Original Article

The Effect Of A "Selected Exercise Training" On Reducing Symptoms Of Dementia Caused By Alzheimer's Disease in People with Down Syndrome

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Objective: The aim of the study was to determine the effect of a selected exercise training on reducing symptoms of dementia caused by Alzheimer's disease in people with Down syndrome.

Methods: 27 men with Down syndrome were randomized to intervention (n=13) and control (n=13) groups. All persons in experimental group followed 12 weeks selected exercise training, three times a week. Prior to the start of the study, and after three-month training, each member in both groups was assessed according to the DSQIID questionnaire filled by caregivers of these peoples. Data were analysed by independent T test.

Results: The results indicated that the first questionnaire subscales that assess memory disorders and confusion in the experimental group between pre and post test showed a significant decrease (P = 0.028). Also in third part of questionnaire that asked about the individual skills, social withdrawal, physical symptoms and speech abnormalities, the variable scores in post-test of experimental group were significantly lower than pre-test scores (P=0.047).

Conclusion: These result showed that the combination of selected exercises training could cause a significant reduction in the incidence of initial dementia symptoms and can be an important step to prevent of the dementia in these people.

Keywords: Selected Exercise training; Dementia; Down syndrome

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Introduction

Down syndrome (DS) is the most common human chromosomal abnormality that was first described one hundred and forty years ago (1). It is the most common genetic cause of intellectual disability and developmental delays (2-5). It occurs equally in all races with an overall incidence of approximately occurring in 1 out of every 700 to 1, 200 live births (3, 6-8). People with DS commonly experience mild to severe intellectual disabilities although the mean level of disability remains mild to moderate (9). Also there are a number of medical and health-related complications that are associated with the syndrome including congenital cardiac and respiratory problems (10, 11), Hypertension (12), low cardiovascular fitness (10), hypothyroidism (13), obesity (14,15), motor developmental problems (16-18), muscle hypotonicity (11,19-21), decreased muscle strength (11, 20-23), joint hypermobility (11, 20, 21, 24), balance and postural deficits, (24-28), nervous system disorders (29), Sensory Impairments (11), cognitive deficits (30,31) and some problems in processing, interpreting, and elaborating information (32), speech (33,34), eye-hand coordination, laterality, visual motor control and reaction time (35).

The brain of an individual with Down syndrome at or shortly before birth is in many respects

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indistinguishable from the brain of a normal individual (36). The learning and memory problems that begin to emerge in late infancy become considerably more noticeable as the infant grows to childhood and adolescence (4).

The most commonly neurological or psychiatric condition associated with aging in adults with DS is Alzheimer disease (5). Dementia of the Alzheimer type is more likely to develop in adults with DS, especially over the age of 30 or 40 years old, than in the general population or in other people with mental retardation (5, 11, 37-41).

Common symptoms associated with diagnosis of dementia in DS include memory loss and deterioration in speech, personality and behavioural changes, disorientation, and functional deterioration (42). Alzheimer's disease is characterised by neuropathological changes in the brain, including the deposition of extracellular β-amyloid in neuritic plaques and the formation of intracellular neurofibrillary tangles, which result the death of the neurons that contain them (43). Direct treatment of the dementia itself remains controversial in Down's syndrome (44). Stanton and Coetzee (2004) reported that the new addition of memantine (an N-methyl-D-aspartate receptor antagonist) for the treatment of moderate to severe Alzheimer's disease may be useful in care of Alzheimer's disease associated with Down's syndrome and initial data on elderly people show that memantine can bring benefits in activities of daily living and cognition (45).

It is well-known that during human ageing the cortex and hippocampus atrophy and this atrophy may be a risk factor for accelerated memory dysfunction (46, 47). These deleterious consequences of ageing might be attenuated by exercise (48). Several studies showed that physical activity has a positive impact on improving cognition and nervous system function and can cause structural changes that lead to the improvement of brain functions (48-55). Dik and colleagues (2003) found a positive correlation between physical activities at ages 15-25 and information processing speed in older (62-85 years) men (56). Cotman and colleagues (2007) assumed that common mechanism underlying the effects of exercise on brain function have focused on inflammation, which can impair growth factor signaling. Through regulation of growth factors and reduction of peripheral and central risk factors, exercise ensures successful brain function (57). Specific to the hippocampus, a brain area important for learning and memory is the robust increase in new neurons with exercise (58). The beneficial effects of some training, such as running, on cognition could be mediated by enhanced hippocampal neurogenesis (58). In conclusion various studies have shown that physical activity improves cognitive function and decrease likely to develop cognitive decline (48, 59, 60). But much more research is needed in this field, especially in the treatment and prevention of Alzheimer's disease in Down's syndrome (45).

