



## Correlation between Conners' Parent Rating Scale and autonomic functions in ADHD before and after methylphenidate

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### Abstract

*The present study was conceived with the objective to study the correlation between the Conners' Parent Rating score and autonomic functions in children with Attention-deficit/hyperactivity disorder (ADHD) before and after treatment with Methylphenidate. ADHD is associated with autonomic dysfunction which gets further modulated by drug therapy. There are few prospective studies to evaluate the correlation between the Conners' Parent Rating score and autonomic functions before and after 12 weeks of methylphenidate treatment in drug-naive patients with ADHD. The parasympathetic reactivity was tested with E: I ratio (Deep Breathing Test) and 30:15 ratio (Heart response to standing). On the Sympathetic reactivity tests, the Increase in Systolic blood pressure (SBP) & diastolic blood pressure (DBP) on exposure to cold (Cold Pressor test) and sustained handgrip (Handgrip test) was performed on the subjects. Cold Pressor Test SBP differences showed a negative correlation with Conners Parent Rating score signifying that the children with lower ADHD scores had higher responsiveness to CPT-induced SBP changes. Post-therapy Cold Pressor Test SBP differences showed a negative correlation with Conners ARS signifying that the children with lower ADHD scores had higher responsiveness to CPT-induced SBP changes. Hence with the improvement as shown by reduction in ADHD scores, the sympathovagal balance shifts towards the sympathetic arm.*

**Keywords:** Conners' Parent Rating score, ADHD, methylphenidate, autonomic functions.

## Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most commonly diagnosed psychiatric disorders in children and adolescents with the worldwide prevalence of 7.2 %<sup>1</sup>. ADHD is a behavioral and neurocognitive condition characterized by developmentally inappropriate and impairing levels of gross motor over activity, inattention, and impulsivity<sup>2</sup>. ADHD is treated with psycho-education, Cognitive behavioral therapy techniques, and pharmacotherapy<sup>3,4</sup>. The Methylphenidate is one of the most commonly used medications for ADHD treatment<sup>5</sup>. Studies on autonomic functions have shown that stimulant-free children with ADHD showed a sympathetic under arousal and parasympathetic over arousal relative to control subjects and Methylphenidate shifted the autonomic balance of children with ADHD towards normal levels<sup>6-8</sup>. The abbreviated version of Conners' rating scale is useful in evaluating the effectiveness of the treatment of ADHD with Methylphenidate<sup>9</sup>. To the best of our knowledge, there are very few prospective studies to systematically evaluate the correlation between the Conners' Parent Rating score and changes of autonomic functions before and after methylphenidate treatment in children suffering from ADHD.

## Aim

To study the correlation between the change in Conners' Parent Rating score and changes of autonomic functions before and after methylphenidate treatment in children suffering from ADHD.

## Methods

The institutional ethics committee for human research of Lady Hardinge Medical College approved the study. This study was conducted in the Department of Physiology in association with the Department of Psychiatry at Lady Hardinge Medical College and Smt. Sucheta Kriplani Hospital, New Delhi. Drug-naive cases of ADHD diagnosed as per DSM-V criteria<sup>2</sup> requiring methylphenidate treatment were recruited. The subjects were

between 6 to 12 years of age, 52 in number. Known patients of cardiovascular diseases, diabetes mellitus systemic inflammatory disorders, and mental retardation were excluded from the study. Patients with other psychiatric co-morbidities including autism, oppositional defiant disorder, and conduct disorder or receiving medication known to affect autonomic function were also excluded from the study. The study group constituted only male patients as no female patient met our inclusion criteria. A parent or legal guardian of the subjects provided the informed written consent in either Hindi or English.

General physical examination and autonomic function tests were carried out in the Physiology department between 9 to 11 am. No psychotropic drug was allowed before the recording of baseline autonomic function tests. The subjects were asked to refrain from tea and caffeinated drinks 2 hours before the tests.

The following autonomic function tests were conducted on the subjects.

### I. Parasympathetic Reactivity tests

The ECG was recorded using BPL CARDIART 6208 ECG machine for the Parasympathetic Reactivity tests.

1. Deep breathing test-E: I ratio<sup>10-13</sup>:- After 10 minutes of rest in the supine position the patient was instructed to take deep and steady breathing at six breaths per minute in lying position comprising of 5 seconds of inspiration and 5 seconds of expiration. During breathing, an electrocardiogram was recorded continuously. With each breathing cycle, the point of beginning of inspiration and the point of beginning of expiration was marked on ECG. The E: I ratio was calculated with the formula-

$$E: I \text{ ratio} = \frac{\text{Longest R-R interval during expiration}}{\text{Shortest R-R interval during inspiration}}$$

In very young children who were unable to follow the above instructions, the values were calculated from single breath cycle.

2. Standing lying test-30:15 ratio<sup>10-13</sup>: The subject was instructed to lie down quietly for 10 minutes, while a continuous electrocardiogram was recorded and then the patient was instructed to stand up and

remain motionless. The point of standing was marked on the ECG. The 30:15 ratio was calculated as-

$$30:15 \text{ ratio} = \frac{\text{R-R interval at beat 30 after assuming an erect posture}}{\text{R-R interval at beat 15 after assuming an erect posture}}$$

## II. Sympathetic Reactivity tests

1. Cold pressor test (CPT)<sup>14,15</sup>: Resting blood pressure was recorded. The patient then dips one hand up to the wrist in cold water at 10 degrees Celsius for one minute. The Systolic and diastolic blood pressures were monitored from the other arm before the procedure and at one minute just before retracting the hand from cold water. The increase in the systolic and diastolic blood pressure was recorded as a response to cold stimulation.

