

# Association between physical activity, cardiovascular fitness and global brain volumes in patients with schizophrenia

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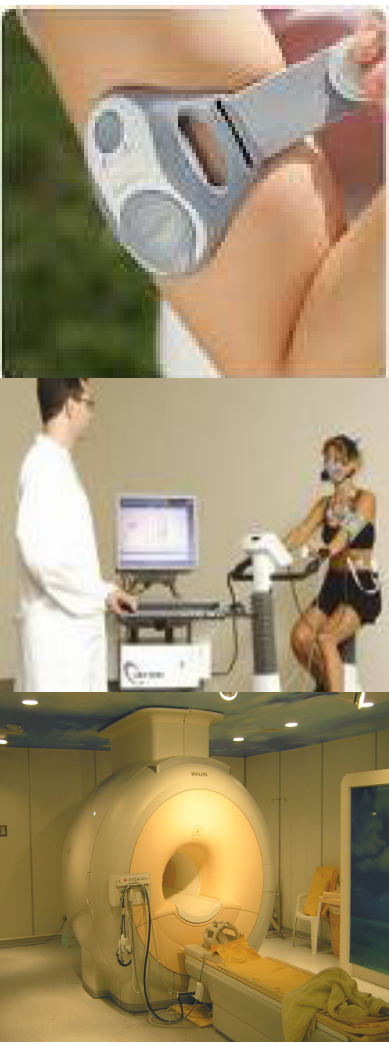
## Background

In schizophrenia brain volume reductions have been found consistently, particularly in the frontal and temporal areas<sup>1</sup>. As suggested by studies in Alzheimer patients and in healthy subjects physical activity might affect global brain volumes. Indeed, physical activity affects hippocampus volume in patients with schizophrenia but other brain structures have not been examined<sup>2</sup>. This study compared real life physical activity and cardiovascular fitness between patients with schizophrenia and matched healthy controls. In addition, the relationship with global brain volumes is investigated.

## Subjects & Methods

**Subjects.** A total of 64 patients (PT) and 55 controls (HC) participated (Table 1). All patients were stable on antipsychotic medication. Controls had no history of psychiatric disorder<sup>3</sup> and no first degree relative with psychotic or mood disorder. HC matched to PT for age, gender, parental education<sup>4</sup> and reported amount of physical activity (PA). All participants gave written informed consent prior to participation.

The following measurements were obtained within a period of two weeks.



-*Real life PA:* SenseWear™ armband, three 24 hour bouts, estimating PA expressed in metabolic equivalents (minutes sedentary vs active PA, steps, time lying down and sleep duration).

-*Maximal Exercise Tolerance Test:* Cardiovascular fitness (CV-fitness) as measured in maximal oxygen uptake capacity per kilogram bodyweight (VO<sub>2</sub>-max) and maximal wattage (WATT).

-*Global brain volumes:* Magnetic Resonance Imaging (MRI) scan, Philips 3-Tesla scanner, quantitative assessment of volume of intracranium (IC), Total brain (TB), cerebrum (BB), cerebral Grey (GM) and White (WM) matter, lateral (LV) and third (V3) ventricles.

**Statistical analysis.** Statistical analysis performed with SPSS 18.0.3. Independent samples T-test and ANOVA analysis determined group differences on PA, VO<sub>2</sub>-max levels and global brain volumes between PT and HC. Multiple linear regressions investigated the correlations between PA and CV-fitness with brain volume measurements in the total sample, as well as in the groups separately. Age, gender and IC volume were entered as covariates.

Table 1: demographic characteristics

	PT (N=64)	HC (N=55)	F	p
Age (years)	29.65 ± 7.3	29.29 ± 7.8	0.708	.79
Sex (M/F)	48/17	36/19	Chi	.33
Length (cm's)	177.8 ± 9.3	178.2 ± 10.1	0.817	.82
Weight (kg's)	82.5 ± 19.3	76.3 ± 14.3	5.151	.05
Body Mass Index	26.1 ± 6.0	24.0 ± 3.3	12.049	.02
Parental education level*	5.1 ± 1.2	5.5 ± 1.2	Chi	.09

Results presented as Mean ± Standard deviation.