Choosing the best training program for these people is very important. The effect of different types of strength (61-63), endurance (64) and aerobic (65) training for these people has been determined. Also several researchers have concluded that a combination of exercises in balance and strength (66-68), strength and aerobic (69, 70) and combined with plyometrics jumps training (71) are more beneficial for these individuals. Other researchers have shown positive effects of some special techniques such as riding and cycling (72,73). Also combining the functionality of physical therapy and the creative aspect of dance with music can stimulate and challenge Down syndrome individuals physically and cognitively which can improve their memory and increase physical fitness while allowing them to express their emotions (74). Therefore according to the results of the several researches in this case, can be concluded that combined training with the use of some special techniques is more useful for these people. The researchers of the present study intend to investigate the effect of Kashi practice (the combination of a variety of specific exercises for people with Down syndrome) on reducing the symptoms of dementia caused by Alzheimer's disease in adults with Down syndrome.

Method

Participants

This interventional research was accomplished in Nemoneh Disability Rehabilitation Centre of Tehran with the financial support of Islamic Azad University of Khodabandeh branch. The samples consisted of 28 individuals with Down syndrome. These individuals live in the above mentioned centre and mainly were non-families. It was obtained the authorization and the consent of the responsible of

this centre. This study examined men with Down syndrome. The inclusion criteria were: individuals with the age of more than 20 years, ability to understand simple instructions and ability to stand and walk independently. The exclusion criteria in experimental group were inability to attend in training sessions over two-thirds or over three sessions in a row. Out of the 34 men 28 met the study criteria in this centre. 28 men with Down syndrome (mean age 26.185± 3.933) were randomly assigned to either a control (n=14) or an experimental group (n=14). However, the data for one person were not used because he missed more than three intervention sessions in a row and as a result he did not participate in the study. All the conditions such as eating, physical activity, sleeping and participation in educational program were exactly the same in control and experimental group except experimental group participating in selected exercise training. Before intervention phase researchers collected some information derived from the hospital files regarding the IQ of each individual as it was measured in previous years by using the Stanford-Binet Test. Sample group were people with mild to moderate retardation. The Iranian professional code of ethics has been followed in this research. A full agreement letter for all participates were signed; it has been agreed that all the data should be kept in private and secure.

Instrument

For assessing the effect of selected exercise training to reduce symptoms of dementia we used the Dementia Screening Questionnaire for Individual with Intellectual Disability (DSQIID). Shoumitro (2008) reported that the DSQIID has high sensitivity and specificity in adults with Down's syndrome. Moreover it is a valid, reliable, user-friendly and an observer-rated questionnaire for screening dementia among adults with Down's syndrome (75). The DSQIID is an observer-rated questionnaire that is it completed by caregivers of people with Down's syndrome and who have known the individual for some time.

The DSQIID is divided into three parts by Shoumitro and colleagues (2007): Part 1 it tends to gain information about the highest capacity ever reached by the person in the study. Part 2 contains 43 questions about behaviour or symptoms that are usually associated with dementia in adults with Down's syndrome (76). These researchers revealed that a four-factor structure was most appropriate for the Part 2 of DSQIID. The first sub-scale includes 19 questions and is related to the memory/confusion. The second sub-scale includes 13 questions and is related to the feelings of insecurity. The third sub-scale includes 7 questions and is related to the sleep problems. The fourth sub-scale includes 5 questions and is related to the behaviour problems (76). Part 3 of the DSQIID contains 10 comparative questions where the response of 'yes' is scored 1 and 'no' is scored 0. According to Shoumitro and colleagues (2007) we carried out an analysis with four factors and we analysed part 3 of this questionnaire separately.

