Review Article

Exercise in Individuals with Down Syndrome: A Brief Review

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ABSTRACT

International Journal of Exercise Science 8(2): 192-201, 2015. Research examining acute and long-term responses to exercise of individuals with Downs Syndrome (DS) is sparse. However, if this group experiences benefits associated with improved quantity or quality of life, it would be important to elucidate specific responses and discourage adoption of a sedentary lifestyle in individuals with DS. Specifically, these individuals have multiple blunted physiological responses to exercise both at the onset and termination of an acute exercise bout. Mechanistically, this could be rooted in hormonal responses which are blunted, in comparison to non-DS participants. Specific studies indicate individuals with DS appear to experience benefits in such hormonal responses, in response to short term (~12 weeks) participation in exercise programs. Damage due to oxidative stress is greater in individuals with DS, as the gene for superoxide dismutase lies on chromosome 21. Current research suggests exercise training can also improve oxidative stress in this population. Although less well-understood, there is potential for improved motor learning in individuals with DS as a result of exercise participation. This paper provides a brief review discussing current research on how individuals with DS respond to exercise. Further, a link is made advocating that blunted acute responses may result in elevated perceptions regarding difficulty of exercise, which in turn contributes to increased likelihood of having a sedentary lifestyle. Adverse effects have not been identified, and with no theoretical arguments against exercise participation, it is concluded that adaptive exercise programs for individuals with DS should be implemented for improving health and quality of life.

KEY WORDS: Trisomy 21, disease, special population, children, disabilities, oxidative stress, sympathovagal imbalance, heart rate variability

INTRODUCTION

Down Syndrome (DS) is a genetic disorder linked with both physical and cognitive disabilities which is caused by a trisomy of chromosome 21. Individuals with DS are commonly physically inactive (19). As with non-DS individuals, this sedentary lifestyle is associated with multiple health consequences and ultimately increased healthcare costs. A mean cost of $4,287 is spent every year on healthcare in the United States for every individual with DS, with diabetes and heart disease being two of the top costs (5). With an estimated 250,000 individuals having DS, costs in the US could surpass $1,071,750,000. Being a preventable risk factor, sedentary lifestyle contributes to disease development and decreases quality of life. This has encouraged scientists to examine how exercise affects individuals with DS physiologically. This review will explore multiple plausible reasons why a physically

inactive lifestyle is prevalent in this population, which contributes to irregular catecholamine responses and blunted vagal withdrawal. An additional focus will be to examine research on physiological benefits of exercise in individuals with DS such as sympathovagal improvement, reduction of oxidative damage, and improved motor learning. In part, it is hoped that outlining the sparse nature of the literature while pointing out the potential exercise-associated benefits for individuals with DS will spawn an increased volume of scientific research in this under-represented population.

CONTRIBUTING FACTORS TO A SEDENTARY LIFESTYLE

The United States has developed a culture which facilitates inactivity. The country as a whole is experiencing an obesity epidemic. The technologically-advanced environment and easily available high-calorie, low-nutrition fast food has contributed to increased obesity and increased risk of associated life-threating diseases. Exposure of individuals with DS to this culture has made it easier for them to live an inactive lifestyle. However, while this presents healthcare challenges to all members of society, this is more problematic for individuals with DS. Physiological differences make exercise participation more difficult in this population. Thus, they may need extra encouragement to participate in a physically activity lifestyle. Living in a society that encourages a sedentary lifestyle has made these physiological differences more of a concern.

