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Autonomic nervous system function assessed by heart rate variability in children and young adults with craniopharyngioma

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OBJECTIVES

Hypothalamic damage due to craniopharyngioma (CRP) and ensuing treatment is associated with obesity. Autonomic dysfunction is implicated in the development of obesity in hypothalamic damage.

AIMS:
1.To evaluate autonomic function using heart rate variability (HRV) parameters according to the grade of hypothalamic damage in CRP.

2. To analyze for relationships of HRV parameters with obesity and insulin resistance.

METHODS

SUBJECTS:
47 patients with longstanding CRP (28 males, mean age 18.5 ± 4.7 years) with median postoperative follow-up of 10.7 years were enrolled.
Patients with comorbidities or medications affecting the autonomic nervous system were excluded.

Anthropometrics, physical activity measures, blood pressure (BP), and fasting blood sample were obtained. HRV indices were measured as follows:
-overall HRV: standard deviation of the NN interval (SDNN), total power (TP)
-sympathetic activity: low frequency (LF)
-parasympathetic activity: root mean squared difference of successive NN intervals (RMSSD), high frequency (HF)

The degree of hypothalamic involvement (mild or severe) was graded on magnetic resonance imaging as defined by a grading system defined by Puget[1] at the time of HRV testing.

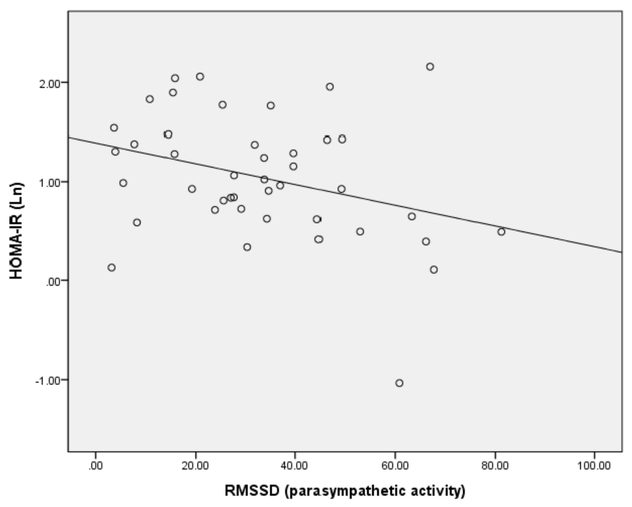
RESULTS

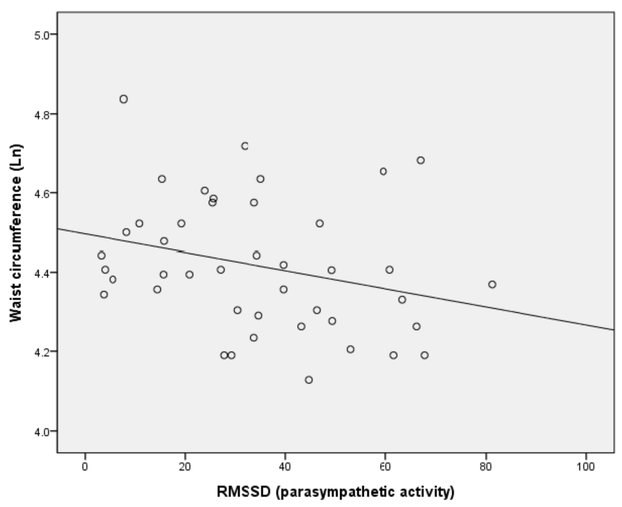
	Mild HI (n=19) Mean ± SD	Severe HI (n=28) Mean ± SD	*P*-value
Age (years)	18.3±4.0	18.7±5.3	0.776
Postoperative years	11.2±5.5	10.1±5.5	0.506
BMI SDS	0.40±1.33	1.48±1.05	**0.006**
HOMA-IR	2.45±1.53	3.96±2.10	**0.033**
Total cholesterol (mg/dL)	185±24	187±38	0.910
Triglyceride (mg/dL)	153±99	171±161	0.678
HDL cholesterol (mg/dL)	45±11	42±13	0.416
LDL cholesterol (mg/dL)	117±20	121±37	0.714
SDNN (ms)	45.48±17.55	33.54±18.00	**0.029**
RMSSD (ms)	40.71±20.51	29.86±18.13	0.062
Total power (ms^2)	1816±1192	1033±1117	**0.008**
Low frequency (ms^2)	360±224	212±212	**0.043**
High frequency (ms^2)	415±323	270±240	**0.050**
LF:HF ratio	1.46±1.67	1.99±2.74	0.453
Systolic BP (mmHg)	99±10	109±12	**0.005**
Diastolic BP (mmHg)	65±7	70±11	0.069

The group with severe HI showed higher BMI SDS, insulin resistance (HOMA-IR) and systolic BP.

Severe HI group showed reduced overall HRV as shown by reduced SDNN and total power. Both sympathetic (low frequency) and parasympathetic (high frequency) measures were decreased with greater hypothalamic involvement.

Multivariate regression analysis
Greater hypothalamic involvement (severe HI) was independently associated with lower markers of overall HRV (P=0.05 for SDNN and P=0.01 for total power) and lower sympathetic activity (P=0.004 for LF), after adjusting for BMI, HOMR-IR and triglycerides.





RMSSD and HF indicating parasympathetic activity correlated negatively with HOMA-IR (P=0.03) and waist circumference (P=0.03) respectively

CONCLUSIONS

Patients with greater hypothalamic damage showed generalized autonomic dysfunction with reduced overall HRV, sympathetic and parasympathetic activities.
The degree of hypothalamic damage was an independent predictor for reduced overall HRV and reduced sympathetic activity.
Increased IR and central obesity were associated with decreased parasympathetic activity.
These results provide deeper understanding of obesity, IR and autonomic dysfunction in CRP patients with hypothalamic damage.

References

1. Puget S, Garnett M, Wray A et al, Pediatric craniopharyngiomas: classification and treatment according to the degree of hypothalamic involvement. J Neurosurg 2007; 106(Suppl 1):3-12

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