Prior to the start of the study, and after having completed a three-month training, each member of the research sample in both groups was assessed according to the DSQIID questionnaire filled by the careers who were working at the centre and they had responsibility for keeping/treating these people.

Procedure (selected exercise training)

The basic elements of all sport activities that should be entailed are cardiovascular exercise, strength training, balance, and flexibility (77, 78). Due to low levels of cardiovascular fitness, poor levels of muscular strength and balance and postural deficits of individuals with DS, our activity program focused mainly on these very important elements However, because of the hyper mobility and joint laxity that is common in DS, flexibility is not a recommended activity for this population (79). According to several studies mentioned above, researchers attempted to design a combined training program (Educational-Training Kashi Practices) for individuals with Down syndrome. The beneficial effect of Educational-Training Kashi Practices in improvement of cardiovascular function (80), balance (81) and muscle strength (82) has been proved. This training program consisted of five parts. Balance training, strength and power training, muscular endurance and aerobic training, the psycho- motor skills training and other exercises such as the use of vibration machines, local dances and games (table 1). This selected training program begins with Fundamental Movement Abilities and is to be completed with specialized movement abilities.

Table1. Selected exercise training (Educational-Training Kashi Package) for Down syndrome adults

selective exercise training for Down Syndrome adults				
Balance training	strength and power training	muscular endurance and aerobic training	psycho- motor skills training	Other training
1- Static balance training 2- walking and running on the line 3- walking and running on the balance beam 4-axial movements 5-hopping 6- cycling	1-exercises with the rehabilitation and medicine ball 2- weight training 3- Calisthenics 4-plyometrics training 5- jumping	1-walking 2-roping 3-running 4-stepping training 5- cycling	1-throwing, catching, kicking and striking eight models of balls 2-galloping, skipping, sliding and leaping 3-targeting 4- implementation of group dancing 5-football and basketball penalty, 6-Football and basketball dribbling 7-volleyball setting	1-use of vibration machines 2-games with rules 3- local dance

Training duration was 50 minutes for initial session and this time rose to 150 minutes in the final weeks. The practice continued for three sessions per week for three months based on a recent study that had reported significant improvements in individual with Down syndrome following a 10-12-week special training (66, 83-86). Considering the usefulness of this type of training, Kashi practices were planned for 12 weeks and led by 14 trainers and assistants (a trainer/assistant per each participant).The intensity of the program rises gradually from light to difficult. Incorporated motivational techniques were used to improve adherence of participants. We have followed the Lotan guidelines on quality physical intervention activity for persons with Down syndrome (2007) to determine the intensity of exercises (79).

Statistical Analysis

All analyses were performed by SPSS 16.0 and the significance level was set at 0.05. Furthermore, all analyses were also executed on the intervention and control groups separately. Descriptive statistics were calculated for all the variables. Group differences were evaluated using t test for dependent samples.

Results

The age of the 27 adults with DS included in this study ranged from 21 to 38 years with an average age of 26.185 ± 3.932 years. These patients living in a care centre for disabled people. They were randomly divided into an experimental and a control group. Experimental group contained 13 patients with a mean age of 25.538 ± 2.436 years and 14 patients participated in the control group with a mean age of 26.785 ± 4.964 years. Analysis of results showed that 2 participants (4.7 %) had problems with vision, 1 person (3.7%) had problems with hearing and 23 (85.18%) persons were treated with psychological and behavioural problems. Their caregivers reported that 2 persons (7.4%) could speak fluently and understandably, 7 persons (25.9%) could make short sentences, 8 persons (29.6%) could speak only a few words and 11 persons (37%) could not speak much but were able to use sign language. The caregivers! also reported that 8 persons (29.6%) of them could live independently with minor help, 6 persons (21.8%) could live independently but needed a lot of help with self-help skills, 8 persons (29.6.8%) could not live independently and needed minor help with self-help skills and 5 persons (18.5) could not live independently and needed a lot of help with self-help skills.

