

RELATIVE ROLES OF THE SYMPATHETIC AND PARASYMPATHETIC SYSTEMS IN THE 4-S EXERCISE TEST

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To evaluate the relative influence of the two branches of the autonomic nervous system on the 4-s exercise test which measures heart rate acceleration at the onset of exercise, 6 healthy male subjects performed the 4-s test under sympathetic blockade with propranolol, parasympathetic blockade with atropine and dual blockade. The magnitude of the 4-s test results (means \pm SD) was significantly different only between the conditions with and without atropine (1.04 ± 0.03 vs 1.53 ± 0.33 , respectively), with no differences between the control (1.60 ± 0.25) and the test under sympathetic blockade (1.51 ± 0.33). These results support the conclusion that the 4-s exercise test is a specific method for the evaluation of parasympathetic activity.

Key words: atropine, exercise test, heart rate, parasympathetic system, propranolol.

The autonomic nervous system (ANS) plays an essential role in the maintenance of homeostasis in human beings and some important clinical features related to various physiological disorders have been attributed to ANS impairment (1-3).

Since there is no practical method for direct assessment of the autonomic fibers in humans, the procedures used to study the ANS consist of applying a known stimulus and quantifying a physiological variable observed at the effector organ of a certain autonomic reflex arch (4). Usually this approach is not capable of detecting isolated disorders of one of the branches of the ANS for the sympathetic and parasympathetic systems are both stimulated or released in parallel. The variable is the intensity of these changes (5). We have overcome this constraint by taking into account the fact that at the onset of dynamic exercise there exist different kinetics for vagal inhibition and sympathetic activation of the heart characterized by distinct latency times and time constants which are faster for vagal inhibition (6,7).

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The present study was carried out to determine the relative roles of the autonomic nervous system branches in the 4-s exercise test.

Six male volunteers aged 21 to 26 years gave informed written consent to participate in the study. All of them were submitted to clinical examination, including a resting electrocardiogram, and none reported use of medications. None of them presented any signs or symptoms compatible with cardiovascular or autonomic dysfunction. The volunteers were instructed not to smoke or exercise on the day of the experiment.

For the 4-s exercise test (8) the subjects were requested to pedal very fast for exactly 4 s, with no resistance set (unloaded cycling) on a cycle ergometer (Siemens, model 380B). The test was performed at maximal inspiratory apnea, beginning 4 s before and ending 4 s after the exercise. An electronic timer provided auditory and visual signals at 4-s intervals to increase the precision of the test performance.

Two R-R intervals in an ECG tracing obtained from a modified CC_5 bipolar lead were measured: B, the last R-R interval before the onset of exercise, and C, the shortest R-R interval during the 4-s effort. The B/C ratio is a dimensionless number that reflects heart parasympathetic activity. Two tests were executed in sequence, separated by an interval sufficient for the heart rate to return to control level.

The tests were performed in the afternoon on two different days, three hours after the last meal. On the first day, after performing a 4-s control test and waiting for 2 min, each subject received intravenously 0.04 mg/kg body weight atropine sulfate divided into four identical doses administered at 3-min intervals. Three min after the last dose, another 4-s test was executed. On the second day, the subjects first performed a control 4-s test. After a 2-min rest, they received *iv* 0.2 mg/kg body weight propranolol hydrochloride infused slowly over a 12-min period. The 4-s test was executed 5 min after the end of infusion. To obtain 4-s results under dual autonomic blockade, atropine sulfate was administered following the same protocol as used on the first day. According to Jose and Taylor (9), these doses of propranolol and atropine are sufficient to completely block the ANS.

The mean values of the B/C ratio in each of the five situations (C1, control 1; A, atropine; C2, control 2; P, propranolol; P+A, propranolol + atropine) were compared by analysis of variance and, when appropriate, by the least significant difference test for post-hoc analysis. We chose 5% of probability as the limit for statistical significance.

The values (means \pm SD) obtained for B/C on the two control occasions were quite similar, i.e., 1.53 ± 0.33 for C1 and 1.60 ± 0.25 for C2, both comparable to the test performed under sympathetic blockade ($P = 1.51 \pm 0.33$). In contrast, when atropine was used to block the parasympathetic system with or without propranolol, the results were very close to unity (A, 1.04 ± 0.03 , and P+A, 1.03 ± 0.01), i.e., the relative tachycardia observed during the first 4 s of dynamic exercise was almost fully abolished. The overall F ratio was 8.68 ($P < 0.05$) and the post-hoc test showed significant differences only between the tests with atropine and the other conditions, with no statistical significance among the conditions within each of these two groups (see Figure 1).

