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The GROUP investigators are Therese van Amelsvoort[a], Behrooz Z. Alizadeh[b], Agna A. Bartels-Velthuis[b], Nico J. van Beveren[c,d,e], Richard Bruggeman[b], Wiepke Cahn[f], Lieuwe de Haan[g], Philippe Delespaul[a], Carin J. Meijer[g], Inez Myin-Germeys[h], Rene S. Kahn[f], Frederike Schirmbeck[g], Claudia J.P. Simons[a,i], Neeltje E. van Haren[f], Jim van Os[j], Ruud van Winkel[h]

[a] Maastricht University Medical Center, Department of Psychiatry and Psychology, School for Mental Health and Neuroscience, Maastricht, The Netherlands;
[b] University of Groningen, University Medical Center Groningen, University Center for Psychiatry, Groningen, The Netherlands;
[c] Antes Center for Mental Health Care, Rotterdam, The Netherlands;
[d] Erasmus MC, Department of Psychiatry, Rotterdam, The Netherlands;
[e] Erasmus MC, Department of Neuroscience, Rotterdam, The Netherlands;
[f] University Medical Center Utrecht, Department of Psychiatry, Brain Center Rudolf Magnus, Utrecht, The Netherlands;
[g] Academic Medical Center, University of Amsterdam, Department of Psychiatry, Amsterdam, The Netherlands;
[h] KU Leuven, Department of Neuroscience, Research Group Psychiatry, Center for Contextual Psychiatry, Leuven, Belgium;
[i] GGzE, Institute for Mental Health Care Eindhoven and De Kempen, Eindhoven, The Netherlands;
[j] King's College London, King's Health Partners, Department of Psychosis Studies, Institute of Psychiatry, London, United Kingdom

Section 1

Linear mixed-model results regarding the association between smoking and neurocognitive tasks.

Speed of processing , WAIS digit symbol coding, Total raw score (0-133)				
	Patients n=928			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	69.75414	1.33591	51.955	< 2e-16
Smoking, yes	-2.37791	0.84000	-2.814	0.004948
Time 1	1.63586	0.68458	2.384	0.017372
Time 2	1.19917	0.77474	1.543	0.123220
Gender, female	6.78526	1.11587	6.063	1.93e-09
Age	-0.43853	0.06461	-6.767	2.32e-11
Antipsychotic medication, yes	-4.67082	1.12619	-4.122	4.00e-05
Cannabis, urine positive	0.49692	1.05769	0.467	0.640584
Education	0.53858	0.09478	5.647	1.97e-08
PANSS, negative subscale	-2.43701	0.53033	-4.566	5.40e-06
PANSS, positive subscale	0.21670	0.62020	0.347	0.728504
PANSS, general subscale	-3.64291	1.02617	-3.527	0.000436
Random effects	*Variance*	*SD*		
Subject Intercept	156.82	12.523		
Time 1	49.07	7.005		
Time 2	12.59	3.548		
Residual	68.53	8.278		

Speed of processing , WAIS digit symbol coding, Total raw score (0-133)								
	Siblings, n=966				**Controls, n=562**			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	77.86130	0.75746	102.592	< 2e-16	80.27217	0.95454	83.809	< 2e-16
Smoking, yes	-1.03890	0.65167	-1.585	0.113	-3.13119	1.06002	-2.929	0.00348
Time 1	3.55702	0.51363	6.912	8.78e-12	2.22904	0.76439	2.905	0.00385

	Estimate	SE	t	p-value	Estimate	SE	t	p-value
Time 2	3.73125	0.62795	5.928	3.97e-09	1.60976	0.84205	1.904	0.05744
Gender, female	3.71918	0.88146	4.208	2.81e-05	7.68024	1.14524	6.675	5.71e-11
Age	-0.27595	0.05286	-5.208	2.32e-07	-0.28940	0.05243	-5.496	5.87e-08
Cannabis, urine positive	1.74959	1.21380	1.434	0.152	-1.88132	2.28876	-0.815	0.41544
Education	0.39841	0.07885	5.027	5.56e-07	0.32818	0.10474	3.102	0.00200
CAPE, negative subscale	0.44816	1.06565	0.418	0.676	-0.20563	1.67858	-0.121	0.90346
Cape, positive subscale	-7.66204	1.80018	-4.234	2.42e-05	-1.59375	2.74585	-0.575	0.56530
CAPE, depressive subscale	1.05468	1.08575	0.966	0.334	-1.75080	1.54189	-1.125	0.26107
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	174.41	13.206			140.85	11.868		
Time 1	29.60	5.441			40.14	6.336		
Time 2	32.41	5.693			34.85	5.904		
Residual	42.69	6.533			52.45	7.243		

Attention/Vigilance, Continuous Performance Test, accuracy (0-100)				
	Patients n=916			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	98.90237	0.38875	253.276	< 2e-16
Smoking, yes	0.03446	0.21564	0.159	0.873812
Time 1	0.09257	0.23063	0.401	0.688780
Time 2	0.31476	0.25821	1.215	0.224507
Gender, female	0.04586	0.24992	0.183	0.855131
Age	-0.05425	0.01433	-3.767	0.000178
Antipsychotic medication, yes	-0.40019	0.32252	-1.234	0.217453
Cannabis, urine positive	0.11347	0.30162	0.374	0.708513
Education	0.08767	0.02751	3.167	0.001576
PANSS, negative subscale	-0.73171	0.15692	-4.634	3.9e-06
PANSS, positive subscale	-0.24641	0.18679	-1.311	0.190068
PANSS, general	0.08243	0.31697	0.258	0.796132

subscale				
Random effects	*Variance*	*SD*		
Subject Intercept	15.166	3.894		
Time 1	12.163	3.488		
Time 2	10.865	3.296		
Residual	8.445	2.906		

