Human brain morphology using MRI: findings in schizophrenia patients and healthy subjects

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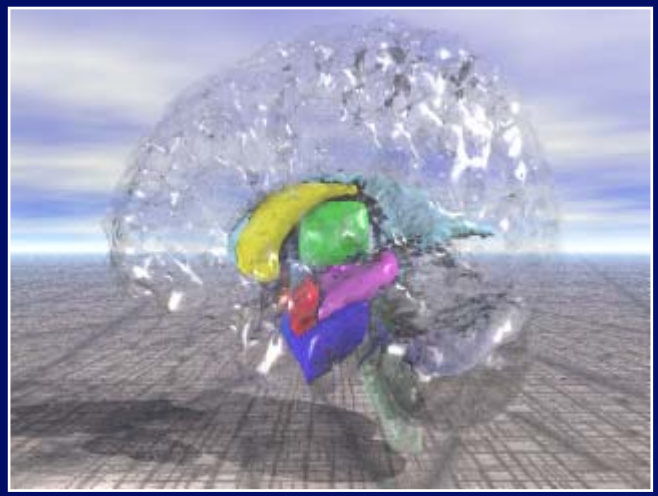
Grey matter abnormalities in schizophrenia

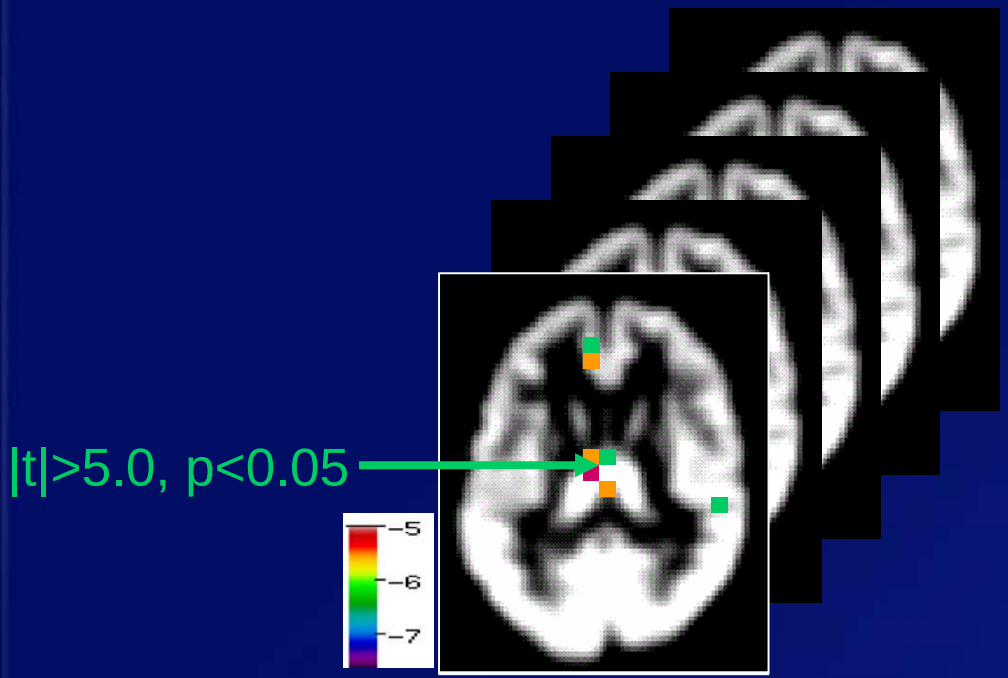


Decreases in:	
overall grey matter	-2%
superior temporal gyrus	-7%
amygdala, hippocampus	-6%
parahippocampal gyrus	-6%
thalamus	-4%
frontal lobes	-2%

Increases in:	
globus pallidus	+24%
putamen	+6%
caudate	+4%

Wright et al. 2000

Voxel based morphometry

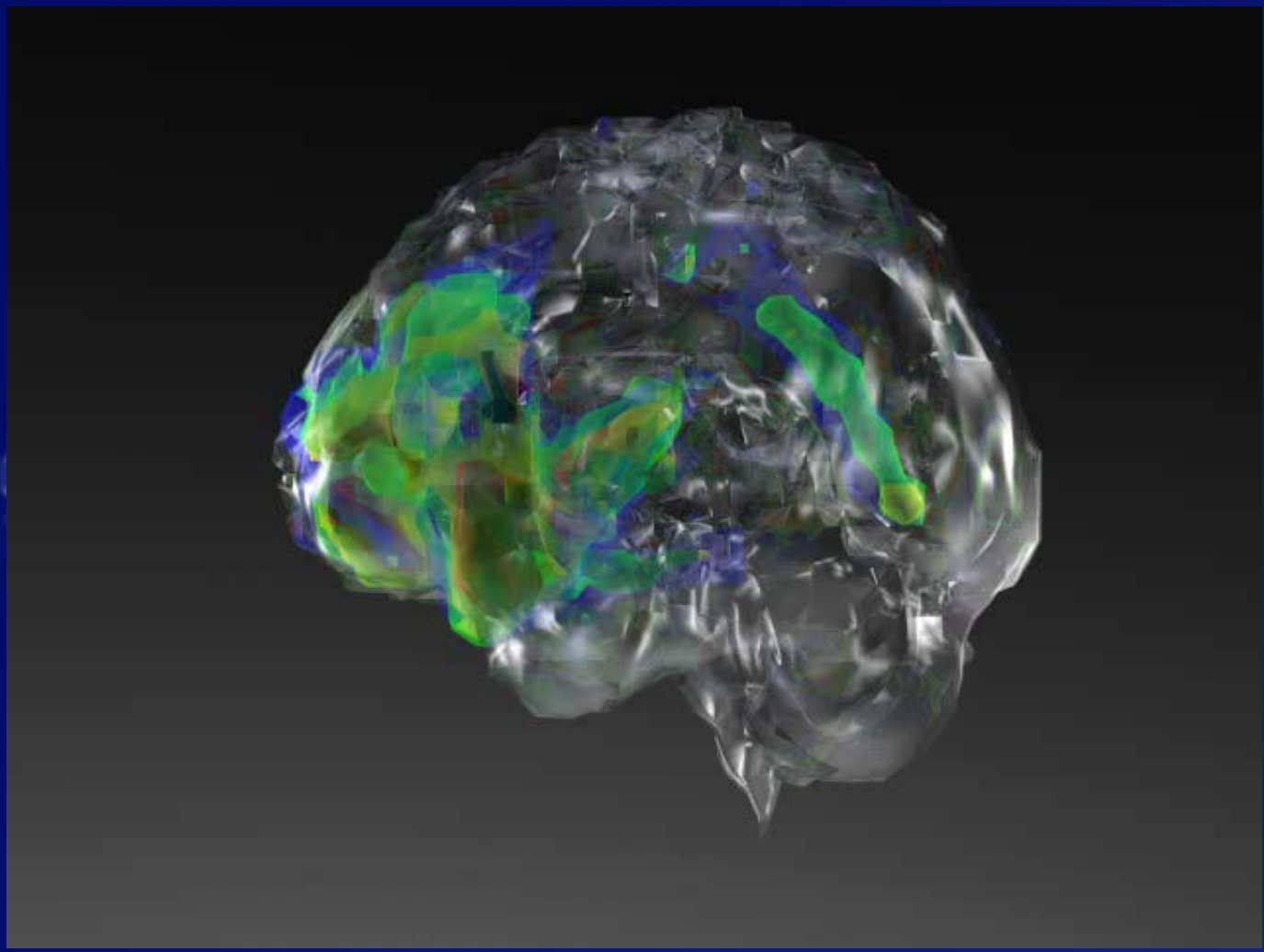


- Grey level images
- Blurred with isotropic Gaussian kernel (fwhm=8mm)
- Transformation to standardised coordinate system using ANIMAL[1]