Individuals with DS are found to have lower aerobic capacities and maximal heart rates when compared to individuals in the general population, observations which emphasize and verify the low physical activity levels in this population (2). Fernhall et al. (2) suggests a potential genetically-related explanation for comparatively low aerobic capacities and maximal heart rates in this population is their irregular catecholamine response to exercise. Catecholamines are hormones produced by the adrenal glands. Two important catecholamines that play a key role in exercise are epinephrine and norepinephrine, also known as adrenaline and noradrenaline respectively. When a healthy, non-DS individual begins to exercise, the adrenal gland releases epinephrine and norepinephrine to increase heart rate to supply more oxygen-rich blood to active muscles. In Fernhall, et. al. (2), DS (n=20) and non-DS (n=21) participants completed a treadmill test from a very low workload to maximal exertion with epinephrine and norepinephrine concentrations measured before and after the test. Catecholamine measurements before the treadmill tests were similar between the groups; while post measurements indicated significant increases in the catecholamines in the non-DS group, only minute increases were noted in the DS group. The DS group showed no increase in epinephrine in response to the treadmill test and only a small, insignificant, increase in the norepinephrine (2). Catecholamines aid non-DS individuals in the ability of the heart meet the oxygen demands of the body while exercising. As intensity (and therefore oxygen demands) increase, these hormones prompt increases in heart rate which results in greater cardiac output and reflects greater oxygen-rich blood delivery to working muscle tissue. Conversely, an

attenuated catecholamine response may contribute to lower aerobic capacities and comparatively lower maximal heart rates in individuals with DS.

Another potential reason for reduced aerobic capacities and lower maximal heart rate is that individuals with DS have a sympathovagal imbalance. Sympathetic nervous system activity increases heart rate in response to exercise. Simultaneous withdrawal of parasympathetic nervous system activity at the initiation of exercise permits elevation of the heart rate, which is necessary for oxygen delivery in support of physical activity. In these individuals, though, the parasympathetic nervous system activity does not abate as in non-DS individuals (6). That is, individuals with DS tend to have blunted vagal withdrawal and reduced sympathoexcitation (6). Research indicates that the impaired vagal modulation and reduced sympathoexcitation are reasons for the initially low heart rate response at the beginning of exercise, but that the irregular catecholamine response alone is the reason for the low heart rate at intense levels of exercise (2). The blunted heart rate response to an exercise stimulus, regardless of the underlying mechanism, may be responsible for impaired aerobic fitness in individuals with DS. Further, dulled physiological responses which typically support physical activity would make exercise more challenging from a subjective standpoint for this population. A potential consequence of greater relative strain is adoption of more sedentary lifestyle due to the greater discomfort associated with physical activity. This assertion, while plausible, is speculative and current literature lacks direct evidence. Future research should investigate these possibilities to reach definitive conclusions and further the understanding of acute responses in this population.

PHYSIOLOGICAL BENEFITS

Exercise can provide individuals with DS with many physiological benefits. For example, adopting a more physically active lifestyle would help reduce the chance of these individuals acquiring chronic diseases such as heart disease, obesity, and diabetes (19). In Ulrich et al. (19) a group of children with DS were taught to ride a bike and compared to a control group of children with DS who were not taught to ride a bike. A year following the intervention the children taught to ride the bike had on average 6 percent less body fat than they had before the intervention and were more physically active than the control group. The reduction in body fat from engaging in physical activity can help decrease risk of lifestyle-associated diseases. Exercise can provide individuals with DS, not only with benefits common to non-DS individuals, but also with benefits unique to their population.

As mentioned above, individuals with DS have a sympathovagal imbalance. The balance between the two branches of the autonomic nervous system can be measured by heart rate variability (HRV) (6). HRV is the measure of the differences in the time intervals between heartbeats. It can be divided in to two components: high frequency (HF), which can be interpreted as vagal tone, and low frequency (LF). LF is still being studied as to what it fully represents. Sympathetic activity can be interpreted as low frequency to high frequency ratio (LF/HF) (4). Multiple studies have examined how the HVR of

individuals with DS is affected by regular exercise training over time; however, these studies only examined HRV at rest. In two of these studies examining HRV (3, 10), a group of individuals with DS participated in an exercise training program with both aerobic and resistance components for 12 weeks. HRV was measured before and after the program and compared to a control group of non-DS who did the exercise training as well. Both studies found similar results. Post training measures indicated an increase in HF and reduced LF/HF and found that their sympathovagal imbalance improved (3, 10). Giagkoudaki et al. conducted a similar study examining HRV in individuals with DS before and after a 6 month exercise training program which showed even greater increases in HF and greater reductions in LF/HF; implying that over time, exercise may result in benefits to some as yet unidentified ceiling (6). The post-training measures in the three previous described studies also indicated LF and HF components in the individuals with DS to be more similar to the non-DS controls (6). This normalization of values similar to that of controls can be interpreted as an improved sympathovagal balance in response to 12 weeks and 6 months of exercise; however, these studies only examined HRV at rest before and after the training period. There is a possibility that exercise training could improve aerobic capacities and maximal heart rate responses for individuals with DS by improving vagal withdrawal and sympathoexcitation, but this is not well-understood (3). As aerobic capacity and heart rate response are improved, systematic increases in exercise volume would result in individuals with DS finding that exercise becomes easier and perhaps increasing their increase voluntary participation in fitness activities.