Attention/Vigilance, Continuous Performance Test, accuracy (0-100)

	Siblings, n=947				*Controls, n=552*			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	99.343505	0.168694	587.842	< 2e-16	99.630307	0.080116	1239.249	<0.001
Smoking, yes	0.004768	0.131931	0.036	0.97134	-0.012765	0.106280	-0.119	0.904928
Time 1	0.197011	0.166959	1.179	0.23878	-0.339489	0.160530	-2.109	0.035627
Time 2	0.256043	0.133573	1.911	0.05623	-0.268963	0.183047	-1.465	0.143937
Gender, female	-0.151213	0.142367	-1.058	0.29041	0.065914	0.097956	0.670	0.503343
Age	-0.011451	0.008632	-1.321	0.18675	-0.012232	0.004455	-2.733	0.006505
Cannabis, urine positive	0.208860	0.258872	0.802	0.42241	0.253400	0.221952	1.136	0.256419
Education	0.018974	0.015758	1.197	0.23149	0.050046	0.012952	3.841	0.000136
CAPE, negative subscale	0.323969	0.223060	1.444	0.14907	-0.422971	0.183461	-2.292	0.022284
Cape, positive subscale	-1.140002	0.401120	-2.828	0.00475	-0.503427	0.292754	-1.710	0.087913
CAPE, depressive subscale	0.069733	0.225882	0.307	0.75898	0.232269	0.173487	1.331	0.183841
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	13.513	3.676			0.4266	0.6531		
Time 1	15.395	3.924			6.5779	2.5647		
Time 2	3.016	1.737			7.8102	2.7947		
Residual	1.645	1.282			0.6204	0.7876		

Attention/Vigilance, Continuous Performance Test, mean reaction time

	Patients n=916			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	434.3436	7.4019	58.405	< 2e-16
Smoking, yes	-3.0286	4.6875	-0.642	0.5207
Time 1	-0.1326	3.6772	-0.036	0.9713

Time 2	-4.5670	4.7275	-0.963	0.3360
Gender, female	6.9429	6.0900	1.136	0.2561
Age	2.6339	0.3488	7.528	1.23e-13
Antipsychotic medication, yes	5.8847	6.1443	0.952	0.3412
Cannabis, urine positive	-1.0761	5.9428	-0.180	0.8572
Education	-0.3702	0.5516	-0.667	0.5048
PANSS, negative subscale	-2.4039	2.9812	-0.801	0.4231
PANSS, positive subscale	-4.4976	3.5564	-1.257	0.2090
PANSS, general subscale	13.5067	5.8704	2.286	0.0224
Random effects	*Variance*	*SD*		
Subject Intercept	4658.6	68.25		
Time 1	860.6	29.34		
Time 2	1406.3	37.50		
Residual	2287.4	47.83		

Attention/Vigilance, Continuous Performance Test, mean reaction time								
	Siblings, n=947				**Controls, n=552**			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	404.4644	4.0972	98.505	< 2e-16	413.9709	5.2818	78.106	<0.001
Smoking, yes	2.1370	3.9068	0.544	0.586412	-2.4708	5.8945	-0.416	0.6778
Time 1	10.7900	3.1470	3.422	0.000649	5.5335	4.2403	1.300	0.1940
Time 2	7.0256	4.1047	1.708	0.088000	-7.5561	4.7855	-1.571	0.1167
Gender, female	17.9449	4.5570	3.926	9.23e-05	14.4015	6.1774	2.320	0.0207
Age	1.7453	0.2722	6.393	2.53e-10	2.2615	0.2842	7.920	<0.001
Cannabis, urine positive	0.9006	7.1493	0.125	0.900241	5.5060	12.1470	0.449	0.6534
Education	-0.9598	0.4846	-1.971	0.048932	-0.1253	0.5773	-0.215	0.8299
CAPE, negative subscale	7.8655	6.4720	1.209	0.226986	-12.8633	9.3617	-1.361	0.1739
Cape, positive subscale	-24.8571	10.9395	-2.262	0.023844	35.7306	15.7201	2.252	0.0246

CAPE, depressive subscale	1.7884	6.5760	0.270	0.786834	7.3586	8.4929	0.858	0.3910
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	4062	63.74			4414.0	66.44		
Time 1	1200	34.65			1448.2	38.05		
Time 2	2673	51.70			870.1	29.50		
Residual	1695	41.17			1685.7	41.06		

Working memory, WAIS arithmetic, Total raw score (0-22)

	Patients n=930			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	14.06719	0.41438	33.784	< 2e-16
Smoking, yes	-0.58901	0.25542	-2.294	0.0220
Time 1	-0.48726	0.21911	-2.218	0.0268
Time 2	-1.30367	0.24469	-5.311	1.39e-07
Gender, female	-2.16025	0.32557	-6.615	6.23e-11
Age	0.01214	0.01880	0.644	0.5197
Antipsychotic medication, yes	-0.38733	0.35928	-1.072	0.2840
Cannabis, urine positive	0.43102	0.32673	1.312	0.1898
Education	0.24959	0.02911	8.522	< 2e-16
PANSS, negative subscale	-0.82740	0.16673	-4.933	9.03e-07
PANSS, positive subscale	-0.41278	0.19270	-2.129	0.0334
PANSS, general subscale	-0.25868	0.32192	-0.799	0.4246
Random effects	*Variance*	*SD*		
Subject Intercept	11.636	3.411		
Time 1	4.970	2.229		
Time 2	2.491	1.578		
Residual	6.925	2.632		