Table 2. Caregivers responses in the second part of questionnaire

questions	Pre test		Post test	
	exp	con	exp	con
Cannot wash and/or bathe without help	0	2	0	1
Cannot dress without help	0	0	0	0
Dresses inappropriately	0	0	0	1
Undresses inappropriately	0	1	0	0

questions	Pre test		Post test	
	exp	con	exp	con
Needs help eating	0	2	0	0
Needs help using the bathroom	0	1	0	0
Incontinent (including occasional accidents)	1	1	1	1
Does not initiate conversation	2	3	1	0
Cannot find words	0	0	3	0
Cannot follow simple instructions	2	0	2	3
Cannot follow more than one instruction at a time	2	1	4	1
Stops in the middle of a task	2	1	2	1
Cannot read	0	0	0	0
Cannot write (including printing own name)	0	0	0	0
Changed sleep pattern	2	0	2	1
Wakes frequently at night	1	0	1	1
Confused at night	0	1	0	0
Sleeps during the day	3	0	3	2
Wanders at night	1	0	1	1
Cannot find way in familiar surroundings	0	3	0	1
Wanders	2	0	2	2
Loses track of time	2	1	5	0
Not confident walking over small cracks	0	1	0	0
Unsteady walk, loses balance	2	0	2	0
Cannot walk unaided	0	2	0	0
Cannot recognize familiar person	0	0	0	0
Cannot remember names of familiar persons	0	0	0	0
Cannot remember recent events	1	3	1	1
Withdraws from social activities	0	2	2	7
Withdraws from persons	2	3	2	7
Loss of interest in hobbies and activities	2	2	2	4
Seems to go into own world	2	3	2	6
Obsessive or repetitive behaviour	2	0	2	0
Hides or hoards objects	0	0	0	0
Loses objects	1	0	1	0
Puts familiar things into wrong places	0	0	0	0
Does not know what to do with familiar objects	0	0	0	0
Appears insecure	1	0	1	2
Appears anxious or nervous	3	6	4	2
Appears depressed	5	7	7	5
Shows aggression	3	4	4	3
Fits/ Epilepsy	0	3	0	1
Talks to self	0	0	0	3

Table 2 shows the responses of caregivers from the second part of the questionnaire. Changes in the experimental group scores that reported by caregivers on this questionnaire has been shown by the seven questions (9, 11, 22, 29, 39, 40 and 41) of the second part. The post-test scores of the second part were lower than pre-test scores in the experimental group. These questions in order were to find appropriate words for conversation (reduction in 3 patients), follow-up of more than one instruction at a time (reduction in 2 patients), the ability to track of time (reduction in 3 patients), withdraws from social activities (reduction in 2 patients), appears anxious or nervous (reduction in 1 patient), appears depressed (reduction in 2 patients) and shows aggression verbal or physical (reduction in 1 patient). Questions 9, 11 and 22 were from first sub-scale, questions 29, 39 and 40 were from second sub-scale and question 41 was from forth sub-scales.

Table 3. Caregivers responses in the third part of questionnaire

questions	Pre test		Post test	
	exp	con	exp	con
Lost some skills (e.g. Brushing teeth)	5	4	6	3
Speaks (or signs) less	0	1	0	0
Seems generally more tired	1	1	2	1
Appears tearful, gets more easily upset	0	0	0	0
Appears generally slower	3	6	3	6
Slower speech	0	1	0	1
Appears more lazy	2	3	4	3
Walks slower	1	3	4	3
Generally appears more forgetful	1	2	1	2
Generally appears more confused	0	1	0	1

In the third section of the questionnaire, that includes 10 questions (table 3), we observed changes in case of 4 questions as compared to the experimental group. These questions asked about the loss of skills (reduction in 1 patient), seem generally more tired (reduction in 1 patient), appear more lazy (reduction in 2 patients) and walks slower (reduced in 3 patients).

Table 4. Comparison of the overall score of DSQIID between pre and posttest in experimental and control group

	Pre test		Post test		dependent t test			
	mean	Std.	mean	Std.	Mean difference	t	df	sig
experimental	6.000	1.776	4.231	1.511	1.769	3.057	12	0.004
control	5.500	0.740	5.428	0.837	0.071	0.201	13	0.844

Table 4 compared total score of questionnaires between pre and post-test in experimental and control group separately. The data presented in this table makes clear that the Kashi practices could cause a significant reduction in the incidence of dementia symptoms in experimental group (P=0.004). Because it is clear that the overall score of the questionnaire in this population reduced from 6.000 to 4.231. But in control group this score in pre-test is 5.500 and in post-test is 5.428 and has not showed a significant change (P=0.844).