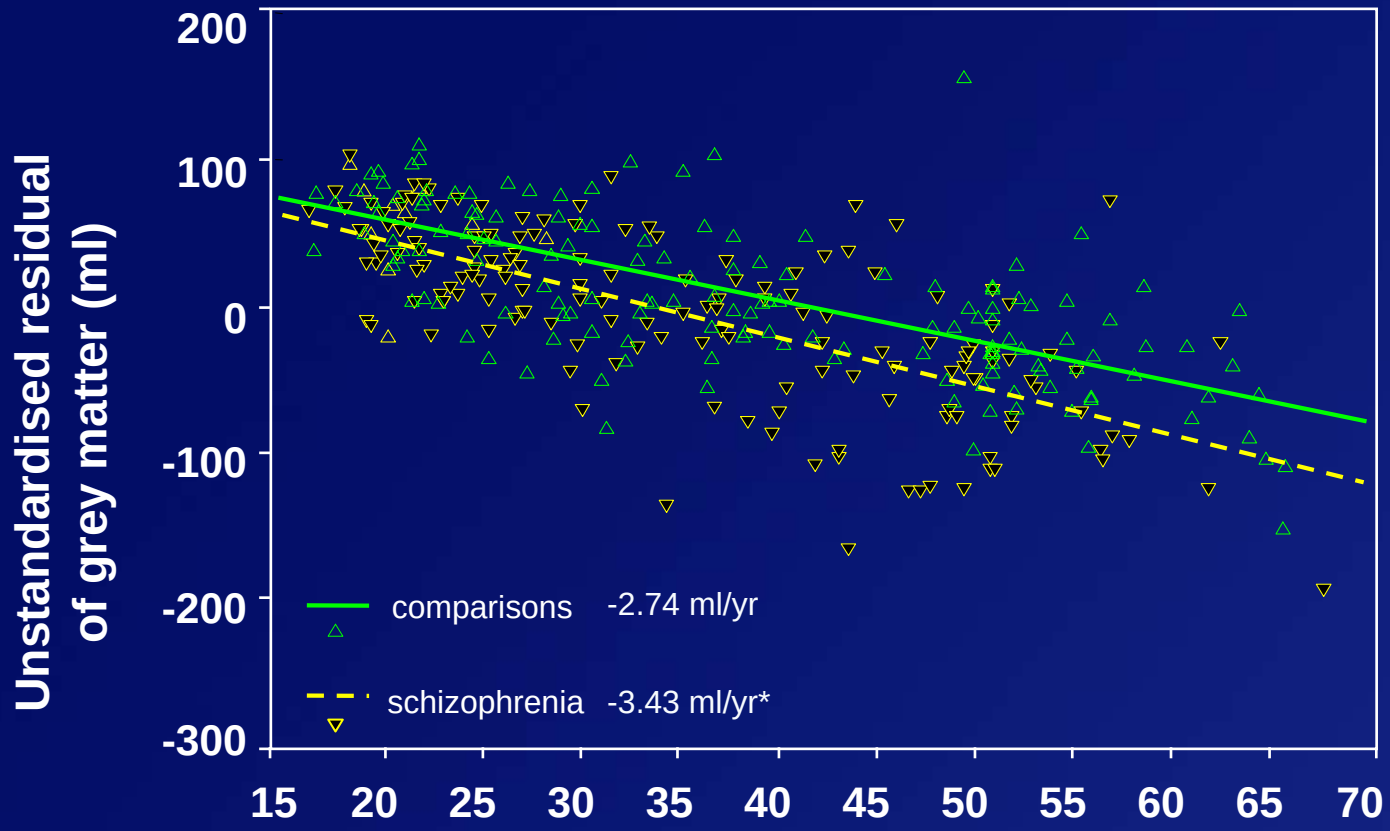
- The critical t-level is dependent of the:
  - number of subjects
  - data resolution
  - voxel size
  - volume of search region
- Determined according to random field theory[2]

1. Collins et al. 1996
2. Worsley et al. 1996

Brain volume decreases in schizophrenia



The regression of grey matter volume on age in schizophrenia and healthy comparisons



* Significant group-by-age interaction

Hulshoff Pol et al. 2002

Patients

Age at first symptoms, years	21.1±6.1
Years of illness	12.3 (0.1–51.8)
Cumulative hospitalisation, median (range), months	6.0 (0–324)

Medication at time of scan	Number of pts	median (range) haloperidol eq.
Typical neuroleptics	79	5.9 (1–50)
Atypical neuroleptics	66	6.3 (0.6–40)
No medication at time of scan	4	
medication information was not available in 10 patients		

Hulshoff Pol et al. 2002

Schizophrenia

- Recent studies suggest schizophrenia to be a progressive brain disease (neurodevelopmental vs neurodegenerative)
- Rapid clinical changes take place during the first (symptomatic) years of the schizophrenic illness
- One would expect these progressive brain changes to be related to outcome

Patient characteristics

Diagnosis (DSM IV)	SCAN 1 (T=0) Mean (SD)	SCAN 2 (T=1) Mean (SD)	T=2
Schizophrenia	23	29	
Schizoaffective	2	5	
Schizophreniform	7		
No. psychotic episodes	2		
Prodromal phase (months)	37.84 ± 51.26		
Psychosis (months)	17.18 ± 30.03		
PANSS +ve symptoms	17.00 ± 4.84	12.87 ± 4.51	
PANSS -ve symptoms	17.92 ± 6.25	15.67 ± 5.17	
PANSS psychopathology	35.58 ± 10.18	29.00 ± 6.69	
Hospitalisation (days; T0-T1)		73.88±72.49	
Cumulative antipsychotic medication mg. haloperidol equiv.	65.89 ±157.60	2077.50 ±962.67	
Total CAN score (professional)			0.33 ± 0.22

CAN=Camberwell Assessment of Need; PANSS=Positive and Negative Syndrome Scale

Demographic data for patients with first-episode schizophrenia and healthy controls

	Patients (n=34)	Controls (n=36)	t or χ^2	p
Sex, No.				
Male	29	30	**χ^2=0.051**	0.822
Female	5	6		
Handedness. No.				
Right	31	31	χ^2=2.230	0.328
Left	2	5		
Mixed	1	0		
Age, scan 1				
Mean	26.18 ± 5.31	24.54 ± 5.83	*t*=-1.228	0.224
Range	19–37	17–40		
Weight, kg scan 1				
Mean	73.00 ± 12.24	76.14 ± 11.35	*t*=1.113	0.270
Range	52–100	57–100		

Demographic data for patients with first-episode schizophrenia and healthy controls (cont.)

	Patients (n=34)	Controls (n=36)	t	p
Height, cm scan 1				
Mean	177.24±9.04	184.14 ±7.46	***t*=3.491**	0.001
Range	160–193	170–199		
Parental education level (completed, years)				
Mean	**13.47**±3.24	**14.03**±2.56	***t***=0.801	0.426
Education (completed, years)				
Mean	11.50±2.72	12.28±3.05	*t*=1.127	0.264
MRI interval, months				
Mean	**12.85±1.15**	**12.44±0.94**	*t*=-1.609	0.112