Working memory, WAIS arithmetic, Total raw score (0-22)

	Siblings, n=967				Controls, n=562			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	15.67515	0.21828	71.669	< 2e-16	16.58802	0.27571	59.964	<0.001
Smoking, yes	-0.60089	0.20144	-2.967	0.00304	-0.38811	0.29908	-1.287	0.199
Time 1	0.13301	0.15185	0.874	0.38237	-0.33362	0.20227	-1.642	0.101

Time 2	-0.4441	0.19754	-2.244	0.02500	-0.99912	0.24258	-4.102	<0.001
Gender, female	-2.09674	0.25830	-8.096	1.63e-15	-1.55274	0.33395	-4.628	<0.001
Age	0.02065	0.01545	1.333	0.18281	0.01585	0.01528	1.033	0.302
Cannabis, urine positive	-0.56929	0.37761	-1.501	0.13363	0.06230	0.65263	0.095	0.925
Education	0.15761	0.02387	6.569	6.94e-11	0.17465	0.03021	5.724	<0.001
CAPE, negative subscale	0.80374	0.33131	2.413	0.01594	0.16389	0.46911	0.346	0.729
Cape, positive subscale	-1.12020	0.54173	-2.057	0.03982	-0.96731	0.77029	-1.244	0.214
CAPE, depressive subscale	-0.65680	0.33782	-1.934	0.05331	-0.13992	0.43561	-0.318	0.750
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	12.5019	3.5358			12.100	3.478		
Time 1	0.4667	0.6684			1.148	1.072		
Time 2	3.6177	1.9020			3.621	1.903		
Residual	4.3672	2.0898			3.887	1.972		

Verbal learning, AVLT, Immediate recall (0-45)				
	Patients n=929			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	25.21101	0.53891	46.556	< 2e-16
Smoking, yes	0.07453	0.33992	0.218	0.82742
Time 1	1.63671	0.27098	6.025	2.59e-09
Time 2	0.53851	0.33609	1.597	0.11054
Gender, female	1.40042	0.43994	3.174	0.00155
Age	-0.12374	0.02539	-4.858	1.39e-06
Antipsychotic medication, yes	-2.61767	0.45860	-5.675	1.72e-08
Cannabis, urine positive	-0.32193	0.43287	-0.739	0.45972
Education	0.20754	0.03901	5.289	1.41e-07
PANSS, negative subscale	-0.48396	0.21721	-2.215	0.02694
PANSS, positive subscale	-0.54978	0.25586	-2.136	0.03287
PANSS, general subscale	-0.66726	0.42527	-1.559	0.11918
Random effects	*Variance*	*SD*		
Subject Intercept	22.359	4.729		

Time 1	4.846	2.201		
Time 2	8.506	2.917		
Residual	12.009	3.465		

Verbal learning, AVLT, Immediate recall (0-45)

	Siblings, n=965				*Controls, n=561*			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	26.56089	0.28812	91.997	< 2e-16	27.38920	0.34628	78.809	<0.001
Smoking, yes	-0.38208	0.28114	-1.352	0.17648	-0.72233	0.40337	-1.776	0.075971
Time 1	1.62037	0.23200	6.971	6.11e-12	1.27019	0.32076	3.945	<0.001
Time 2	1.68166	0.28204	5.949	3.64e-09	1.16338	0.33793	3.428	<0.001
Gender, female	1.29515	0.32750	3.944	8.59e-05	2.11655	0.40310	5.223	<0.001
Age	-0.11130	0.01954	-5.680	1.78e-08	-0.12651	0.01842	-6.835	<0.001
Cannabis, urine positive	-0.52472	0.52793	-0.989	0.32256	-0.97774	0.87036	-1.114	0.265561
Education	0.22187	0.03428	6.440	1.54e-10	0.14096	0.04224	3.305	<0.001
CAPE, negative subscale	0.20034	0.47421	0.420	0.67436	-0.13999	0.66481	-0.209	0.834757
Cape, positive subscale	-2.22388	0.77781	-2.845	0.00449	-0.92594	1.08041	-0.850	0.395736
CAPE, depressive subscale	0.28466	0.48358	0.586	0.55823	-0.03243	0.61080	-0.053	0.958050
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	19.188	4.380			15.946	3.993		
Time 1	4.253	2.062			7.740	2.782		
Time 2	7.693	2.774			3.884	1.971		
Residual	10.440	3.231			9.873	3.142		

Verbal learning, AVLT, Delayed recall (0-15)

	Patients n=926			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	8.54152	0.25400	33.460	< 2e-16
Smoking, yes	0.05122	0.15993	0.318	0.750225
Time 1	0.41602	0.13027	3.186	0.001499
Time 2	0.10951	0.15609	0.699	0.484437
Gender, female	0.75255	0.20803	3.607	0.000327

Age	-0.02720	0.01200	-2.261	0.024012
Antipsychotic medication, yes	-1.21266	0.21590	-5.583	2.89e-08
Cannabis, urine positive	0.08608	0.20438	0.419	0.675494
Education	0.09317	0.01847	5.013	5.97e-07
PANSS, negative subscale	-0.20505	0.10225	-1.993	0.046465
PANSS, positive subscale	-0.23710	0.12046	-1.956	0.050678
PANSS, general subscale	-0.24198	0.20021	-1.201	0.230056
Random effects	*Variance*	*SD*		
Subject Intercept	5.259	2.293		
Time 1	1.912	1.383		
Time 2	2.188	1.479		
Residual	2.461	1.569		