Another indication that exercise training improves sympathovagal balance is the improvement of heart rate recovery (HRR) among individuals with DS. When compared to non-DS individuals, individuals with DS tend to have slower HRR, such as in the one to two minutes after exercise cessation (10). Just as individuals with DS have trouble increasing their heart rate when beginning an exercise bout, heart rate reduction at the termination of exercise, or HRR, is also problematic in this population. In non-DS individuals HRR follows a predictable pattern, as it returns to near pre-exercise levels shortly following exercise cessation. A more rapid reduction reflects a greater capacity of the cardiovascular system to restore the homeostasis disrupted by the exercise. Individuals with DS, though, tend to have an abnormally slow HRR, reflecting an impaired ability to restore homeostasis (10). This impairment may be linked with abnormal vagal reactivation and sympathetic withdrawal. Further research needs be conducted to more firmly determine the direct cause of impaired HRR in this population. The HRR in all individuals at one minute is thought to be due to vagal reactivation and at two minutes tends to be due to sympathetic withdrawal (10). In the same 12 week training study described earlier, the post-training HRR showed an improvement at one minute but not at two minutes (10). No improvement in HRR at two minutes may be explained by this populations' irregular catecholamine response. Because these individuals have a blunted catecholamine response, the rate of catecholamine removal will also be slow and thus contribute to a blunted sympathetic withdrawal, resulting in a slower than normal HRR (10). Therefore, the improvement in HRR at 1

minute may indicate that exercise training improves vagal reactivation and sympathovagal balance. Thus, this adaptation allows individuals with DS to return to their resting HR more quickly. Slow removal of catecholamines post exercise may disrupt the nervous system's influence, as seen in HRR at two minutes. The overall result is impairment in the heart rate response following exercise which mitigates the ability acute recovery from a bout of exercise in comparison to non-DS individuals.

OXIDATIVE DAMAGE

Oxidative damage, or oxidative stress, is cellular damage caused by free radicals derived from oxygen and tends to occur more often in the DS population (20). Oxidative stress contributes to many negative health problems such as atherosclerosis, Parkinson's disease, Alzheimer's disease, diabetes, autoimmune dysfunctions, neurodegeneration, and accelerated cell aging (12; 13; 14; 15). The greater risk of oxidative damage in individuals with DS can be attributed to an excess of super oxide dismutase (SOD). SOD is an enzyme that catalyzes the reaction of superoxide anion to hydrogen peroxide in the body, and which is coded genetically on chromosome 21 (13). The trisomy of chromosome 21, which causes DS, also causes an excess of SOD which in turn causes an excess of hydrogen peroxide, leading to greater oxidative damage relative to non-DS individuals (13). Exercise may aid individuals with DS in reducing oxidative damage. Three different studies examining different variables detailed below all concluded that aerobic training reduces oxidative damage in these individuals.

