Blunted Heart Rate Response to Upright Tilt in People With Down Syndrome

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ABSTRACT. Fernhall B, Figueroa A, Collier S, Baynard T, Giannopoulou I, Goulopoulou S. Blunted heart rate response to upright tilt in people with Down syndrome. Arch Phys Med Rehabil 2005;86:813-8.

Objectives: To determine whether heart rate and blood pressure responses to upright tilt would be lower in subjects with Down syndrome (DS) than in control subjects with no disabilities.

Design: Comparative study.

Setting: University research laboratory.

Participants: Nineteen people with DS (mean age, 25.1±7.3y) and 17 control subjects without disabilities (mean age, 28.4±5.6y).

Interventions: Not applicable.

Main Outcome Measures: Heart rate and blood pressure recordings were obtained at rest and during a 2-minute period of passive head up tilt to 80°.

Results: Heart rate and blood pressure increased significantly during the first 30 seconds of upright tilt in both groups ($P<.05$) and then stabilized for the remainder of the test. The initial heart rate response to head up tilt (first 30s) was significantly higher in controls compared with subjects with DS ($P<.05$), whereas the blood pressure response did not differ between groups ($P>.05$). Controlling for heart rate reserve showed a blunted heart rate response through the tilt period in subjects with DS.

Conclusions: These data show a blunted heart rate response to upright tilt in people with DS, despite similar changes in blood pressure, consistent with reduced sympathoexcitation and possibly altered baroreceptor function in these people with DS.

Key Words: Blood pressure; Down syndrome; Heart rate; Orthostasis; Rehabilitation.

PEOPLE WITH DOWN SYNDROME (DS) usually exhibit a number of physiologic perturbations of the cardiovascular system, even in the absence of congenital heart disease.[1-4] These perturbations include low levels of aerobic capacity, accompanied by low maximal heart rates, low resting blood pressures, and reduced heart rate and blood pressure responses to isometric exercise and cold pressor testing.[3-8] Recent studies of the heart rate response to exercise have established that people with DS exhibit chronotropic incompetence,[4,7,9] which is related to the reduced aerobic capacity in this subject population.[4,10] Furthermore, chronotropic incompetence is related to mortality and morbidity in nondisabled populations,[11] although the clinical outcome of chronotropic incompetence per se is unknown in populations with DS.

It has been suggested that chronotropic incompetence in people with DS is caused by cardiovascular autonomic dysfunction.[3,4,9,12] A recent study of blood pressure and heart rate responses to hand grip exercise and cold pressor testing showed reduced responses in persons with DS compared with controls with no disabilities,[12] which is consistent with altered cardiovascular autonomic function. These findings could be explained by reduced sympathetic responsiveness in persons with DS. Others have also found a reduction in sympathoactivation in response to exercise in this population.[2,13] Although the mechanism of the reduced sympathetic response is unknown, it is possible that altered baroreceptor control of heart rate could be involved.[12]

Orthostatic stress is an adrenergic stressor. The effect of adrenergic stress on the cardiovascular system depends on baroreceptor function[14] to maintain adequate blood pressure.[15,16] There are anecdotal reports of orthostatic hypotension in persons with DS,[1] which support the notion of reduced sympathoexcitation in this population, but few systematic investigations exist. Although the orthostatic index (heart rate response to standing) may be lower in people with DS,[17] no difference has been found in the heart rate and blood pressure responses of a sit-to-stand task between subjects with DS and control subjects.[18,19] However, these studies enrolled too few subjects to achieve adequate statistical power.

Passive head-up tilt is a standard test used to assess autonomic cardiovascular function.[16,20] A short 1- to 2-minute period of passive head-up tilt will yield valuable information about autonomic control of heart rate and blood pressure.[16] If the low blood pressure and heart rate responses to sympathetic stress in people with DS are indicators of cardiovascular autonomic dysfunction, then altered blood pressure and/or heart rate responses to passive head-up tilt would be expected. However, this has never been investigated in a population of DS subjects.

Therefore, the purpose of our study was to evaluate the blood pressure and heart rate responses to passive head-up tilt in subjects with DS without congenital heart disease and compare these responses with controls of similar age without disabilities. Based on previous studies, we hypothesized that subjects with DS would exhibit lower blood pressure and a blunted heart rate response to upright tilt compared with controls.

METHODS

Participants

Thirty-six healthy subjects (19 with DS, 17 controls without disabilities), aged 17 to 40 years, volunteered for the study. There were 9 men and 10 women in the group with DS and 8

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men and 9 women in the control group. Subjects in both groups were either sedentary or moderately active, but none were involved in any extensive exercise endurance training. Subjects with DS were recruited from local organizations and community support groups. Control subjects were recruited from the local and university communities. Based on medical history, all subjects were free from any overt disease, and for subjects with DS, only those classified with mild mental retardation were included.

Subjects were excluded from the study if they exhibited any form of cardiovascular disease including congenital heart disease, if they were smokers, if they were taking any heart rate– or blood pressure–altering medications, if they had any pulmonary disorders including asthma, if they had severe or profound mental retardation, or if they exhibited any contraindications to exercise. All subjects signed informed consent forms after listening to an explanation of the nature of study participation and initial eligibility screening. The parents and/or guardians of the subjects with DS also signed informed consent forms prior to participation. The study was approved by the university institutional review board.