Verbal learning, AVLT, Delayed recall (0-15)								
	Siblings, n=966				**Controls, n=559**			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	9.124151	0.134283	67.807	< 2e-16	9.059068	0.172263	52.401	< 2e-16
Smoking, yes	-0.264589	0.129838	-2.027	0.042765	0.013625	0.200268	0.067	0.94620
Time 1	0.564195	0.110373	5.102	4.09e-07	0.395185	0.154238	2.552	0.01103
Time 2	0.589210	0.126473	4.648	3.76e-06	0.546373	0.166178	3.274	0.00113
Gender, female	0.708465	0.152432	4.635	4.05e-06	1.270315	0.200333	6.309	<0.001
Age	-0.035604	0.009101	-3.902	0.000102	-0.051067	0.009135	-5.564	<0.001
Cannabis, urine positive	-0.083223	0.244112	-0.339	0.734358	-0.625248	0.431462	-1.437	0.15100
Education	0.085324	0.015835	5.362	9.35e-08	0.063856	0.020607	3.069	0.00222
CAPE, negative subscale	0.113924	0.220076	0.515	0.606701	-0.467491	0.326436	-1.419	0.15621
Cape, positive subscale	-0.872051	0.360517	-2.407	0.016182	-0.977728	0.536281	-1.807	0.07103
CAPE, depressive subscale	0.209871	0.223510	0.934	0.350429	0.421681	0.299429	1.395	0.16319
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	4.249	2.061			4.070	2.017		
Time 1	1.433	1.197			1.374	1.172		

	1.042	1.021			1.145	1.070		
Time 2	1.042	1.021			1.145	1.070		
Residual	2.226	1.492			2.295	1.515		

Reasoning and problem solving, WAIS block design, Total raw score (0-68)

	Patients n=929			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	44.95469	1.18468	37.769	< 2e-16
Smoking, yes	-1.66310	0.78962	-2.092	0.036580
Time 1	1.41998	0.51855	2.730	0.006454
Time 2	2.66746	0.78024	3.409	0.000678
Gender, female	-4.11172	1.24252	-3.300	0.001001
Age	-0.26928	0.07193	-3.733	0.000200
Antipsychotic medication, yes	-2.23207	0.89491	-2.478	0.013394
Cannabis, urine positive	0.84196	0.94954	0.881	0.378520
Education	0.38990	0.08391	4.617	4.35e-06
PANSS, negative subscale	-1.90246	0.46030	-4.105	4.33e-05
PANSS, positive subscale	-1.28408	0.53882	-2.367	0.018107
PANSS, general subscale	0.77186	0.87176	0.879	0.379401
Random effects	*Variance*	*SD*		
Subject Intercept	227.44	15.081		
Time 1	13.02	3.608		
Time 2	78.91	8.883		
Residual	32.44	5.696		

Reasoning and problem solving, WAIS block design, Total raw score (0-68)

	Siblings, n=967				Controls, n=562			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	47.61066	0.74445	63.833	< 2e-16	47.31807	0.92838	50.801	<0.001
Smoking, yes	-1.72685	0.61048	-2.813	0.004969	-1.92091	0.94125	-2.022	0.0435
Time 1	2.95875	0.44489	6.636	5.43e-11	3.00718	0.59777	5.008	<0.001

Time 2	5.76778	0.60055	9.581	< 2e-16	4.60245	0.77802	5.891	<0.001
Gender, female	-3.43068	0.88510	-3.866	0.000118	-1.65361	1.13737	-1.448	0.1483
Age	-0.23245	0.05306	-4.370	1.37e-05	-0.34411	0.05224	-6.561	<0.001
Cannabis, urine positive	1.68253	1.15135	1.454	0.146100	1.10146	2.06853	0.527	0.5980
Education	0.32062	0.07247	4.401	1.16e-05	0.37323	0.09271	3.983	<0.001
CAPE, negative subscale	3.32067	0.98246	3.361	0.000798	1.28468	1.44432	0.880	0.3789
Cape, positive subscale	-1.32536	1.64068	-0.804	0.421793	-3.98439	2.41446	-1.634	0.1026
CAPE, depressive subscale	-2.29414	1.00453	-2.271	0.023294	-1.07230	1.33693	-0.794	0.4276
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	174.66	13.216			153.14	12.375		
Time 1	2.65	1.628			17.56	4.190		
Time 2	30.60	5.532			59.55	7.717		
Residual	35.60	5.966			29.19	5.403		

Section 2

Results of linear mixed models regarding the cross-sectional association between number of cigarettes and neurocognitive tasks.

Effects	Patients				Siblings				Controls			
	Estimate	SE	P	N	Estimate	SE	P	N	Estimate	SE	P	N
Speed of processing, WAIS Digit Symbol Coding (0-133)												
Intercept	69.37	1.30	< 0.001	921					80.36	0.95	<0.001	561
Cigs/day	-0.10	0.03	0.002						-0.25	0.07	0.001	
Attention/Vigilance, Continuous Performance Test, Accuracy (0-100)												
Intercept												
Cigs/day												
Attention/Vigilance, Continuous Performance Test, Mean reaction time												
Intercept												
No. of cigs												
Working memory, WAIS Arithmetic (0-22)												
Intercept					15.60	0.22	<0.001	964				
No. of cigs					-0.30	0.01	0.026					
Verbal learning, AVLT immediate recall (0-45)												
Intercept												
No. of cigs												
Verbal learning, AVLT delayed recall (0-45)												
Intercept					9.10	0.13	<0.001	962				
No. of cigs					-0.01	0.01	0.171					
Reasoning and Problem solving, WAIS Block Design (0-68)												
Intercept	44.68	1.14	<0.001	922	47.62	0.74	<0.001	964	47.38	0.92	<0.001	561
No. of cigs	-0.05	0.03	.086		-0.13	0.04	0.002		-0.14	0.07	0.03	

Section 3

Results of linear mixed models regarding the association between change in smoking status and change in performance of neurocognitive tasks.