\* Parental education: highest level of one of both parents according to Verhage method<sup>4</sup>

## Results

Table 2: physical activity in PT vs HC

	PT (N=64)	HC (N=55)	t	p
Sedentary (1>3 MET)	1300 ± 71	1258 ± 69	3.217	<.00
Physical activity (SUM>3 MET)	140 ± 71	181 ± 69	-3.158	<.00
Steps (number)	8138 ± 3031	8838 ± 2775	-1.305	.194
Time lying down (minutes)	675 ± 124	517 ± 70	8.409	<.00
Sleeping time (minutes)	544 ± 114	389 ± 61	9.003	<.00
On body time (percentage)	98.3 ± 1.4	97.7 ± 1.8	1.999	.048

Results presented as Mean ± Standard deviation.

Table 3: CV-fitness in PT vs HC

	PT (N=64)	HC (N=55)	t	p
VO <sub>2</sub> -max specific (ml/min/kg)	32.0 ± 10.0	35.2 ± 6.1	-2.076	.04
WATT Maximum	219 ± 53	255 ± 54	-3.707	<.00
RER Maximum (respiratory Exchange rate)	1.26 ± .15	1.37 ± .09	-4.821	<.00

Results presented as Mean ± Standard deviation.

Table 4: Global brain volumes in PT vs HC

	PT (N=60)	HC (N=54)	F	p
IC	1493.11 ± 132.30	1515.11 ± 134.19	2.875	.093
TB	1227.40 ± 117.50	1278.21 ± 113.20	25.254	.000
BB	.89 ± 8.31	14.35 ± 8.37	19.469	.000
LV	17.89 ± 8.31	14.35 ± 8.37	7.018	.009
V3	0.83 ± 0.40	0.64 ± 0.28	9.763	.002
GM	581.46 ± 54.16	609.78 ± 55.81	22.500	.000
WM	494.42 ± 64.82	507.87 ± 55.34	1.029	.313

Mean (±SD) volumetric measurements (cm<sup>3</sup>) corrected for age, gender and IC volume in PT vs HC.

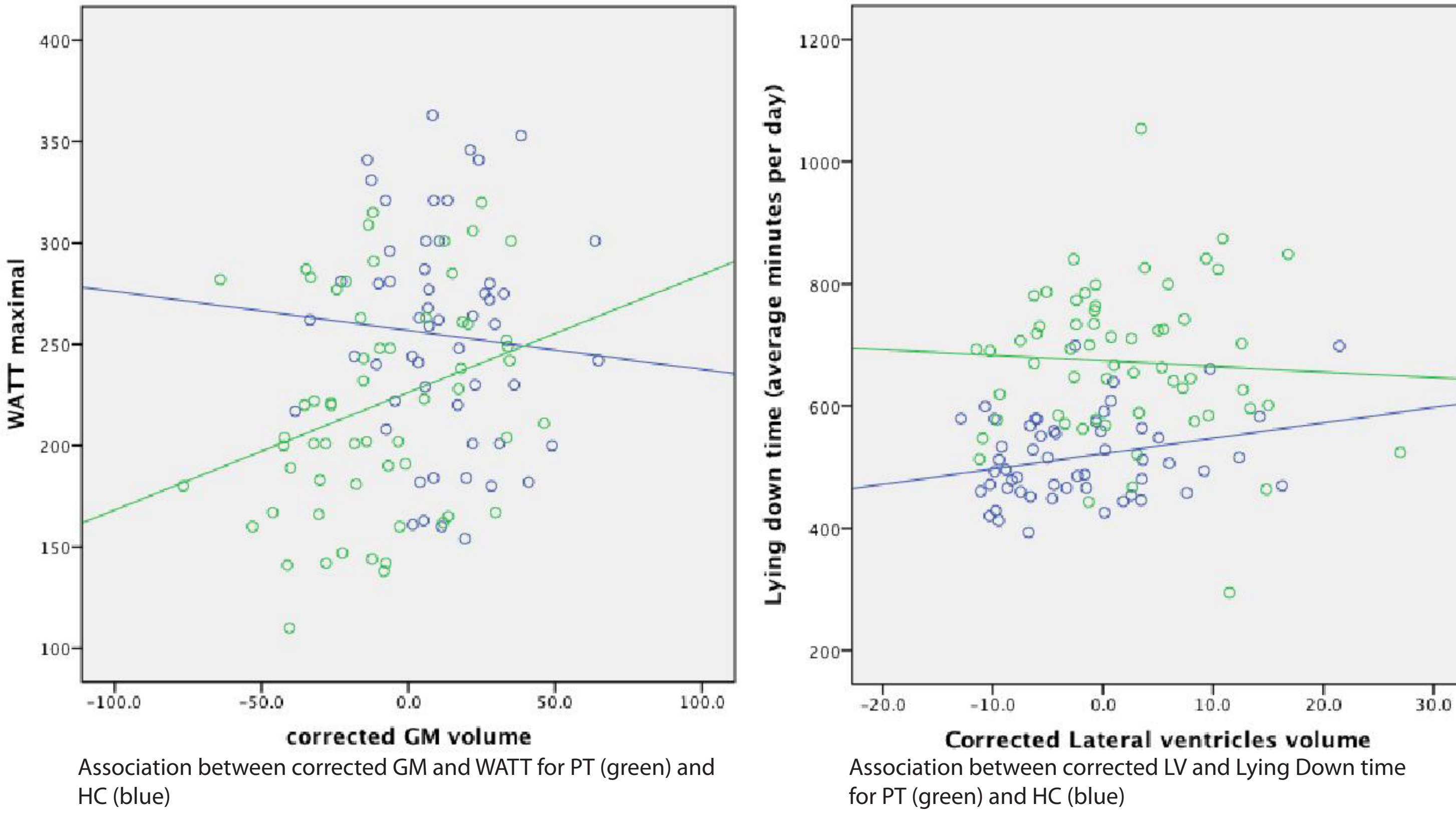
Table 5: Brain volume correlations with Lying, Sleeping time & WATT in HC and PT

