.26	-0.09, 0.61	0.145	
Migraine, yes	0.03	-0.11, 0.17	0.674	
Depression, yes	0.04	-0.14, 0.23	0.641	
Anxiety or other mental disorder ³ , yes	-0.08	-0.30, 0.14	0.461	
Obesity ⁴ , yes	-0.01	-0.13, 0.10	0.856	
Δ Reaction time				0.39
(Intercept)	0.99	0.54, 1.43	<0.001	
Sex, male	-0.01	-0.09, 0.07	0.826	
Age, years	-0.02	-0.03, -0.02	<0.001	
Education, years	0.01	-0.00, 0.02	0.230	
Reaction time 2011	-0.59	-0.63, -0.55	<0.001	
Cardiovascular disease ¹ , yes	0.02	-0.08, 0.11	0.750	
Brain disease ² , yes	-0.09	-0.41, 0.22	0.551	
Type 2 diabetes, yes	-0.08	-0.28, 0.12	0.416	
Cancer, yes	0.05	-0.23, 0.32	0.734	
Migraine, yes	0.18	0.07, 0.29	0.001	
Depression, yes	-0.03	-0.18, 0.12	0.740	
Anxiety or other mental disorder ³ , yes	-0.14	-0.31, 0.03	0.114	
Obesity ⁴ , yes	0.03	-0.06, 0.12	0.551	

<i>Δ Information processing</i>			0.11
(Intercept)	0.11	-0.35, 0.58	0.630
Sex, male	0.15	0.06, 0.23	0.001
Age, years	-0.02	-0.03, -0.01	<0.001
Education, years	0.04	0.03, 0.05	<0.001
Information processing 2011	-0.23	-0.28, -0.19	<0.001
Cardiovascular disease ¹ , yes	0.01	-0.08, 0.11	0.832
Brain disease ² , yes	0.11	-0.24, 0.45	0.542
Type 2 diabetes, yes	-0.15	-0.35, 0.05	0.140
Cancer, yes	0.09	-0.19, 0.37	0.526
Migraine, yes	0.13	0.02, 0.24	0.022
Depression, yes	0.00	-0.15, 0.16	0.975
Anxiety or other mental disorder ³ , yes	-0.13	-0.31, 0.05	0.161
Obesity ⁴ , yes	-0.06	-0.16, 0.03	0.178
<i>Δ Working memory</i>			0.044
(Intercept)	1.05	-0.03, 2.13	0.058
Sex, male	0.41	0.21, 0.60	<0.001
Age, years	-0.05	-0.07, -0.03	<0.001
Education, years	0.04	0.01, 0.06	0.003
Working memory 2011	-0.13	-0.23, -0.03	0.009
Cardiovascular disease ¹ , yes	-0.30	-0.52, -0.08	0.008
Brain disease ² , yes	-0.06	-0.80, 0.69	0.880
Type 2 diabetes, yes	0.19	-0.27, 0.65	0.421
Cancer, yes	-0.25	-0.89, 0.38	0.436
Migraine, yes	-0.02	-0.27, 0.24	0.908
Depression, yes	-0.16	-0.51, 0.20	0.391
Anxiety or other mental disorder ³ , yes	-0.31	-0.73, 0.11	0.146
Obesity ⁴ , yes	0.04	-0.17, 0.26	0.685

Δ: Delta change of cognitive performance between years 2018 and 2011. Values are β estimates and their 95% confidence intervals and p values from linear models. All variables are entered simultaneously into the model. Variables related to illnesses are defined the same way as in Supplementary Table 4. For illnesses, reference value is “No”. R^2 values represent the goodness of fit of each full model. Statistically significant p values are bolded.

¹Cardiac infarction, coronary heart disease, hypertension, insufficiency of heart, atrial fibrillation, other arrhythmia, valvular defect, congenital heart defect, dilation of aorta, constriction of carotid artery, and/or claudication.

²Cerebral thrombosis, cerebral hemorrhage, and/or cerebrovascular accident in the past.

³Anxiety or other mental disorder was asked as a one question in self-reported questionnaire. Therefore, this group includes individuals diagnosed with anxiety as well with other affective and non-affective psychotic disorders and personality disorders.

⁴If body mass index is greater than 30 m²/kg, participant is considered obese.

Online Resource 7 Association between change in cognitive performance, sex, age, and education adjusted for gross yearly income in the year 2018 and year 2011 result for the respective cognitive domains.

	<i>β estimate</i>	<i>95% confidence interval</i>	<i>p value</i>	<i>R²</i>
Δ Overall cognition				0.081
(Intercept)	0.23	-0.24, 0.70	0.339	
Sex, male	0.04	-0.04, 0.13	0.307	
Age, years	-0.03	-0.04, -0.02	<0.001	
Education, years	0.03	0.02, 0.04	<0.001	
Gross income, 5000 €	0.01	-0.00, 0.02	0.068	
Overall cognition 2011	-0.18	-0.23, -0.14	<0.001	
Δ Learning and memory				0.095
(Intercept)	0.28	-0.28, 0.85	0.324	
Sex, male	-0.10	-0.20, 0.01	0.067	
Age, years	-0.03	-0.04, -0.02	<0.001	
Education, years	0.02	0.01, 0.04	0.001	
Gross income, 5000 €	0.01	-0.00, 0.02	0.256	
Learning and memory 2011	-0.30	-0.35, -0.25	<0.001	
Δ Reaction time				0.39
(Intercept)	1.02	0.58, 1.46	<0.001	
Sex, male	-0.06	-0.14, 0.02	0.148	
Age, years	-0.02	-0.03, -0.02	<0.001	
Education, years	0.00	-0.01, 0.01	0.586	
Gross income, 5000 €	0.01	0.00, 0.02	0.018	
Reaction time 2011	-0.59	-0.63, -0.55	<0.001	
Δ Information processing				0.11
(Intercept)	0.14	-0.31, 0.60	0.534	
Sex, male	0.11	0.02, 0.19	0.012	
Age, years	-0.02	-0.03, -0.01	<0.001	
Education, years	0.04	0.03, 0.05	<0.001	
Gross income, 5000 €	0.01	0.00, 0.02	0.037	
Information processing 2011	-0.24	-0.28, -0.20	<0.001	
Δ Working memory				0.039
(Intercept)	1.27	0.20, 2.33	0.020	
Sex, male	0.37	0.17, 0.56	<0.001	
Age, years	-0.06	-0.08, -0.04	<0.001	
Education, years	0.03	-0.00, 0.05	0.059	
Gross income, 5000 €	0.02	-0.00, 0.04	0.111	
Working memory 2011	-0.13	-0.23, -0.03	0.008	

Δ: Delta change of cognitive performance between years 2018 and 2011. Values are β estimates and their 95% confidence intervals and *p* values from linear models. All variables are entered simultaneously into the model. Gross yearly income was reported as 5000 € intervals (the highest group > 100 000 €). *R²* values represent the goodness of fit of each full model. Statistically significant *p* values are bolded.