Effects	Patients				Siblings				Controls			
	Estimate	SE	P	N	Estimate	SE	P	N	Estimate	SE	P	N
Speed of processing, WAIS Digit Symbol Coding (0-133)												
Intercept	5.52	1.48	<0.001	517	4.13	0.59	<0.001	891	2.89	0.93	0.002	278
Ceased smoking	4.90	1.73	0.005		0.61	1.13	0.592		-0.11	2.15	0.960	
Started smoking	-2.15	2.23	0.340		0.29	1.32	0.829		-3.01	2.59	0.247	
Attention/Vigilance, Continuous Performance Test, accuracy (0-100)												
Intercept	0.48	0.43	0.260	583	0.28	0.19	0.141	656	-0.35	0.21	0.090	372
Ceased smoking	0.13	0.46	0.774		-0.09	0.33	0.788		0.04	0.52	0.925	
Started smoking	0.12	0.60	0.841		-0.08	0.39	0.836		0.30	0.60	0.618	
Attention/Vigilance, Continuous Performance Test, mean reaction time												
Intercept	19.68	8.12	0.016	583	11.72	3.73	0.002	655	8.74	4.96	0.080	372
Ceased smoking	1.30	9.88	0.191		0.89	7.22	0.968		7.02	10.88	0.522	
Started smoking	-2.34	12.95	0.072		2.57	8.65	0.767		10.64	13.79	0.444	
Working memory, WAIS Arithmetic (0-22)												
Intercept	0.38	0.45	0.393	516	0.36	0.17	0.029	587	-0.13	0.22	0.551	278
Ceased smoking	-0.70	0.53	0.185		-0.15	0.33	0.666		-0.56	0.55	0.314	
Started smoking	-1.40	0.68	0.041		0.15	0.39	0.701		1.48	0.64	0.022	
Verbal learning, AVLT Immediate recall (0-45)												
Intercept	3.87	0.62	<0.001	515	2.03	0.27	<0.001	592	1.51	0.37	<0.001	277
Ceased smoking	0.53	0.72	0.462		-0.40	0.53	0.450		0.14	0.86	0.869	
Started smoking	0.71	0.94	0.452		-0.74	0.61	0.230		-0.23	1.01	0.824	
Verbal learning, AVLT Delayed recall (0-45)												
Intercept	1.45	0.30	<0.001	512	0.63	0.13	<0.001	584	0.71	0.18	<0.001	276
Ceased smoking	-0.37	0.34	0.284		0.05	0.24	0.829		-0.51	0.44	0.256	

Started smoking	-0.05	0.45	0.906		-0.39	0.28	0.167	0.82	0.51	0.111	
<u>Reasoning and Problem solving, WAIS Block Design (0-68)</u>											
Intercept	2.77	1.06	0.009	513	3.47	0.47	<0.001	3.03	0.72	<0.001	278
Ceased smoking	1.93	1.33	0.151		0.80	0.95	0.399	0.03	1.72	0.988	
Started smoking	0.92	1.72	0.596		1.46	1.13	0.197	0.81	2.04	0.693	

Abbreviations: WAIS= Wechsler Adult Intelligence Scale; AVLT= Auditory Verbal Learning Test.

Section 4

Results of linear mixed models regarding the association between change in smoking status and change in neurocognitive outcomes.

Speed of processing , WAIS digit symbol coding, raw change score				
	Patients n=517			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	5.523186	1.484439	3.706	0.000229
Smoking, quitted	4.901402	1.731217	2.814	0.005053
Smoking, started	-2.146612	2.233497	-0.956	0.339679
Time 2	-3.498907	1.145470	-3.052	0.002392
Gender, female	-0.252586	0.909742	-0.276	0.782434
Age	-0.216389	0.051216	-4.206	3.37e-05
Antipsychotic medication, yes	-2.962062	1.493131	-1.974	0.048772
Cannabis, urine positive	-0.826331	1.178056	-0.698	0.485683
Education	0.003568	0.107446	0.033	0.973665
PANSS, negative subscale	-0.616166	0.681366	-0.899	0.368888
PANSS, positive subscale	0.347047	0.877304	0.393	0.694205
PANSS, general subscale	-1.733190	1.472475	-1.170	0.242412
Random effects	*Variance*	*SD*		
Subject Intercept	110.73	10.52		
Time 2	386.06	19.65		
Residual	72.77	8.53		

Speed of processing , WAIS digit symbol coding, raw change score								
	Siblings, n=891				*Controls, n=278*			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	4.12829	0.58967	6.992	5.77e-12	2.88892	0.92531	3.114	0.00200
Smoking, quitted	0.60943	1.13166	0.536	0.59193	-0.11017	2.15272	-0.051	0.95955
Smoking, started	0.28648	1.32163	0.216	0.82917	-3.01951	2.58711	-1.158	0.24745
Time 2	-3.38540	0.78195	-4.327	1.77e-05	-3.34552	1.23797	-2.699	0.00738