It is still a matter of controversy whether a reflex mediated by peripheral

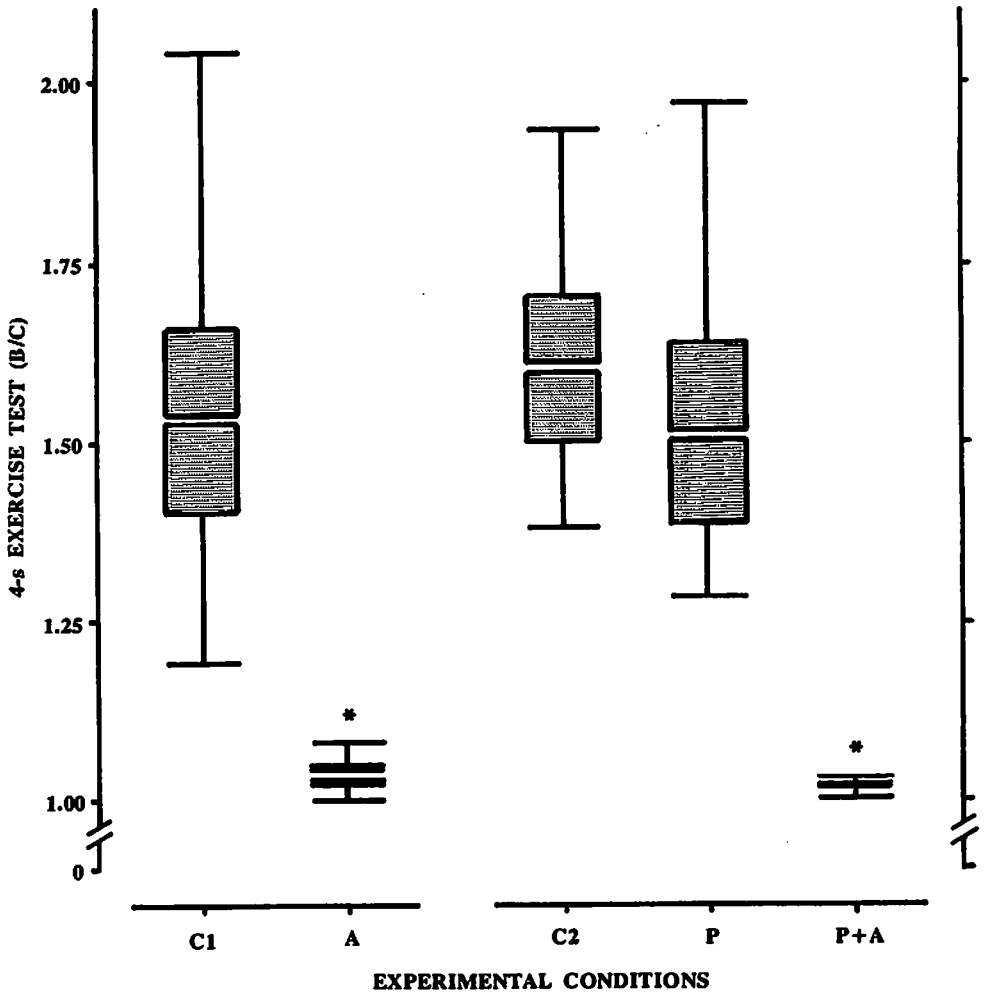


Figure 1 - Effect of autonomic blockade on the B/C ratio obtained during the 4-s exercise test. Data reported as means, SEM (boxes) and range (brackets) for 8 subjects tested under the five different conditions. C1, Control on the first day; A, atropine; C2, control on the second day; P, propranolol; P+A, propranolol plus atropine. * $P < 0.05$ (ANOVA).

somatoreceptors or a direct discharge from the motor cortex on the cardiac inhibition center is responsible for the heart rate acceleration response (10,11). Most of the research in the field, however, points to a so-called muscle-heart reflex, meaning that muscle receptors constitute the structure involved in the heart rate acceleration at the start of exercise (6,12). While the afferent path of this reflex remains to be elucidated, it has been established that the heart rate response is exclusively brought about by withdrawal of the predominant resting

vagal tone (13,14). Based on this premise, the 4-s test was proposed as a pure method to evaluate vagal activity. The present results support this idea.

An isolated study of the parasympathetic system is not only of physiological interest but also of clinical relevance. For instance, a negative correlation between vagal tone and sudden death in patients with diabetes (1), acute myocardial infarction (2), and AIDS (3) has been noted. Furthermore, no other simple test in the literature has been shown to be dependent only on vagal integrity (5). One could argue that an exception is the R-R interval variation measured during normal respiration patterns (15) or during respiratory efforts of 5-cycles/min (16). Nevertheless, the rationale is that during inspiration the vagal tone is decreased and sympathetic activity is increased, the opposite occurring during expiration (17,18). Thus, it seems correct to think that the respiratory sinusual arrhythmia mechanism is also dependent on sympathetic system function (19).

In conclusion, the present results clearly show that the 4-s exercise test response depends only on a vagal-mediated reflex and therefore can be used by physiologists and clinicians for evaluation of vagal tone.

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