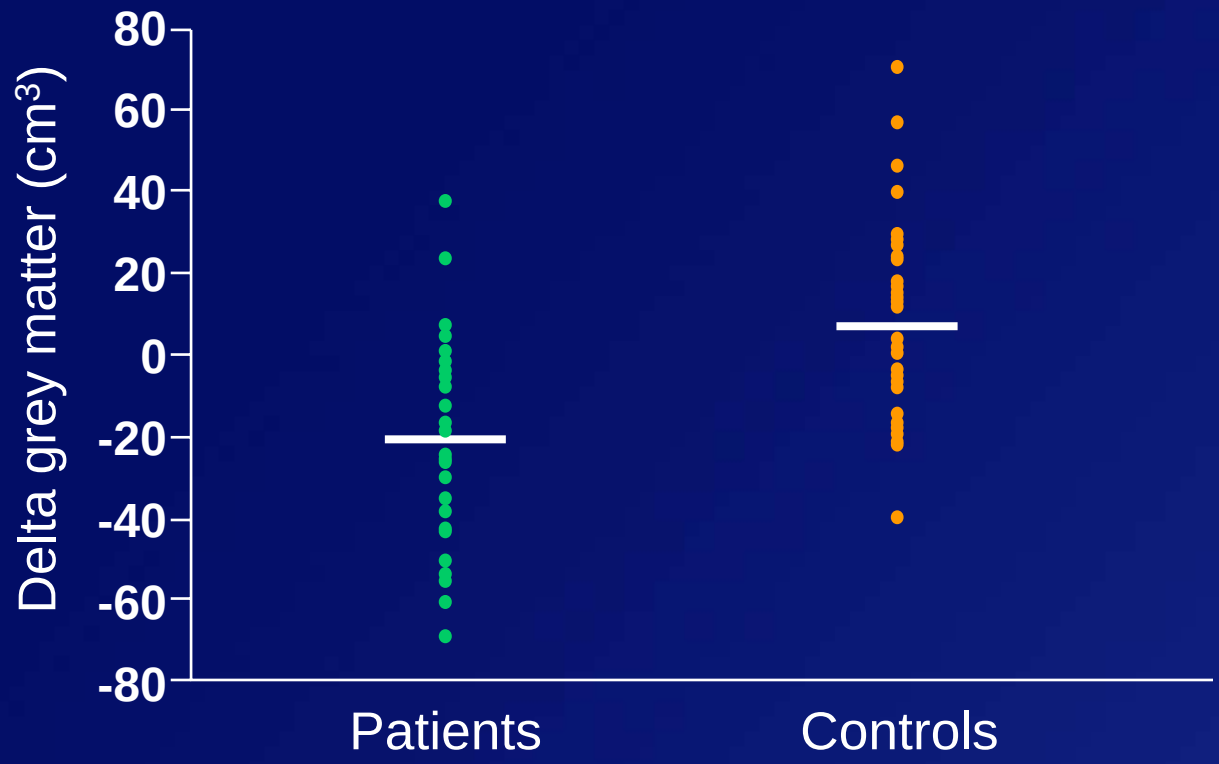
Results

Anatomic brain MRI measures for patients with first-episode schizophrenia and healthy controls at baseline and 1 year rescan

MAN(C)OVA Group; x time			AN(C)OVA T0; Volume in cm^3 (SD)				AN(C)OVA T1; Volume in cm^3 (SD)			
	Ft	*p*	Patients n=34	Control n=36	*F*	*p*	Patients n=34	Control n=36	*F*	*p*
Total brain	**25.64**	**<0.001**	1318.71 ±109.33	1347.18 ±114.21	0.29	0.59	1303.21 ±113.96	1360.51 ±112.96	**4.41**	**0.04**
Grey	**20.55**	**<0.001**	685.56 ±52.13	693.21 ±56.75	0.37	0.55	665.81 ±57.76	700.84 ±52.84	**5.70**	**0.02**
White	0.01	0.92	474.04 ±62.39	490.32 ±69.19	0.07	0.80	476.41 ±59.51	492.18 ±65.80	0.22	0.64
Lateral ventricles	**11.58**	**0.001**	14.53 ±6.54	14.40 ±9.88	0.96	0.33	15.66 ±7.46	14.41 ±10.37	2.94	0.09
3rd ventricle	2.83	0.10	0.85 ±0.39	0.64 ±0.27	**11.51**	**0.01**	0.90 ±0.36	0.63 ±0.29	**21.54**	**<0.001**

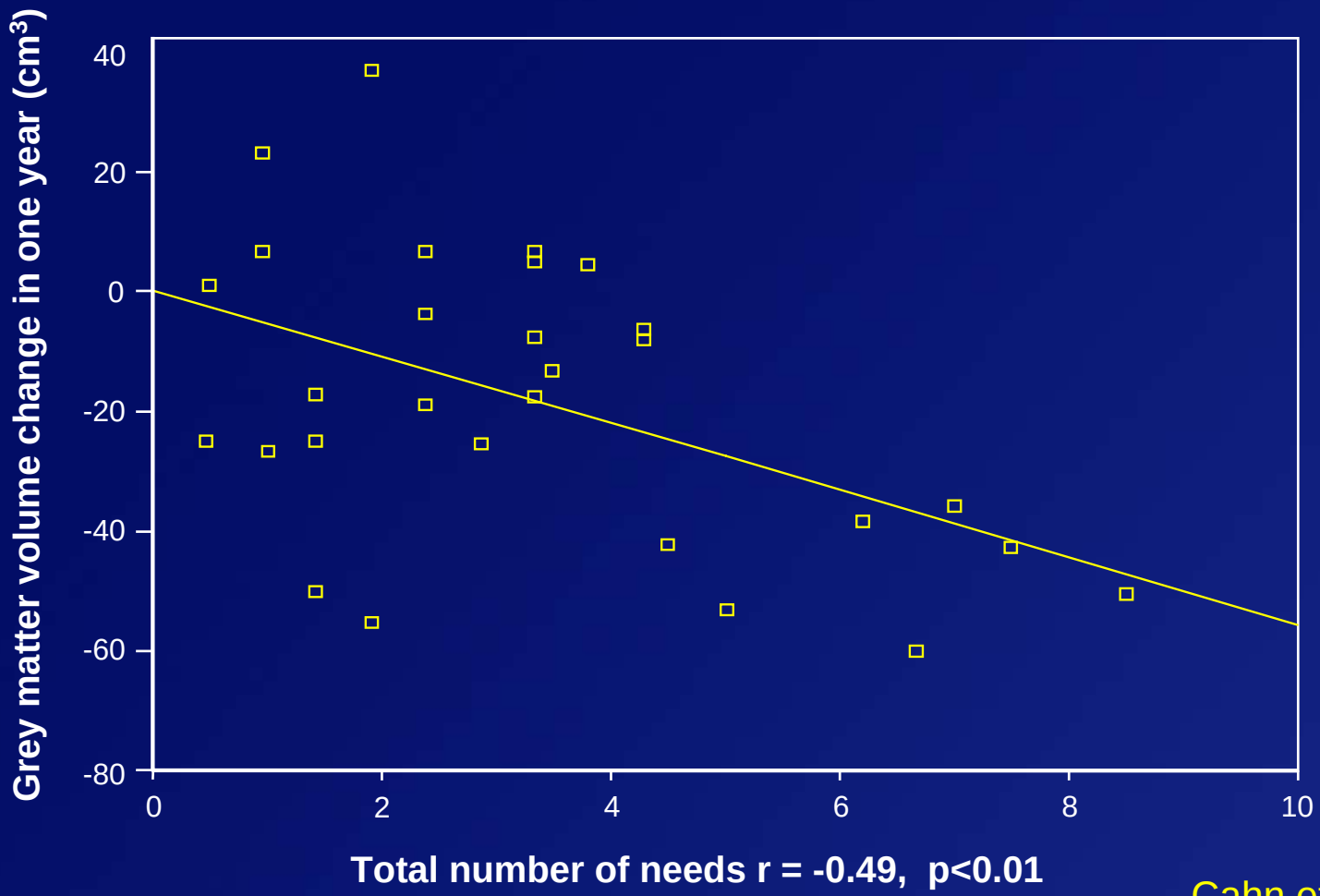
Cahn et al. 2002

Global changes in grey matter volume after 1-year follow-up in first-episode schizophrenia