	Estimate	SE	t	p-value	Estimate	SE	t	p-value
Gender, female	-0.34787	0.56671	-0.612	0.54081	-0.13381	0.96563	-0.138	0.89060
Age	-0.09389	0.03495	-2.679	0.00765	-0.12887	0.04619	-2.772	0.00604
Cannabis, urine positive	1.35639	1.29508	1.043	0.29713	3.03678	2.37479	1.270	0.20534
Education	-0.17841	0.08227	-2.161	0.03112	-0.06211	0.12971	-0.475	0.63519
CAPE, negative subscale	-0.29092	1.15609	-0.251	0.80212	-1.47727	2.30358	-0.636	0.52511
CAPE, positive subscale	-2.16014	1.82143	-1.182	0.23775	-5.95615	4.28839	-1.378	0.16932
CAPE, depressive subscale	2.27531	1.20306	1.884	0.06003	1.32829	2.11738	0.622	0.53426
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	65.81	8.112			68.98	8.305		
Time 2	180.25	13.426			186.35	13.651		
Residual	55.33	7.439			76.01	8.719		

Attention/Vigilance, Continuous Performance Test, accuracy change score			
Patients n= 583			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	0.48117	0.42512	1.127	0.2602
Smoking, quitted	0.13283	0.45958	0.287	0.7740
Smoking, started	0.12017	0.59596	0.200	0.8412
Time 2	-0.19154	0.36098	-0.530	0.5960
Gender, female	0.02872	0.22368	0.128	0.8984
Age	-0.01043	0.01278	-0.812	0.4174
Antipsychotic medication, yes	-0.13415	0.40679	-0.328	0.7431
Cannabis, urine positive	-0.50718	0.29835	-1.691	0.0918
Education	-0.01525	0.02810	-0.540	0.5896
PANSS, negative subscale	0.03011	0.17236	0.174	0.8622
PANSS, positive subscale	-0.31899	0.22338	-1.420	0.1564
PANSS, general subscale	0.42189	0.37767	1.111	0.2674

Random effects	Variance	SD		
Subject Intercept	21.483	4.635		
Time 2	60.473	7.776		
Residual	3.692	1.921		

Attention/Vigilance, Continuous Performance Test, accuracy change score								
	Siblings, n=656				Controls, n=372			
Fixed effects	Estimate	SE	t	p-value	Estimate	SE	t	p-value
Intercept	0.283257	0.192235	1.472	0.141	-0.35142	0.20604	-1.700	0.0899
Smoking, quitted	-0.088608	0.328273	-0.269	0.788	0.04959	0.52220	0.094	0.9249
Smoking, started	-0.081915	0.394713	-0.207	0.836	0.30298	0.60377	0.499	0.6182
Time 2	-0.234262	0.236618	-0.990	0.323	0.33189	0.35677	0.929	0.3533
Gender, female	-0.181960	0.162476	-1.117	0.265	0.09595	0.22466	0.425	0.6715
Age	0.011531	0.009923	1.159	0.247	-0.01757	0.01045	-1.671	0.0959
Cannabis, urine positive	0.109280	0.372373	0.292	0.770	0.16945	0.54520	0.309	0.7576
Education	0.029398	0.023518	1.246	0.213	-0.01381	0.03460	-0.396	0.6921
CAPE, negative subscale	-0.539042	0.326133	-1.647	0.100	-0.34528	0.55802	-0.615	0.5393
CAPE, positive subscale	0.079537	0.616974	0.128	0.898	0.19836	106.128	0.186	0.8528
CAPE, depressive subscale	0.431732	0.331351	1.298	0.195	0.16034	0.50804	0.314	0.7541
Random effects	Variance	SD			Variance	SD		
Subject Intercept	11.821	3.438			3.749	1.936		
Time 2	23.624	4.860			30.346	5.509		
Residual	3.529	1.879			4.030	2.015		

Attention/Vigilance, Continuous Performance Test, mean reaction time change score				
	Patients n=583			
Fixed effects	Estimate	SE	t	p-value
Intercept	19.6810	8.1235	2.414	0.0160
Smoking, quitted	1.30070	9.8794	1.309	0.1908
Smoking, started	-2.34145	12.9496	-1.798	0.0726

Time 2	-1.05012	5.8974	-1.779	0.0758
Gender, female	-5.0013	5.4100	-0.920	0.3580
Age	0.1337	0.3154	0.422	0.6732
Antipsychotic medication, yes	-12.8588	8.2241	-1.557	0.1200
Cannabis, urine positive	-2.4076	7.0906	-0.338	0.7356
Education	-0.3127	0.6654	-0.468	0.6403
PANSS, negative subscale	-0.7720	3.9301	-0.195	0.8451
PANSS, positive subscale	3.8832	5.0421	0.766	0.4439
PANSS, general subscale	-6.7240	8.4907	-0.788	0.4311
Random effects	*Variance*	*SD*		
Subject Intercept	2582	50.81		
Time 2	8812	93.87		
Residual	3038	55.12		

Attention/Vigilance, Continuous Performance Test, mean reaction time change score								
	Siblings, n=655				**Controls, n=372**			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	11.7219	3.7264	3.141	0.001747	8.7380	4.9637	1.756	0.0799
Smoking, quitted	0.2866	7.2217	0.040	0.968482	7.0244	10.8799	0.641	0.5219
Smoking, started	2.5705	8.6506	0.296	0.767317	10.6421	13.7899	0.766	0.4439
Time 2	-16.0877	4.7398	-3.392	0.000734	-11.7717	6.2913	-1.869	0.0623
Gender, female	0.8328	3.7571	0.221	0.825177	1.6494	4.8645	0.337	0.7364
Age	0.4026	0.2301	1.744	0.081671	-0.1082	0.2237	-0.481	0.6312
Cannabis, urine positive	15.5800	8.3695	1.855	0.064031	6.0958	11.8602	0.511	0.6100
Education	-0.4963	0.5402	-0.916	0.360264	-0.4084	0.6723	-0.603	0.5468
CAPE, negative subscale	3.4922	7.5383	0.462	0.644551	1.9755	11.9244	0.165	0.8694
CAPE, positive subscale	-20.2363	13.5560	-1.488	0.137264	7.0131	22.7128	0.307	0.7593
CAPE, depressive subscale	2.7178	7.6832	0.352	0.724624	0.2904	10.9612	0.026	0.9790
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	1893	43.51			2734	52.29		
Time 2	5716	75.61			7198	84.84		
Residual	2795	52.87			2205	46.96		