Ordonez et al. conducted two studies examining the effects of a 12 week aerobic training program on oxidative stress in individuals with DS by examining fasting blood samples before and after the program (13; 14). The first study analyzed glutathione peroxidase (GPX), an enzyme that helps convert hydrogen peroxide to water, a process which combats oxidative stress. Blood samples showed that after a 12 week training program of moderately intense aerobic exercise GPX activity significantly increased in individuals with DS, leading to less oxidative damage (13). Ordonez et al.'s next study (14) examined protein oxidation by analyzing the concentration of carboxyl groups in the blood sample before and after the 12 week training program. Protein oxidation can lead to the formation of carboxyl groups, which is an indicator of oxidative stress (14). This study also found that a 12 week training program of moderately intense aerobic exercise reduced protein oxidation in individuals with DS, which could be an indication of a decrease in oxidative stress (14). Rosety-Rodriguez et al. conducted a similar study examining fasting blood samples before and after a 12 week program. Samples were analyzed for allantoin, or oxidized uric acid, another indicator of oxidative stress (12). Again a 12 week training program of moderately intense aerobic exercise reduced allantoin (12). All three studies noted above also showed that while moderately intense exercise decreases oxidative damage, acute exhaustive exercise increased it (12; 13; 14). There is little information on how acute exhaustive exercise effects oxidative stress and the antioxidant defense system in individuals with DS due to their difficulties with exercise (14). However, based on current literature, exercise participation in

the appropriate context appears to offer benefits to these individuals with regard to oxidative stress. Future research should examine how exercise affects the natural elevation of other endogenous defenses against oxidative stress in individuals with DS and perhaps the associated disease development from a long term perspective.

Exercising provides multiple physiological benefits to individuals with DS. No negative effects from moderate exercising have been identified in any of the studies previously described (6). Therefore, prescribing exercise for this population has the potential to improve quality of life and reduce disease risk. No studies or currently available information suggests that moderate exercise participation is contraindicated for individuals with DS.

MOTOR LEARNING

In addition to having a lower aerobic capacity, individuals with DS tend to have weaker fine and gross motor skills, which may interfere with the ability to perform certain exercise tasks. Their movements are often described as "clumsy" or slow, compared to an individual without DS (9). Latash explains that when asked to complete a task as quickly as possible, individuals with DS have slower times pursuant to slower movement velocities than individuals without DS. These individuals tend to treat any gross movement as a sequence of individual tasks (8). This difference in motor coordination and movement may be attributable to individuals with DS possessing different neuromuscular activation patterns (8; 9). Some evidence suggests this difference may be linked to trisomy 21-based genetic changes to the cerebellum (9). However, when teaching motor tasks to individuals with DS, progressing from and building on simple tasks has shown to enhance form and coordination of motor tasks performance, which is often also the technique used when learning skill-based sport or exercise tasks (8). Because of their similar teaching styles, sport skills and exercising are potentially effective ways to help individuals with DS improve their motor skills. More work is certainly warranted to more definitively establish this link.

Little research has been conducted on the potential exercise-associated benefits to motor learning and development in individuals with DS. However, existing research shows improved memory and learning of motor skills (18). Kida et al. conducted a study involving a genetically modified mouse used to model DS, and found that after voluntarily running for 5 months the mouse's motor balance on a rotating rod apparatus improved (18). Continued successive testing on the mice showed further improvement in motor balance, implying that learning and memory of motor skills also improved (18). However, effects of running on motor learning in individuals with DS have only been observed in mice and no direct evidence on human participants currently exists.

Research has been conducted on the link between sport ability and improvement in motor learning in individuals with DS. Due to their popularity in the Special Olympics, swimming and gymnastics are two sports which have been studied. Chera-Ferrario (1) found similar results to Kida et al. (18) while observing children with DS in an adaptive swimming program. The group of

Table 1. Summary of studies regarding physical activity and individuals with Down syndrome.

Study	Central focus	Participants "n" and age	Principle Limitations	General conclusions
10. Mendonca, et al. (2013)	Effects of combined aerobic and resistance exercise on HRR and HRV in adults with and without DS	N=13 DS N= 12 non-DS Participants similar in age	Low participant number	12 wks moderate exercise improved HRR in participants with DS but not non-DS
14. Ordonez, et al (2012)	Influence of moderate intensity aerobic training on protein oxidation in adolescents w/DS	N=31 16.3±1.1 yrs old	No control group	12 wks aerobic training significantly reduced protein oxidation, expressed as carbonyl group content
19. Ulrich, et al. (2011)	PA benefits of learning to ride a two wheel bike for children with DS: a randomized trial	N=81 8-15 yrs old	Large dropout rate, no record of frequency or total volume of exercise per participant	Children with DS can learn to ride a bike. Moderate exercise can decrease body fat percentage.
6. Giagkoudaki, et al. (2010)	Effects of exercise on HRV indices in individuals with Down syndrome	N= 10 DS 24.5 ±5.1 yrs old N= 10 Non- DS 23.3± 4.6 yrs old	Low participant number, Non-DS group only tested once, lack of estimation of individuals DS VO2	Exercise training in individuals with DS will restore vagal modulation and improve sympathovagal to Non-DS levels
2. Fernhall et al. (2009)	Catecholamine response to maximal exercise in persons with DS	N=20 DS 24±7 yrs old N= 21 Non-DS 26±6 yrs old	Venous sampling reflects global systematic measurement rather than atrial catecholamine concentrations	Blunted catecholamine response is a major contributor to low per heart rates and low VO2s in individuals with DS