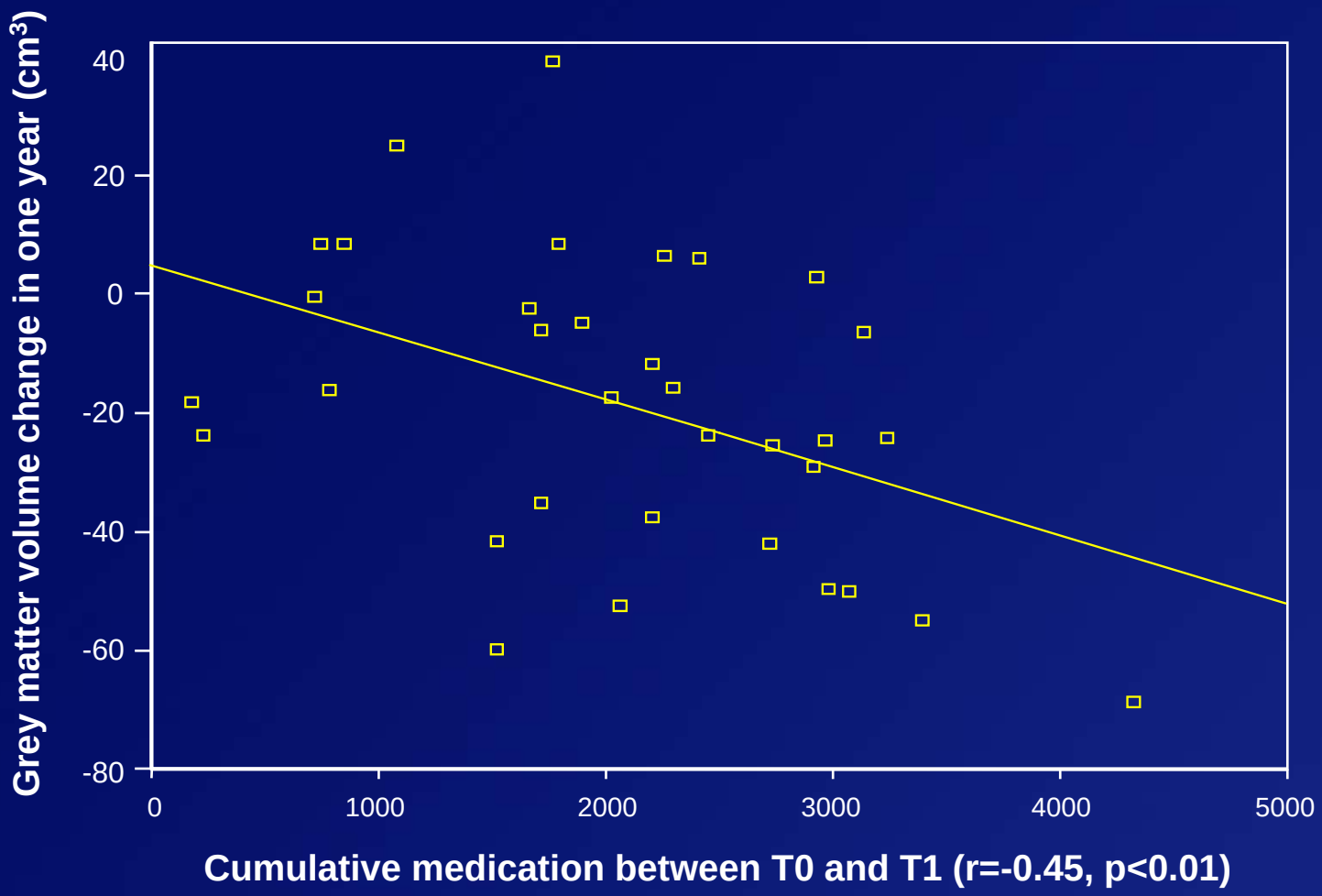
Cahn et al. 2002

Grey matter volume change and outcome



Cahn et al. 2002

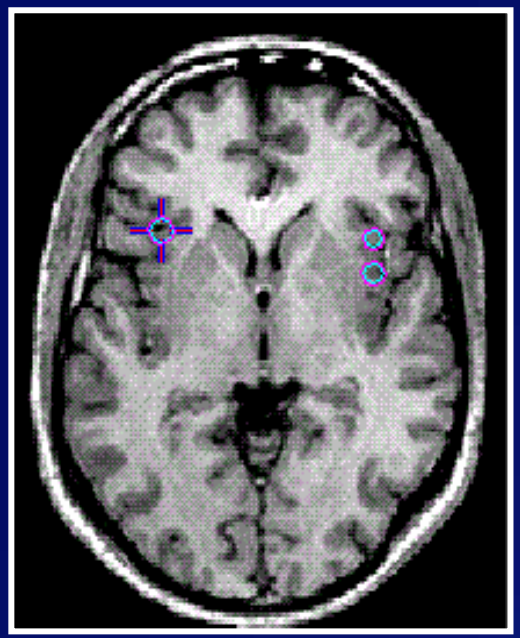
Grey matter volume change and outcome



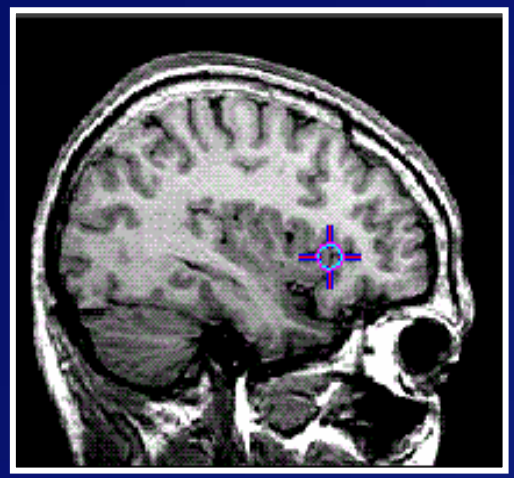
Cahn et al. 2002

Significant voxels T1

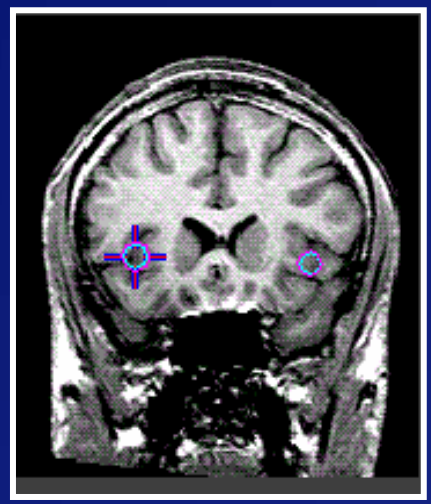
Left inferior frontal



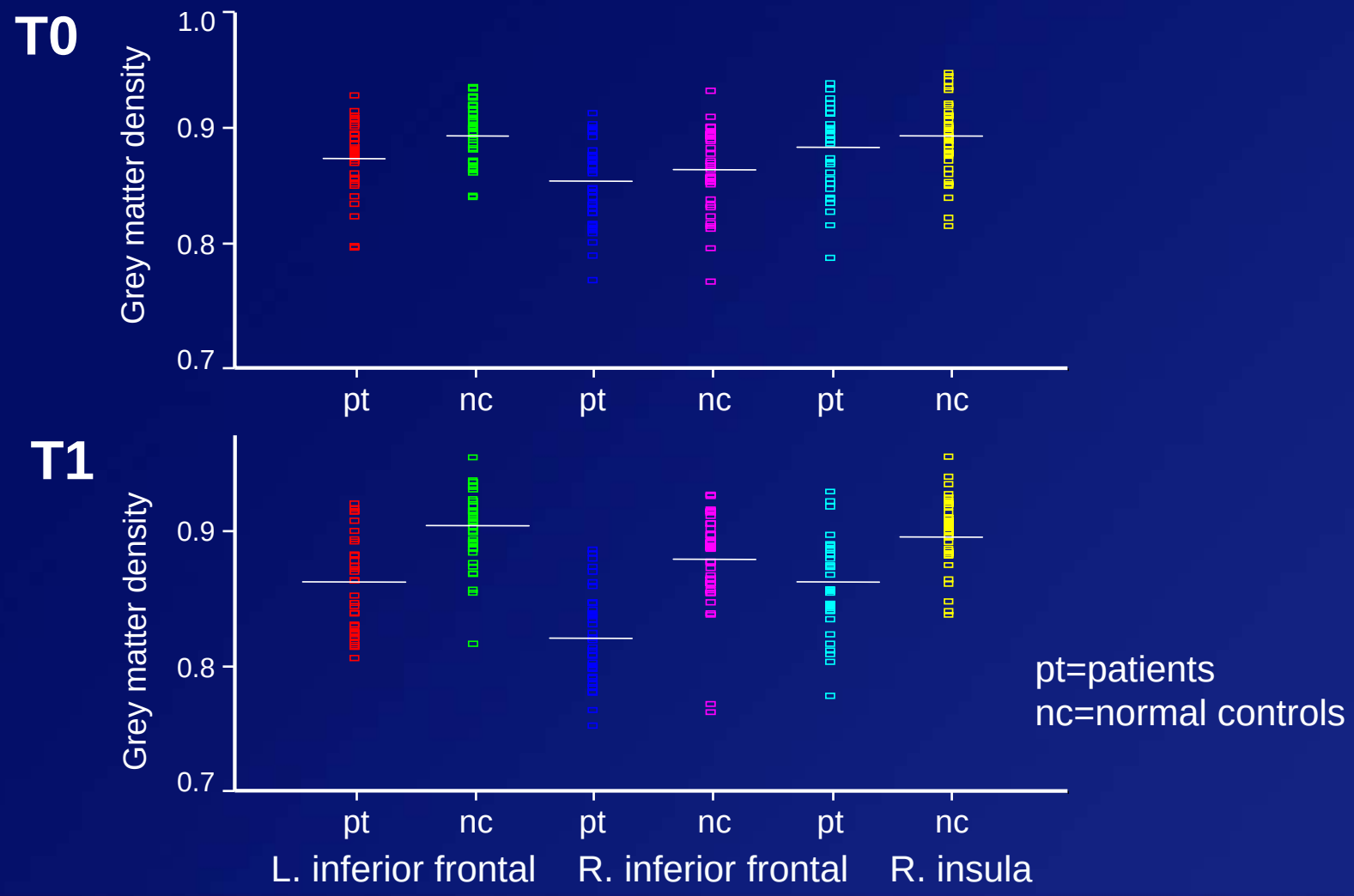