Working memory, WAIS arithmetic, raw change score				
	Patients n=516			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	0.38239	0.44537	0.855	0.39276
Smoking, quitted	-0.70040	0.52518	-1.326	0.18546
Smoking, started	-1.40364	0.68206	-2.047	0.04121
Time 2	-0.56501	0.37357	-1.511	0.13136
Gender, female	0.17260	0.26844	0.640	0.52261

Age	-0.04747	0.01524	-3.100	0.00211
Antipsychotic medication, yes	0.01883	0.44773	0.042	0.96662
Cannabis, urine positive	-0.06772	0.35251	-0.191	0.84852
Education	-0.05730	0.03237	-1.761	0.07907
PANSS, negative subscale	-0.05335	0.20718	-0.256	0.79796
PANSS, positive subscale	-0.18405	0.26433	-0.693	0.48900
PANSS, general subscale	-0.32834	0.44653	-0.731	0.46503
Random effects	*Variance*	*SD*		
Subject Intercept	10.872	3.297		
Time 2	45.532	6.748		
Residual	6.041	2.458		

Working memory, WAIS arithmetic, raw change score

	Siblings, n=587				Controls, n=278			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	0.36466	0.16636	2.189	0.02890	-0.13397	0.22404	-0.596	0.5513
Smoking, quitted	-0.14569	0.33418	-0.434	0.66425	-0.55716	0.54867	-1.007	0.3144
Smoking, started	0.15187	0.39397	0.384	0.70118	1.48409	0.63846	2.308	0.0216
Time 2	-0.69249	0.25591	-2.704	0.00704	-0.38610	0.34933	-1.104	0.2706
Gender, female	0.20666	0.16435	1.254	0.21058	0.14042	0.23690	0.589	0.5564
Age	-0.01607	0.01009	-1.588	0.11300	-0.02702	0.01132	-2.372	0.0185
Cannabis, urine positive	0.81048	0.37517	2.153	0.03174	0.05663	0.58273	0.097	0.9232
Education	-0.04925	0.02412	-2.035	0.04235	0.02117	0.03390	0.620	0.5360
CAPE, negative subscale	-0.16458	0.34175	-0.480	0.63151	0.13914	0.57174	0.242	0.8093
CAPE, positive subscale	-0.25682	0.52963	-0.483	0.62907	-0.15248	1.06670	-0.142	0.8873
CAPE, depressive subscale	0.14441	0.35809	0.402	0.68797	-0.26790	0.52922	-0.502	0.6158
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	4.210	2.052			3.989	1.997		
Time 2	21.114	4.595			18.549	4.307		
Residual	4.959	2.227			4.399	2.097		

Verbal learning, AVLT, Immediate recall change score				
Patients n=515				
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	3.87496	0.61697	6.258	7.11e-10
Smoking, quitted	0.53191	0.71835	0.736	0.46195
Smoking, started	0.71006	0.93871	0.752	0.45226
Time 2	-3.73624	0.44784	-8.334	7.61e-16
Gender, female	-0.15799	0.39570	-0.397	0.69126
Age	-0.03049	0.02247	-1.351	0.17759
Antipsychotic medication, yes	-1.9.063	0.62492	-3.124	0.00186
Cannabis, urine positive	0.47527	0.51088	0.926	0.35521
Education	0.02463	0.04629	0.529	0.59688
PANSS, negative subscale	-0.25099	0.29014	-0.860	0.38994
PANSS, positive subscale	0.01043	0.37539	0.028	0.97797
PANSS, general subscale	-0.62910	0.62289	-1.004	0.31569
Random effects	*Variance*	*SD*		
Subject Intercept	16.91	4.113		
Time 2	51.93	7.206		
Residual	12.31	3.509		

Verbal learning, AVLT, Immediate recall change score								
	Siblings, n=592				**Controls, n=277**			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	2.03009	0.27309	7.424	2.95e-13	1.51346	0.37030	4.078	5.58e-05
Smoking, quitted	-0.40205	0.52933	-0.756	0.44964	0.14253	0.85504	0.165	0.8688
Smoking, started	-0.74158	0.61410	-1.202	0.22954	-0.22719	1.01341	-0.222	0.8241
Time 2	-1.99676	0.38487	-5.185	2.94e-07	-1.45348	0.57334	-2.533	0.0119
Gender, female	-0.07921	0.26045	-0.303	0.76186	-0.65375	0.35046	-1.853	0.0652
Age	-0.03459	0.01599	-2.157	0.03150	-0.04293	0.01665	-2.563	0.0111

Cannabis, urine positive	-0.62959	0.59912	-1.047	0.29548	0.60740	0.86016	0.701	0.4838
Education	0.10975	0.03790	2.886	0.00406	0.01241	0.04924	0.250	0.8028
CAPE, negative subscale	-0.11157	0.52937	-0.210	0.83374	0.27724	0.85032	0.324	0.7465
CAPE, positive subscale	-1.47952	0.84051	-1.755	0.07996	-3.37761	1.57093	-2.135	0.0339
CAPE, depressive subscale	0.34081	0.55572	0.611	0.54141	1.11867	0.79532	1.396	0.1640
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	12.89	3.591			15.705	3.963		
Time 2	45.47	6.743			58.048	7.619		
Residual	13.03	3.610			9.837	3.136		