	Volume in HC Subjects (N=54) With Lying Down Time (ml/min) <sup>a</sup>				Excess Volume in PT With Lying Down Time (ml/min) <sup>b</sup>			
	b	SE(b)	t	p	b	SE(b)	t	p
LV	.030	.015	1.301	.05	-.034	.017	-1.953	.05
	Volume in HC Subjects (N=54) With Sleeping Time (ml/min) <sup>a</sup>				Excess Volume in PT With Sleeping Time (ml/min) <sup>b</sup>			
	b	SE(b)	t	p	b	SE(b)	t	p
LV	.044	.017	2.532	.01	-.056	.019	-2.869	.01
	Volume in HC Subjects (N=54) With WATT maximum (ml/WATT) <sup>a</sup>				Excess Volume in PT With WATT maximum (ml/WATT) <sup>b</sup>			
	b	SE(b)	t	p	b	SE(b)	t	p
GM	-.011	.075	-.146	.88	.186	.086	2.127	.04

<sup>a</sup> Regression slopes in unstandardized (raw) regression coefficients b ± SE(b) for HC with Lying Down, Sleeping Time and WATT maximum after addition of the predictor variable for interaction between Lying Down, Sleeping Time and WATT and group to the regression and correction for sex and total IC volume.

<sup>b</sup> Regression slopes in unstandardized (raw) regression coefficients b ± SE(b) for schizophrenia patients with Lying Down, Sleeping Time and WATT maximum after addition of the predictor variable for interaction between Lying Down, Sleeping Time and WATT and group to the regression and correction for sex, age, and total IC volume.

Graph 1: GM volume association with WATT in HC and PT



## Conclusion

- Patients are less physically active and have worse cardiovascular fitness levels than matched, inactive controls.
- Patients have smaller total brain, cerebrum, lateral and third ventricle, and grey matter volumes than controls.
- More lying down and sleeping time is associated to larger lateral ventricles in controls, not in patients.
- Better CV-fitness (measured by WATT maximum) is associated with larger grey matter volumes in patients, not in controls.

## References

[1] Hulshoff Pol, H.E. Kahn, R.S. 2008 Schizophrenia Bulletin 34, 354-366; [2] Pajonk, F.G. et al. 2010 Archives of General Psychiatry 67, 133-143; [4] APA. Diagnostic and Statistical Manual of Mental Disorders 4th edition TR 2000 Washington DC, American Psychiatric Association; [3] Verhage 1983 Revised scoring method for educational level. University Hospital Groningen: Department of Neuropsychology; [4] Kay et al. 1987 Psychiatry Research vol. 23 pp. 99-110.

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