Study Design

Subjects were familiarized with tests (treadmill exercise test, passive head-up tilt) before data collection. For subjects with DS, 1 or more familiarization sessions were conducted until each subject could satisfactorily perform each test. For both tests, all subjects were tested in a postprandial state, approximately 4 hours after their last meal. Subjects refrained from exercise 24 hours before testing and from caffeine ingestion on testing days. All subjects were tested on 2 different days, more than 1 but less than 21 days apart. The first day of testing consisted of a maximal exercise test on a motorized treadmill.[a] This test was used to confirm chronotropic incompetence in subjects with DS and whether subjects in the control group had a normal heart rate response to peak exercise. The head-up tilt was performed on the second day, after a 10- to 15-minute supine rest.

Protocol

Treadmill test. The treadmill protocol is both valid and reliable for maximal exercise testing of both people with DS and control subjects without disabilities.[3,10,12,21-23] The protocol was individualized to the capabilities of each person by using a comfortable walking speed for each subject. The initial stage consisted of comfortable walking for 3 minutes, followed by a 2-minute stage of fast walking. From this point, treadmill grade was increased by 2.5% every 2 minutes until 12.5% grade was reached, and thereafter the speed was increased by 26.8m/s every minute until exhaustion. Oxygen uptake ($\dot{V}O_2$) was measured by using an on-line breath-by-breath system[b] and the data were expressed in 20-second averages. The metabolic system was calibrated with a known gas and known volume of air before each test. Heart rate was measured by using a Polar heart rate monitor.[c] The test was terminated when the subject could no longer keep up with the treadmill speed and was considered a peak effort if VO_2 or heart rate plateaued with an increase in work rate, concomitant with a respiratory exchange ratio (RER) of greater than 1.0.

Tilt table testing. Subjects rested in a supine position on an electrically controlled tilt table[d] for 10 minutes before head-up tilt was initiated and were secured on the table with straps. Resting data were collected during the last 1 minute of the 10-minute period. Subjects were then tilted to 80° for 2 minutes. Heart rate and blood pressure data were collected in 30-second averages during the head-up tilt. Heart rate was collected by using a single electrocardiogram lead (CM5) interfaced with a computer.[e] Blood pressure was collected by using arterial tonometry[d] in 13 subjects with DS and 12 control subjects. This method uses a collar with several sensors applied around the wrist at the site of the radial artery. The collar is inflated until the artery is flattened and the pressure required to maintain the flattened region are measured, creating an arterial waveform similar to intra-arterial blood pressure measurements. For the remaining 6 subjects with DS and 5 control subjects, blood pressure was measured by using finger plethysmography.[f] For both measurement methods, the arm was kept at heart level during data collection. Because of problems with equipment availability, blood pressure was measured by using 2 different methods; however, both methods have been shown to exhibit similar validity compared with intra-arterial pressures.[24,25]

Table 1: Resting Characteristics and Exercise Responses of All Subjects

Variable	Subjects With DS	Controls
Age (y)	25.1±7.3	28.4±5.6
Height (m)	1.5±0.1	1.7±0.1*
Weight (kg)	81.4±19.9	71.9±12.2
BMI (kg/m^2)	34.7±8.4	24.3±3.9*
Vo_2peak (mL·kg^{-1}·min^{-1})	19.7±6.4	41.2±8.1*
HRpeak (beats/min)	159±16.8	188±8.2*
$V_E$peak (L/min)	59.5±18.1	114.4±25.6*
RERpeak	1.1±0.1	1.2±0.1*
HRR (beats/min)	88.3±15.9	125.0±9.9*

NOTE. Values are mean ± standard deviation (SD).
Abbreviations: BMI, body mass index; HRpeak, peak exercise heart rate; HRR, heart rate reserve; $V_E$peak, peak exercise ventilation.
*Subjects with DS differ from controls ($P<.05$).

Statistical Analyses

Means and standard deviations were calculated for each variable. Descriptive characteristics and treadmill exercise responses of the 2 groups were compared by using *t* tests. The heart rate and blood pressure responses to passive tilt were evaluated by comparing 30-second averages that started from rest to the end of the 2-minute tilt by using a 2×5 analysis of variance (ANOVA) with repeated measures (group DS vs non-DS) by time (rest, 30s, 60s, 90s, and 120s of tilt). Because resting heart rate and maximal heart rate differed between groups, the ANOVA was repeated by using resting heart rate and maximal heart rate as covariates. Because aerobic fitness can influence the cardiovascular responses to an orthostatic challenge, Vo_2peak was also covaried. Statistical significance was set at *P* less than .05 throughout.

RESULTS

Subjects' characteristics and peak exercise data are shown in table 1. Both groups were of similar age and body weight, but all other variables differed significantly between groups. The control group exhibited significantly higher Vo_2peak, peak heart rate, and heart rate reserve compared with the subjects with DS.

The heart rate response to passive tilt is shown in figure 1A. There was a statistically significant group by time interaction, indicating that subjects with DS exhibited a smaller change in heart rate during passive tilt. The change in heart rate between rest and the initial 30 seconds of passive tilt was significant for both groups, but the change in the control group was statisti-