Verbal learning, AVLT, Delayed recall change score				
Patients n=512				
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	1.450691	0.298218	4.846	1.58e-06
Smoking, quitted	-0.368193	0.341140	-1.073	0.2838
Smoking, started	-0.053523	0.448358	-0.119	0.9056
Time 2	-1.019370	0.208550	-4.883	1.41e-06
Gender, female	-0.321603	0.191998	-1.667	0.0963
Age	-0.019388	0.010865	-1.776	0.0765
Antipsychotic medication, yes	-0.693536	0.302336	-2.284	0.0227
Cannabis, urine positive	0.008898	0.247581	0.036	0.9715
Education	0.002143	0.022216	0.096	0.9236
PANSS, negative subscale	-0.243758	0.140479	-1.726	0.0850
PANSS, positive subscale	-0.187435	0.180395	-1.033	0.3020
PANSS, general subscale	0.108567	0.298676	0.361	0.7179
Random effects	*Variance*	*SD*		
Subject Intercept	3.448	1.857		
Time 2	9.868	3.141		
Residual	3.260	1.805		

Verbal learning, AVLT, Delayed recall change score								
	Siblings, n=584				*Controls, n=276*			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	0.630201	0.129052	4.878	1.3e-06	0.70674	0.17991	3.918	0.000107
Smoking, quitted	0.052358	0.241847	0.216	0.82938	-0.50515	0.44036	-1.138	0.255965
Smoking, started	-0.389337	0.280379	-1.383	0.16719	0.81555	0.50704	1.596	0.111241
Time 2	-0.697138	0.183449	-3.798	0.00016	-0.20606	0.26794	-0.768	0.443049
Gender, female	0.037314	0.115781	0.321	0.74812	-0.54780	0.18407	-2.957	0.003439
Age	-0.021592	0.007104	-3.030	0.00259	-0.02440	0.00881	-2.752	0.006424
Cannabis, urine positive	-0.072474	0.273740	-0.264	0.79203	-0.18680	0.47779	-0.388	0.698200
Education	0.044231	0.016980	2.596	0.00971	-0.01655	0.02579	-0.637	0.525028
CAPE, negative subscale	-0.066966	0.237211	-0.281	0.77860	-0.11754	0.44765	-0.261	0.794619
CAPE, positive subscale	-1.182766	0.374356	-3.149	0.00174	-1.26891	0.82456	-1.528	0.127967
CAPE, depressive subscale	0.252664	0.248102	1.015	0.31071	0.21584	0.41458	0.516	0.605947
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	3.633	1.906			2.720	1.649		
Time 2	11.646	3.413			10.509	3.242		
Residual	2.472	1.572			2.858	1.690		

Reasoning and problem solving, WAIS block design, raw change score				
	Patients n=513			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*
Intercept	2.76905	1.05968	2.605	0.00941
Smoking, quitted	1.93344	1.33621	1.439	0.15061
Smoking, started	0.91502	1.71683	0.530	0.59607
Time 2	-0.46998	0.77899	-0.602	0.54718
Gender, female	0.70468	0.77815	0.902	0.36755
Age	-0.08695	0.04488	-1.930	0.05434
Antipsychotic medication, yes	-0.81926	1.08870	-0.750	0.45359
Cannabis, urine positive	0.30188	0.98800	0.304	0.76117

Education	-0.17346	0.09064	-1.905	0.05734
PANSS, negative subscale	-1.51025	0.55809	-2.693	0.00727
PANSS, positive subscale	-1.21500	0.71147	-1.699	0.08981
PANSS, general subscale	0.58613	1.18515	0.492	0.62289
Random effects	*Variance*	*SD*		
Subject Intercept	10.88	3.299		
Time 2	70.47	8.395		
Residual	64.07	8.005		

Reasoning and problem solving, WAIS block design, raw change score								
	Siblings, n=589				*Controls, n=278*			
Fixed effects	*Estimate*	*SE*	*t*	*p-value*	*Estimate*	*SE*	*t*	*p-value*
Intercept	3.47111	0.47336	7.322	6.26e-13	3.03088	0.71786	4.209	3.26e-05
Smoking, quitted	0.80388	0.94792	0.845	0.3985	0.02701	1.71847	0.016	0.98757
Smoking, started	1.46161	1.12820	1.290	0.1974	0.81099	2.03633	0.395	0.69276
Time 2	0.18477	0.67741	0.273	0.7853	-1.16102	0.94072	-1.232	0.21900
Gender, female	-1.23893	0.48714	-2.536	0.0115	-0.34861	0.81828	-0.423	0.67235
Age	-0.13678	0.03000	-4.547	6.91e-06	-0.10426	0.03936	-2.633	0.00901
Cannabis, urine positive	0.23059	1.09807	0.209	0.8343	1.61553	2.00710	0.799	0.42485
Education	-0.02189	0.07072	-0.308	0.7578	-0.03456	0.11024	-0.311	0.75610
CAPE, negative subscale	-0.49155	0.99463	-0.492	0.6226	1.16927	1.92476	0.603	0.54718
CAPE, positive subscale	1.81006	1.56790	1.151	0.2504	-2.09246	3.62243	-0.573	0.56706
CAPE, depressive subscale	-0.67553	1.04198	-0.646	0.5186	-1.51656	1.74802	-0.860	0.39011
Random effects	*Variance*	*SD*			*Variance*	*SD*		
Subject Intercept	24.97	4.997			18.31	4.279		
Time 2	119.44	10.929			61.07	7.815		
Residual	45.35	6.734			60.38	7.770		