

SUPPLEMENTARY TABLES AND LEGENDS

SUPPLEMENTARY TABLE 1

CHARACTERISTIC	GROUP			STATISTICAL COMPARISONS ACROSS GROUPS	STATISTICAL COMPARISONS BETWEEN GROUPS	
	HC	COS	SIB		HC vs COS	HC vs SIB
<i>Number</i>	208	83	62			
<i>Sex, No</i>				$\chi^2=0.64, p=0.73$	$\chi^2=0.03, p=0.90$	$\chi^2=0.5, p=0.5$
<i>F</i>	90	35	30			
<i>M</i>	118	48	32			
<i>Handedness, No</i>				$\chi^2=9.7, p=0.05$	$\chi^2=7.2, p=0.03$	$\chi^2=0.5, p=0.78$
<i>L</i>	27	21	6			
<i>R</i>	181	62	56			
<i>Race, No</i>				$\chi^2=39.8, p=0.0005$	$\chi^2=32, p=0.0005$	$\chi^2=21.3, p=0.0005$
<i>Caucasian</i>	173	43	36			
<i>African</i>	19	23	11			
<i>Asian</i>	6	5	3			
<i>Hispanic</i>	7	6	6			
<i>Other</i>	3	6	6			
<i>IQ, mean (SD)</i>	114 (12.8)	74.5 (18.7)	-		t-statistic=19.7, p=0.0005	
<i>VOCABULARY SCORE, mean (SD)</i>	12.3 (2.8)	6.4 (3.55)	11.2 (2.9)	F=105.8, P=0.0005	t-statistic=14.5, p=0.0005	t-statistic=2.4, p=0.02
<i>SES</i>	42 (19.9)	60 (30.2)	55 (26.5)	F=21.5, P=0.0005	t-statistic=-6.3, p=0.0005	t-statistic=-4.44, p=0.0005
<i>Total number of scans</i>	475	193	124			
<i>Number of scans, No</i>						
<i>1 scan</i>	67	22	29			
<i>2 scans</i>	61	23	13			
<i>≥3 scans</i>	80	38	29			
<i>Age at each scan in years, mean (SD)</i>						
<i>1st scan</i>	12.6 (2.9)	14.6 (2.3)	14.3 (3.9)	F=16.2, P=0.0005	t-statistic=-5.4, p=0.0005	t-statistic=-3.7, p=0.0005

2nd scan	15.1 (2.8)	17.1 (2.5)	15.9 (3.4)	F=10.3, P=0.0005	t-statistic=-4.7, p=0.0005	t-statistic=-1.5, p=0.13
3rd scan	17.2 (2.6)	18.5 (2.4)	18.2 (2.7)	F=4.0, P=0.02	t-statistic=-2.7, p=0.01	t-statistic=-1.6, p=0.12
4th scan	18.7 (2.4)	20.5 (1.4)	20.5 (2.2)	F=3.4, P=0.05	t-statistic=-2.1, p=0.04	t-statistic=-1.8, p=0.08
<i>Age distribution of scans, years</i>						
Mean (SD)	14.7 (3.6)	16.7 (3.0)	15.8 (3.9)			
Range	9.0-22.8	9.2-22.9	9.1-22.7			
<i>Genotype, No participants</i>					$\chi^2=6.7, p=0.04$	$\chi^2=1.5, p=0.5$
MM	60	12	13			
VM	91	42	30			
VV	57	29	19			
<b>Test for difference between genotype groups</b>						
Sex	$\chi^2= 3.3, p=0.22$	$\chi^2 = 8.6, p=0.13$	$\chi^2 = 1.5, p=0.48$			
Handedness	$\chi^2 = 2.4, p=0.67$	$\chi^2 = 5.1, p=0.28$	$\chi^2 = 2.3, p=0.68$			
Race	$\chi^2 = 17.0, p=0.03$	$\chi^2 = 11.9, p=0.15$	$\chi^2 = 3.3, p=0.91$			
IQ	F=0.05, p=0.96	F=0.5, p=0.62	F=0.5, p=0.61			
SES	F=2.2, p=0.11	F=2.2, p=0.12	F=0.5, p=0.60			
<i>Age at each scan</i>						
1st scan	F=0.72, p=0.5	F=2.1, p=0.13	F=2.4, p=0.10			
2nd scan	F=1.91, p=0.15	F=1.7, p=0.20	F=0.6, p=0.58			
3rd scan	F=1.33, p=0.27	F=0.2, p=0.84	F=1.1, p=0.35			

**Full details of Study Participant Characteristics.** Socioeconomic status (SES) was quantified using Hollingshead scales (Hollingshead, 1975). Participants were of mixed handedness (handedness established using Physical and Neurological Examination of Soft Signs).

SUPPLEMENTARY TABLE 2

CONTRAST	REGIONS	PEAK VERTEX: MNI CO-ORDINATES			BRODMANN AREA
		X	Y	Z	
<b><i>Differences in rate of CT change in HCs according to Val dose</i></b>	Left dorsolateral prefrontal cortex, extending through frontal pole, medial superior frontal and cingulate cortices	-25	53	-1	10
	Left superior temporal gyrus	-56	-2	-11	22
	Left planum temporale	-54	-32	14	41
	Left inferior temporal gyrus	-60	-44	-18	20
	Left primary sensorimotor cortices	-41	-32	68	2
	Left superior parietal lobule into intraparietal lobule	-27	-75	44	19
	Left medial occipital cortex	-11	-77	-6	18
	Left parahippocampal cortex	-28	-20	-30	36
	Right dorsolateral prefrontal cortex, extending through frontal pole into medial superior frontal	24	67	6	10
	Right cingulate cortices extending into precuneus	3	-33	39	31
	Right contiguous medial temporal region	17	-30	-15	
	Right superior temporal sulcus	61	-28	-6	21
	Right inferior frontal	48	19	25	46
<b><i>Differences between HCs and COS probands in the influence of Val dose on rate of CT change</i></b>	Left inferior frontal	-43	42	2	46
	Left medial superior frontal extending into cingulate and supplementary motor cortex	-9	-12	51	6
	Right medial superior frontal extending into cingulate	7	-2	48	24

**Differences between HCs and SIBs in the influence of Val dose on rate of CT change**

Left inferior frontal	-44	50	-11	10
Left precentral sulcus	-61	9	20	44
Left inferior temporal gyrus	-61	-45	-18	20
Left superior parietal lobule into intraparietal lobule	-26	-75	37	19
Left parahippocampal cortex	-29	-20	-29	36
Right anterior cingulate	3	18	-8	25
Right inferior frontal gyrus	41	45	-16	47
Right inferior frontal sulcus	43	20	24	9
Right superior temporal sulcus	60	-32	-6	21
Right middle temporal sulcus	53	-57	6	37
Right temporo-occipital junction	36	-85	2	18

**Differences between SIBs and COS probands in the influence of Val dose on rate of CT change**

Left intraparietal sulcus	-26	-82	21	19
Right middle temporal sulcus	50	-57	5	37

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*Test-statistics, Stereotactic Coordinates corresponding Brodmann Areas labels for Cortical Regions Shown in Figures 1, 2 and 3, and. The co-ordinates are given in MNI space for the maximum vertex within each contiguous cortical region where statistically significant effects were found. Corresponding Brodmann areas (BA) were determined by converting to Talairach co-ordinates. Talairach Daemon and visual inspection of the Talairach atlas were used to assign BA label to each vertex of interest.*