Abbrevaitions: PA = Physical Activity, DS = Down syndrome, HRR= Heart Rate Recovery, HRV= Heart Rate Variability

children was tested before and after the swimming program for speed, coordination, and their ability to bend the torso forward and bring an arm to the opposite leg. The test following the swimming program showed significant improvement in these motor skills in all participants.

Improvement in motor learning has also been seen in studies that used gymnastic as the exercise mode (11; 17). In Popescu et al. (17) observed a group of individuals with DS (n=12) during a14 week gymnast training program that required 3-6 days of training and then compared their performance to a group of (n=12) non-DS individuals. After 14 weeks the individuals

with DS were able to perform 8 gymnastic motor tasks to a level such that they demonstrated no statistically-significant differences when compared to the non-DS group (17). In the second study, Moraru et al. tested a group of individuals with DS (n=3) before and after an 8 month adaptive gymnastic program; the dependent variables included; speed completing 10 leg lifts, spine mobility, force of abdominal muscle contraction, and single leg balance. After the program all participants had significantly improved for all dependent measures (11). One limitation to both studies mentioned above is small sample size. Further studies are needed to definitively determine the potential for exercise and sports to improve motor learning and skill acquisition particularly in younger individuals with DS.

ACSM EXERCISE RECOMMENDATIONS

The ACSM exercise recommendation for individuals with DS are similar to the ACSM exercise recommendations for non-DS adults, but these recommendations take into account their lower aerobic capacity and unique physiological responses to exercise. The ACSM recommends an exercise expenditure of greater than 2000 kcal a week, achieved across 3 to 7 days a week through aerobic exercise, with at least 3 to 4 of these days consisting of moderate to intense exercise. Exercise intensity should be 40%-80% of VO2 reserve or HR reserve. The ACSM recommends that RPE should not be used with this population. Individuals with DS should exercise for 30 to 60 min a day by completing bouts of 10 to 15 min. Walking and gradually progressing to moderate intensity running, along with swimming are the recommended exercise modes for individuals with DS (16).

CONCLUSION

Individuals with DS have a lower exercise capacity, which is thought to be linked to abnormal catecholamine response and a sympathovagal imbalance. Exercise has been found to improve sympathovagal imbalance as well as improve heart rate recovery and reduce oxidative damage in individuals with DS. This evidence shows that exercise training can help ease the difficulties that individuals with DS experience when exercising and thus increase the chance that they will participate in physical activity which would have multiple positive influences on their health, including a reduction in risk of serious chronic diseases such as heart disease and cancer. More research should be conducted examining heart rate variability of individuals with DS during exercise to see how exercise training affects sympathovagal responses during exercise. More research is also needed to further observe the potential effect of acute and long-term exercise participation on memory and learning of motor skills in this population; which could help improve walking abnormalities that these individuals tend to develop when learning to walk. These benefits of exercise outlined in this review provide strong introductory evidence that moderate exercise programs should be considered and implemented to help improve the health of people with DS. The ACSM recommends daily aerobic exercise for individuals with DS, with a weekly exercise expenditure of at least 2000 kcal. Future investigations are needed which examine and attempt to identify the optimal volume and intensity of exercise

associated with benefits in individuals with DS. Such research has the potential to greatly enhance the quality of life in this population which has received minimal attention in research literature.

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