Right inferior frontal



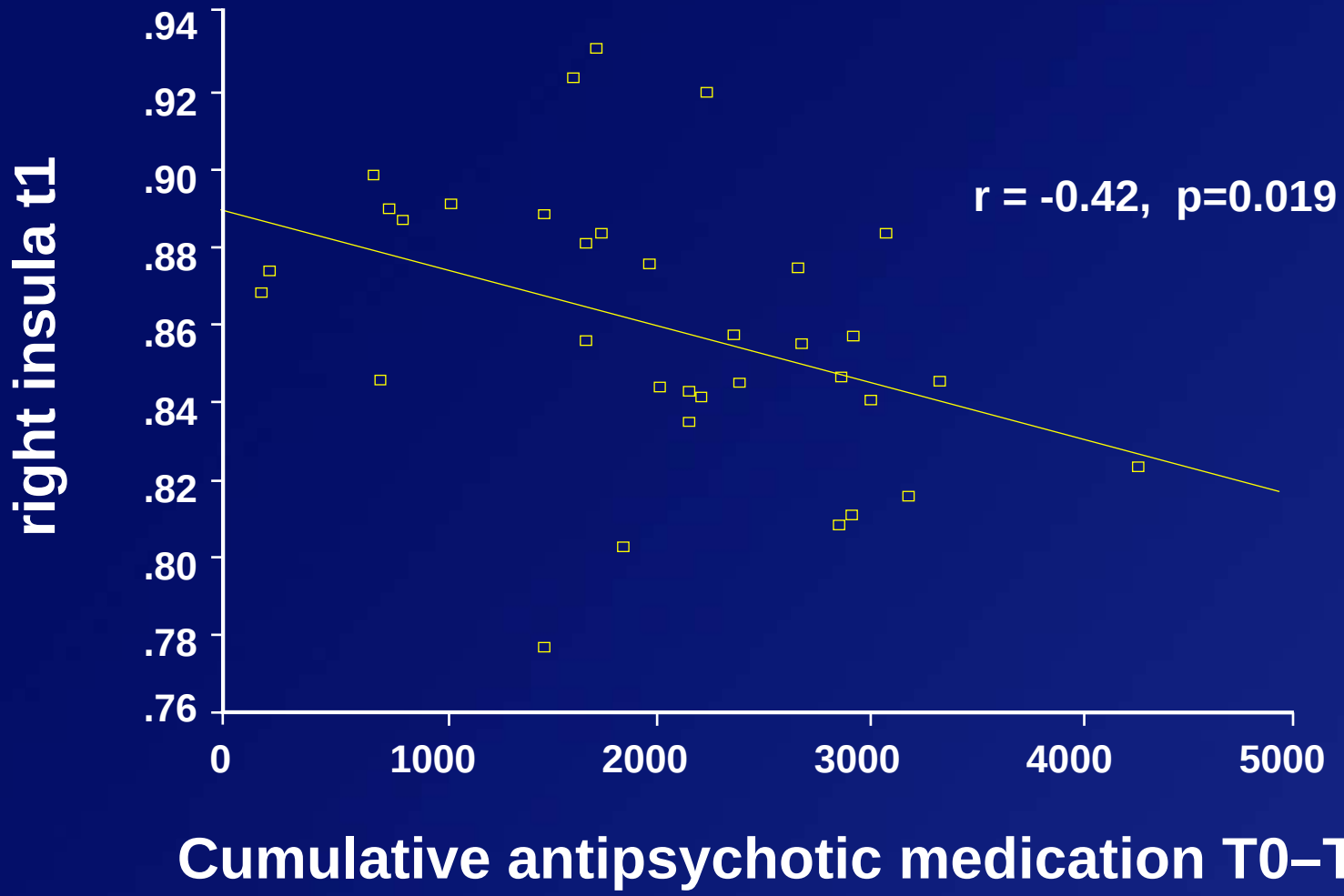
Right insula



Significant voxels: grey matter density in patients and healthy comparison subjects T0 and T1

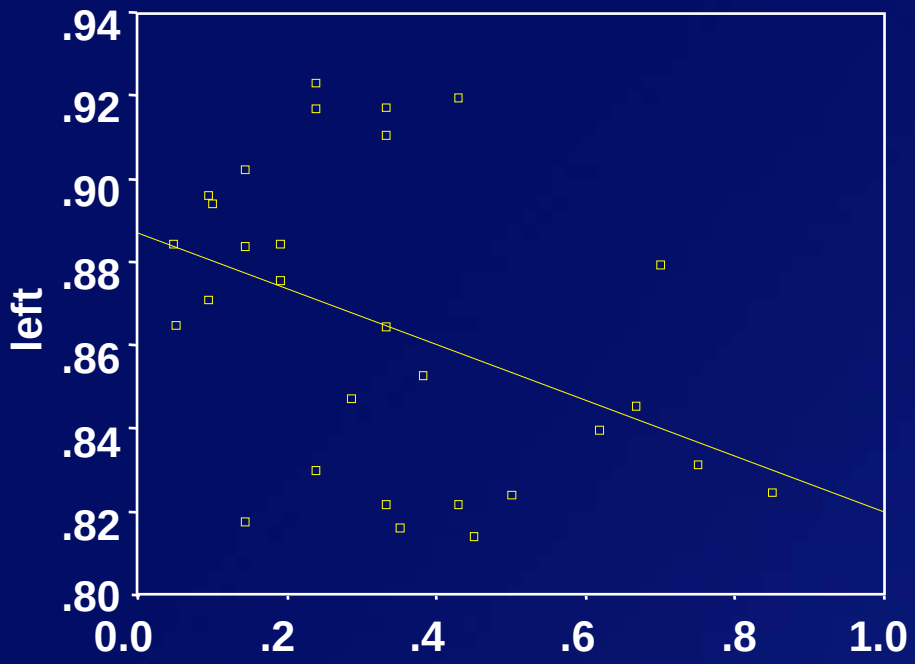


Insula T1 and cumulative antipsychotic medication

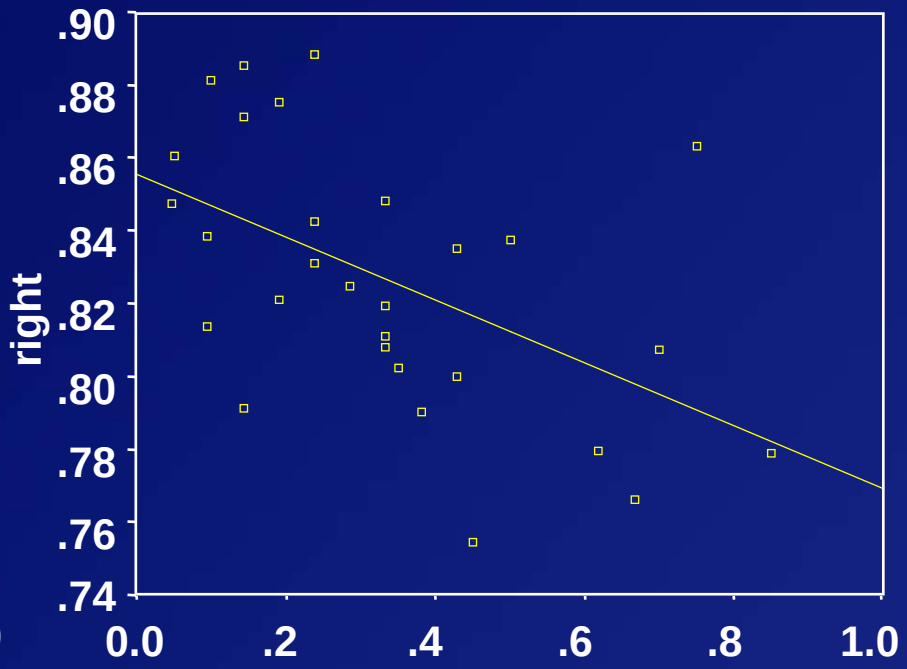


Focal grey matter changes (Broca left and right) T1 and outcome T2 (CAN)