2. Hand grip test<sup>16,17</sup>: The test was performed in sitting position. Resting blood pressure was recorded. Then, the patient was instructed to grip the Hand grip dynamometer with the dominant hand with and contract maximally. Three successive trials were performed at an interval of 30 seconds. The highest value of three contractions was taken as a maximum voluntary contraction. After an interval of five minutes, handgrip exercise was again done, but this time contraction was maintained steadily by the subject at 30% of maximum voluntary contraction for up to 4 minutes. During this maneuver, both systolic and diastolic blood pressure was recorded at first, 2nd and at the 4th minute from the non-exercising arm. The maximum rise in systolic and diastolic blood pressure was taken as an index of response to the hand grip.

The patients were then put on methylphenidate for 12 weeks. Mean dose of methylphenidate at the endpoint of the study was  $0.70 \pm 0.09$  mg/ Kg.

Conners' parent rating scale<sup>18-19</sup>:- The short version of Conners' rating scale was used as it is the most useful diagnostic tool for ADHD because of its brevity and high accuracy. This scale has ten questions regarding the child's behavior in the last one month with four possible answers: Not at all (0), Just a little (1), Pretty much (2) and very much (3). The questions were read one by one to the parents, and the responses were marked on the rating scale accordingly. Conners' abbreviated parent rating

scale has a maximum score of 30. A score of more than 15 is suggestive of ADHD. Reduction in the score after treatment signifies clinical improvement. Autonomic function tests and Conners' Parent Rating score was repeated at 12 weeks of study period.

Data obtained was subject to statistical evaluation using a Graph Pad Prism Version 7 software. The D'Agostino & Pearson normality test, Shapiro-Wilk normality test and KS normality test were applied to test for normal Gaussian distribution. Correlations between Conners' score and Autonomic Function Tests were assessed with Spearman correlation coefficient.

Adherence to 'p' values was followed as stated below:

p >0.05-Non-Significant (NS)

p <0.05-Significant (\*)

p <0.01-Highly Significant (\*\*)

p <0.001-Very Highly Significant (\*\*\*)

## Results

In our study, the correlation analysis showed following essential observations:

A significant negative correlation was observed between the change in Cold Pressor Test DBP and the change in Conners' score at baseline. The Spearman's Correlation test did not yield any significant correlation in Conners' score and other autonomic reactivity tests at baseline (Table 1).

A significant negative correlation was observed between the Cold Pressor Test SBP with Conners' score after 12 weeks of methylphenidate treatment. The Spearman's Correlation test did not yield any significant correlation in Conners' score and other autonomic reactivity tests after 12 weeks of methylphenidate treatment (Table 2).

**Table 1:** Correlation between baseline Autonomic reactivity tests with Conners' score in ADHD patients (n=52)

PARA-METERS	Conner's ARS	
	Correlation Co-efficient(r)	P value
E : I ratio	0.208	0.138
30:15ratio	-0.236	0.092
CPT S Difference	-0.290	0.037*
CPT D	-0.394	0.364
HGD S	-0.129	0.315
HGD D	-0.034	0.176

\* Significant p value

**Table 2:** Correlation between Autonomic reactivity tests with Conners' score after 12 weeks of methylphenidate treatment in ADHD patients (n=52).

PARA-METERS	Conner's ARS	
	Correlation Co-efficient(r)	P value
E : I ratio	0.157	0.265
30:15ratio	-0.004	0.978
CPT S Difference	-0.457	0.027*
CPT D	0.015	0.919
HGD S	-0.159	0.259
HGD D	-0.011	0.940

\* Significant p value

## Discussion

Pretherapy Conners' score showed a significant negative correlation with the CPT-induced changes in SBP. Hence higher ADHD score was associated with lesser sympathetic responsiveness in patients.

Post Therapy CPT SBP differences showed a negative correlation with Conners' ARS signifying that the children with lower Conners' score had higher responsiveness to CPT-induced SBP changes. Thus, in our study ADHD children showed an increase in sympathetic activity with methylphenidate treatment. This increased sympathetic activity was associated with the improvement in the Conners' score.

Though the mechanism by which autonomic tests are altered in ADHD cannot be deciphered from this study but the possible mechanisms that could play a role in autonomic functions may be postulated. Psychological state is known to influence the autonomic nervous control of the cardiovascular system in patients with mental disorders and

psychological state also can influence autonomic functions because the central nervous system modulates the autonomic nervous system<sup>20</sup>. Accordingly, a change in the mental state can also affect the autonomic nervous system and can thus affect autonomic functions, whether the treatment causes it or not.

## Limitations

This study had some limitations. The foremost being the lack of a control group and non-blinded study design. Moreover, this study included a homogeneous group of male patients with ADHD, and distinct neurobiological deficits may underlie the developmental course of ADHD in males and females. Thus, our results are representative of only male ADHD patients. Further research in this field is warranted to elicit ADHD linked gender differences in autonomic functions. Further research on larger sample size and a control group is warranted.

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