Y axis = inferior frontal T1



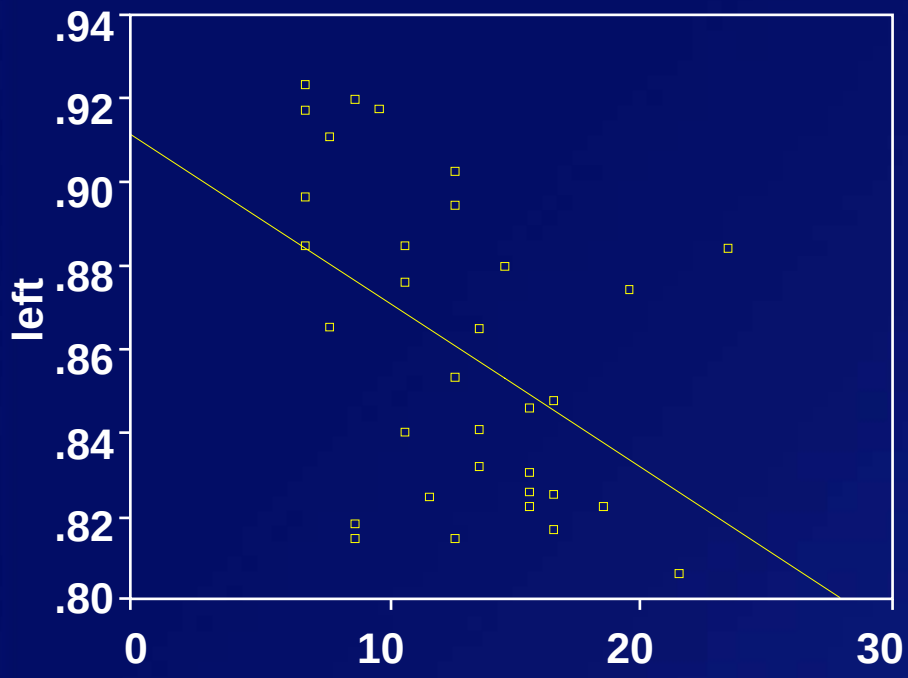
Total number of needs (r =-0.41, p=0.038)



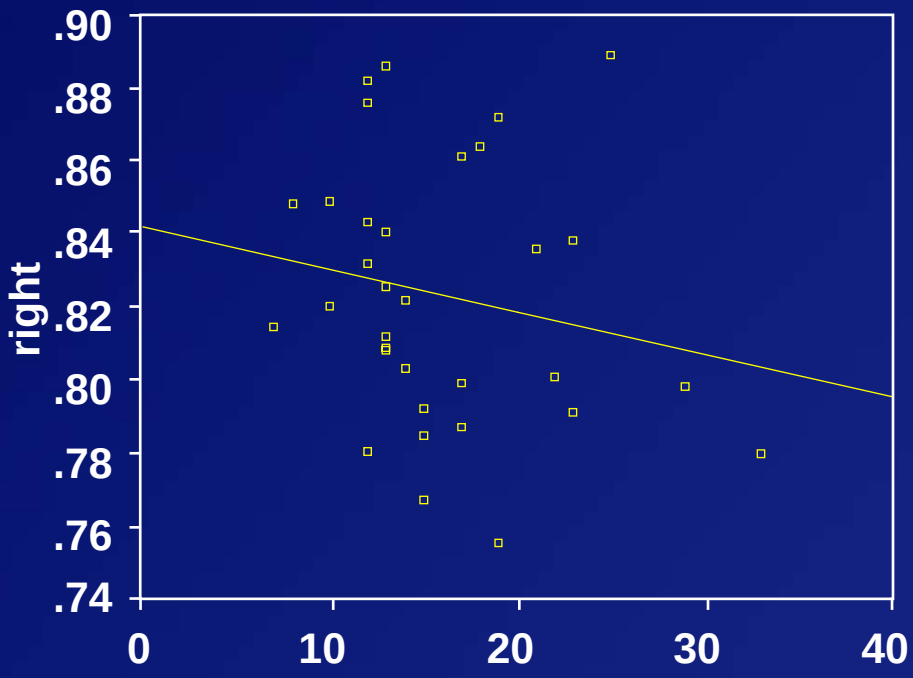
Total number of needs (r =-0.55, p<0.01)

Focal grey matter changes (Broca left and right) T1 and symptoms T1 (PANSS)

Y axis = inferior frontal T1

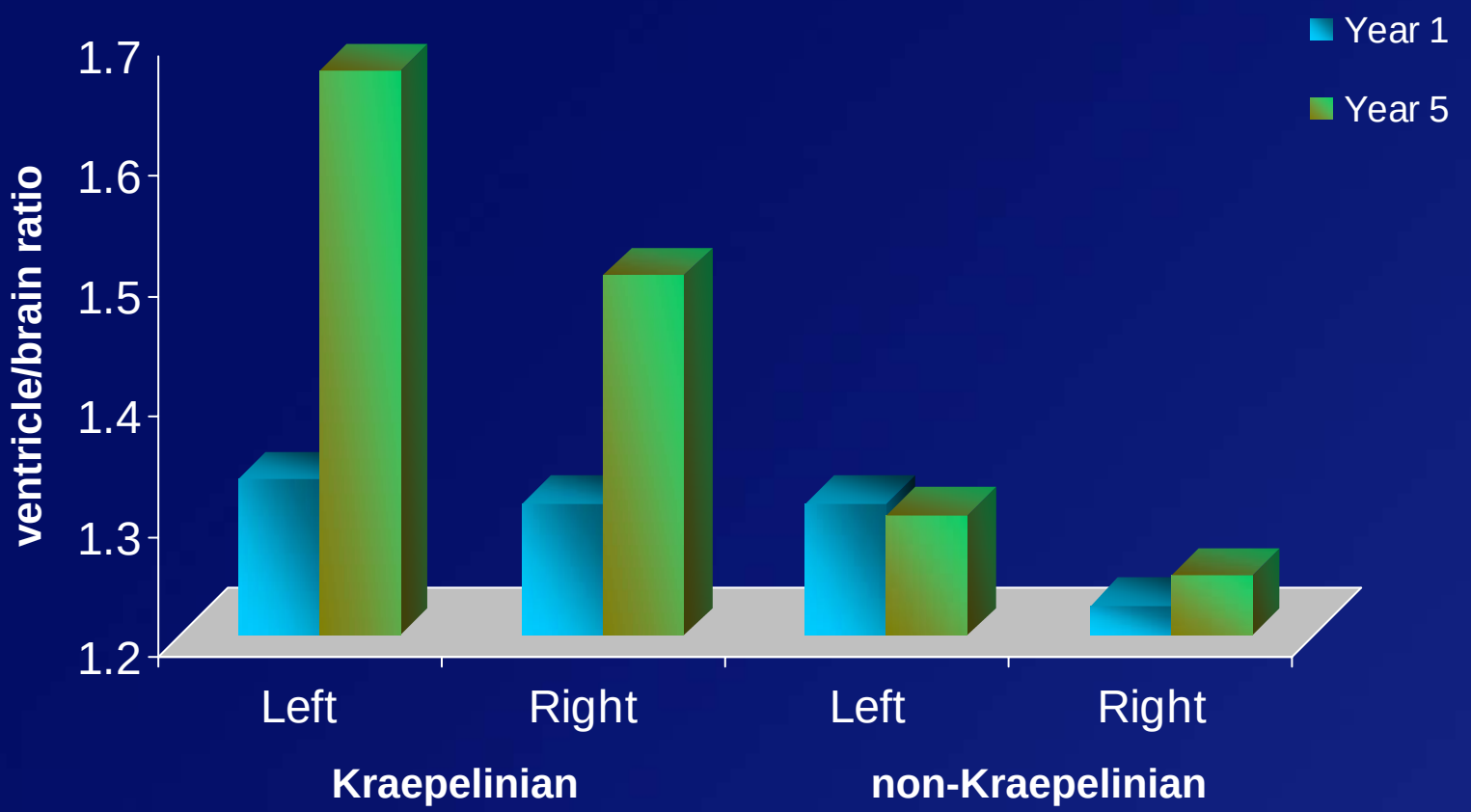


positive symptoms (r =-0.48 p=.007)



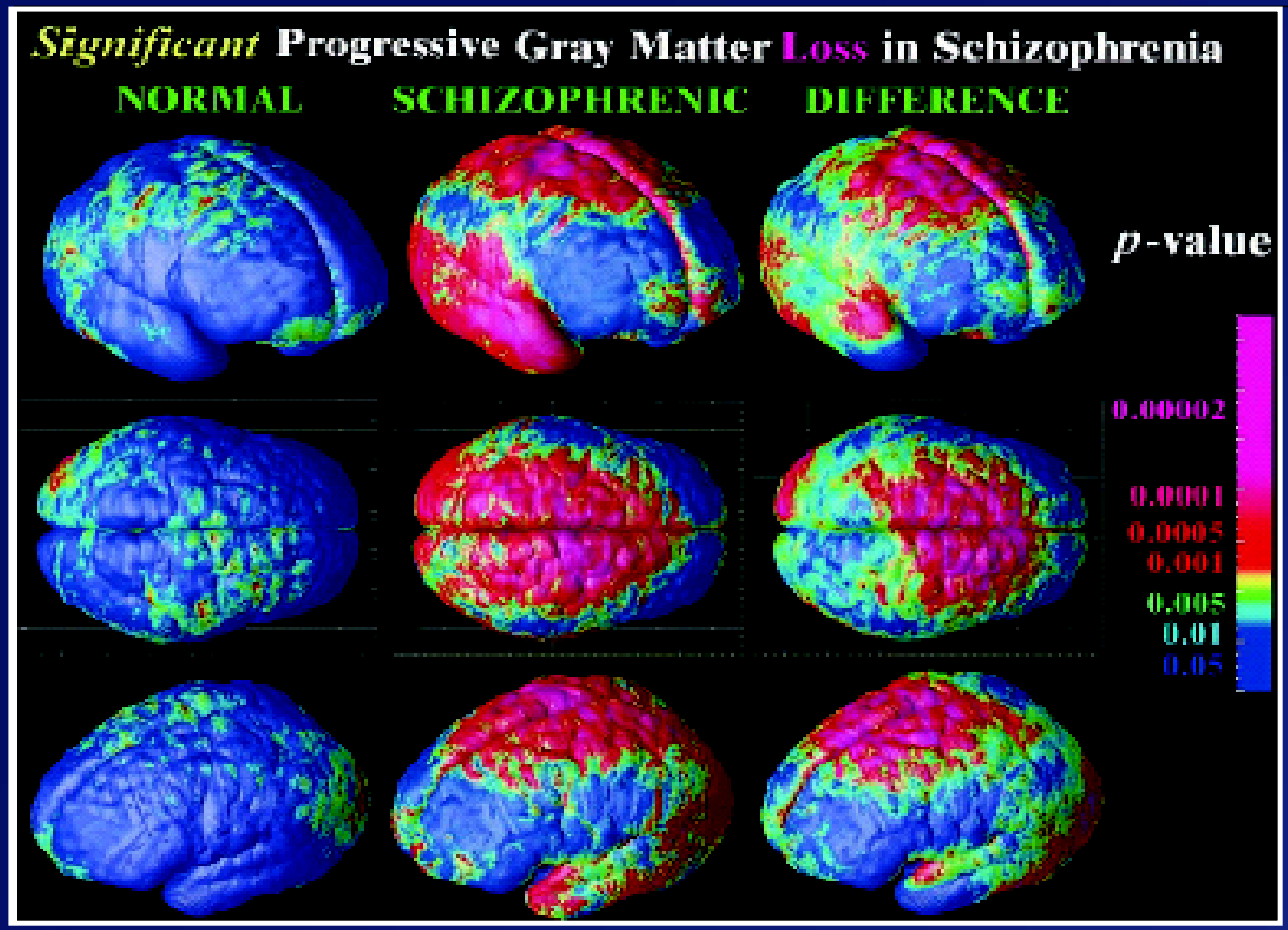
negative symptoms (r =-0.37, p<0.05)

Ventricle change over 5 years



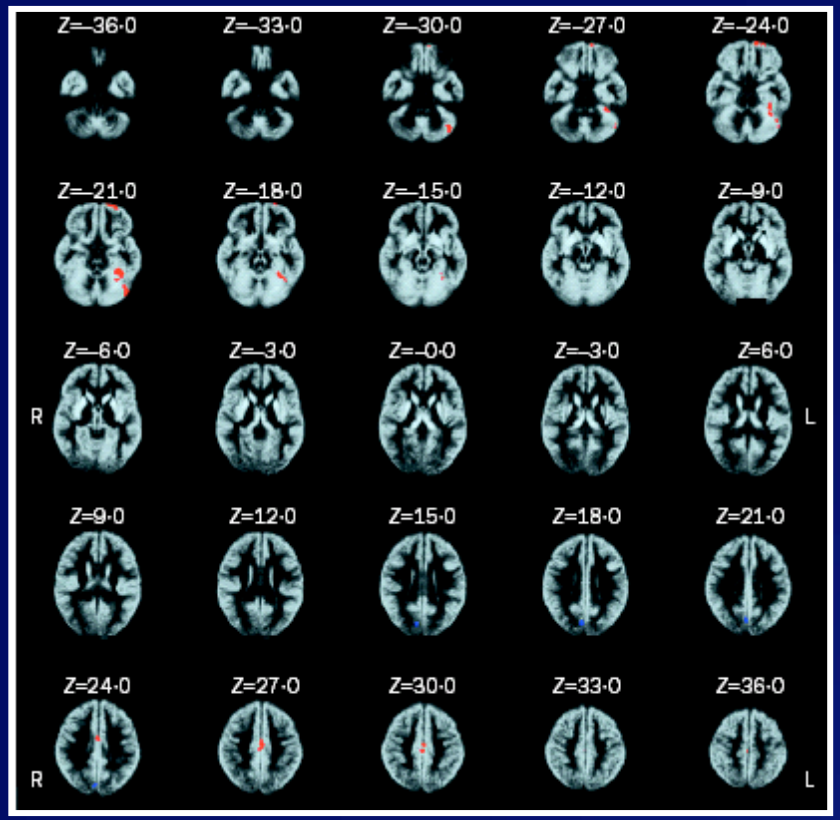
Davis et al, 1998

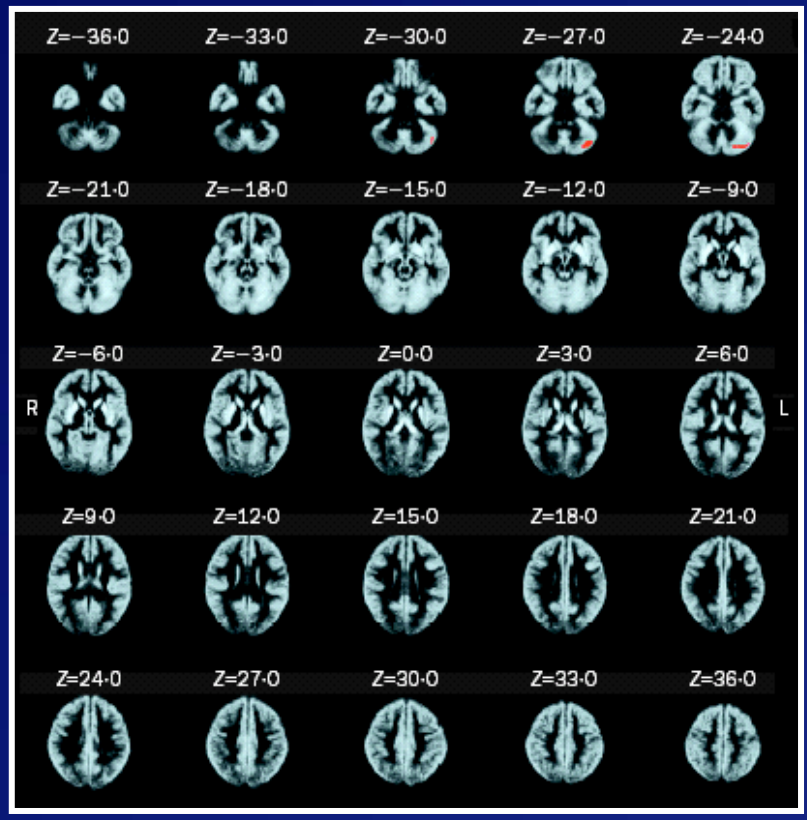
Significance of dynamic grey matter loss in normal and schizophrenic adolescents



Thompson et al, 2001

Neuroanatomical abnormalities before and after onset of psychosis





Pantelis et al, 2003

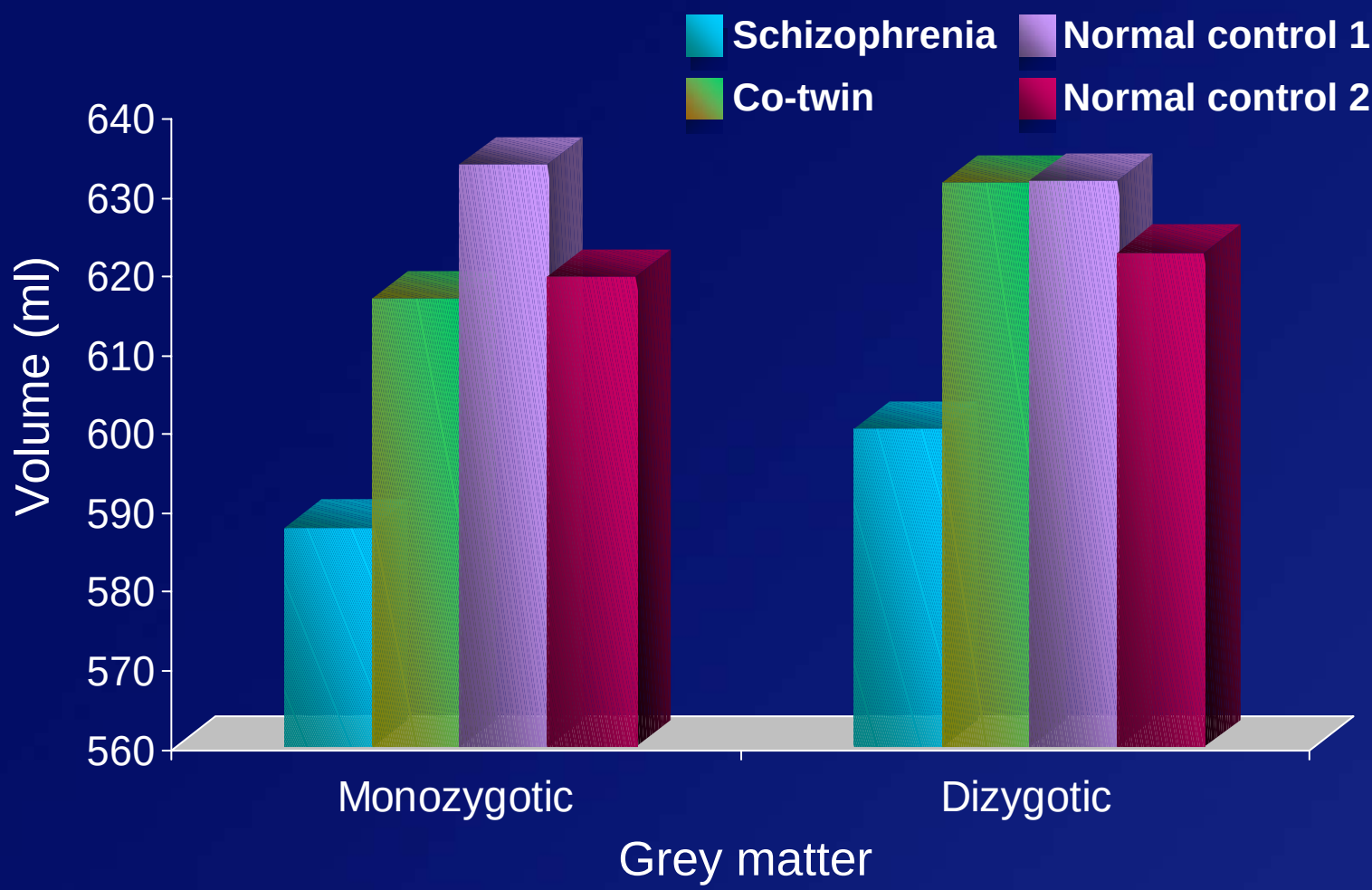
Summary of findings

- Grey matter brain changes in schizophrenia are progressive
- These changes are related to illness, outcome and medication
- White matter changes are static

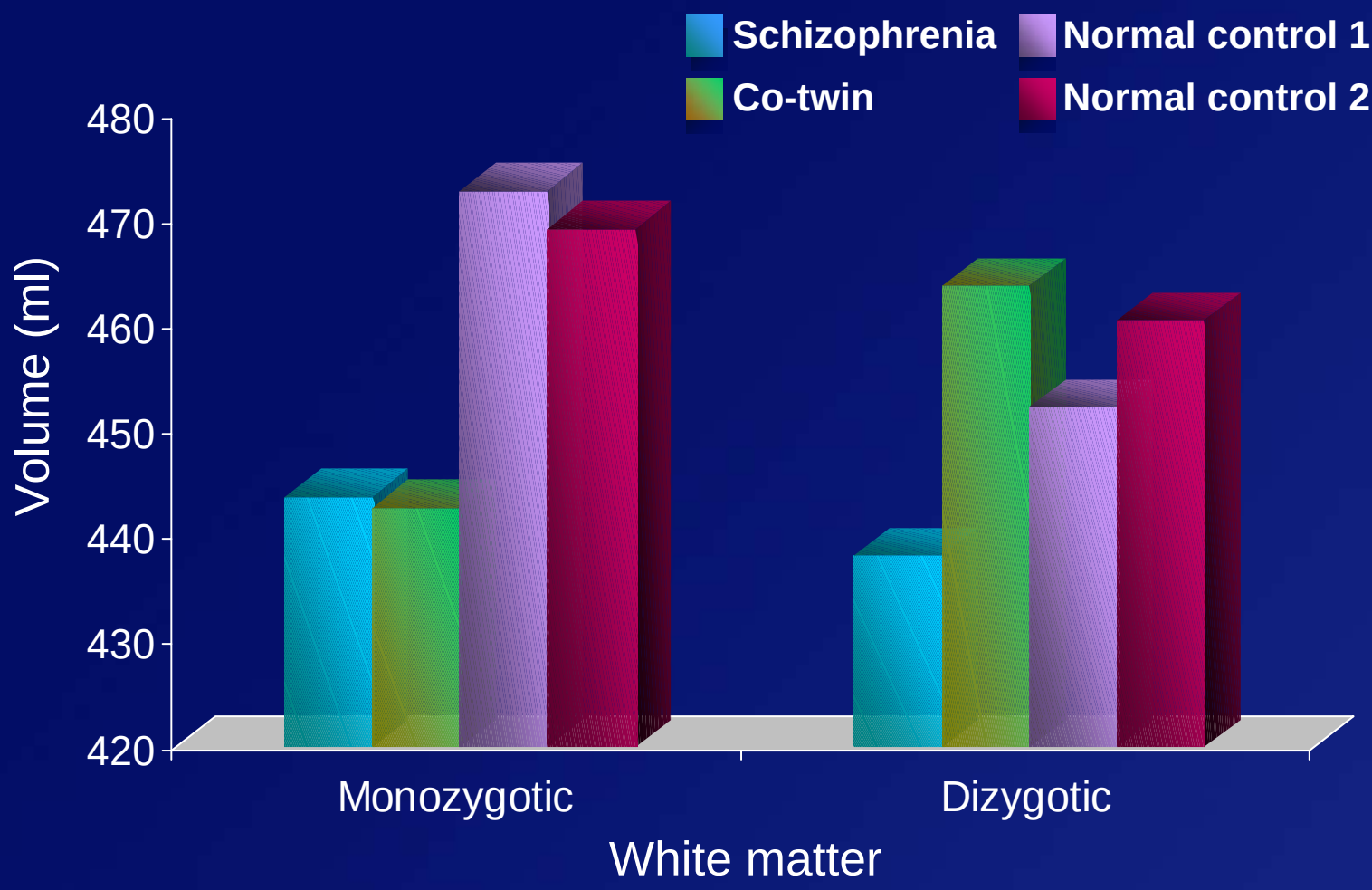
Risk versus illness

- Are the brain changes related to illness or (also) to risk
- Twin study design can address this issue

Twin studies



Twin studies



Conclusions

- Grey matter changes in schizophrenia are progressive and illness-related
- White matter changes in schizophrenia are static and risk-related