Table 5. Comparison of subscales of DSQIID between pre and posttest in experimental and control groups

		Pre test		Post test		dependent t test			
		mean	Std.	mean	Std.	Mean difference	t	df	sig
Memory/	control	1.357	0.386	1.143	0.329	0.214	0.715	13	0.487
confusion	experimental	1.539	0.447	0.000	0.277	0.538	2.501	12	0.028
Feelings of	control	2.000	0.555	2.143	0.404	-0.143	-0. 396	13	0.699
insecurity	experimental	1.692	0.559	1.385	0.560	0.307	1.477	12	0.165
Sleep	control	0.429	0.202	0.357	0.199	0.071	0.322	13	0.752
problems	experimental	0.692	0.398	0.385	0.310	0.308	1.760	12	0.104
Behaviour	control	0.214	0.113	0.286	0.125	-0.071	-0.434	13	0.671
problems	experimental	0.539	0.216	0.461	0.215	0.076	1.000	12	0.337
loss of skills, social	control	1.429	0.272	1.571	0.272	-0.143	-0.472	13	0.165
withdrawal	experimental	1.539	0.526	1.000	0.392	0.538	2.214	12	0.047

Table 5 compares the four subscale scores and the third section of this questionnaire between pre and post-test in experimental and control groups. The information presented in this table revealed that only two of the five comparisons made in this table show significant differences. First subscale assessing memory disorders and confusion that in the experimental group between pre and post-test is significant difference (P=0.028). And test scores in post test showed significant decrease compared with pre-test scores. But in this subscale we can't find significant changed in the control group (P=0.0487). The second significant compression in the table 3 is the third part of questionnaire. It includes 10 questions and asked about the individual skills, social withdrawal, physical symptoms and speech

abnormalities. The data presented in this table indicate that the variable scores in post-test of experimental group were significantly lower than in the pre-test scores (P=0.047) and this change is not significant in the control group (P=0.165).

Discussion

According to the data presented in this study it is clear that the combination of specific exercises (Kashi practices) could cause a significant reduction in the first signs of dementia in the experimental group (P=0.004). Since the overall score of the questionnaire in the experimental group reduced from 6.000 to 4.231. In the experimental group 10 of 13 patients had at least one sign of dementia. Another very important result was that in 8 of 10 patients, dementia symptoms decreased after three months training, although reduce symptoms were not observed in two patients. No meaningful changes were observed in the control group. The pre-test score of control group was 5.500 and this score in post-test reached 5.430, in other words these changes were not significant (P = 0.844). This result shows that the changes were only significant in the experimental group and in reducing symptoms of dementia. It can be concluded that this significant decrease in score of the experimental group was in response to the selected exercise training. Thus implementing our training could have a significant effect in reducing symptoms of dementia.

Several researchers have used sequential cognitive assessments to track the changes that occur with the development of dementia in adults with DS. Memory change appears to be an early symptom in DS and is present before the persons meet the full clinical criteria for dementia. Cognitive decline associated with early and middle stage dementia involved progressively more areas of cognitive functioning, starting with complex cognitive functions, followed by visual organization as well as verbal memory before affecting semantic and short term memory (42). Shoumitro et al. (2007) made a qualitative summary of caregiver's reports of early symptoms. Forgetfulness and confusion were the most prominent symptoms but many 'frontal lobe'-related symptoms that are usually manifest later in the course of dementia among the general population, were also common. These included slowness in activities and speech, loss of interest and withdrawal, along with the emergence of emotional and behaviour problems (76).

Many studies have shown the impact of physical activity on improving cognitive and nervous system function (48, 59, 60). According to neuronal group selection theory, the cortical and subcortical networks within the brain are dynamically organized, and it is hypothesized that the neural networks and connections are established and/or strengthened by afferent information produced via behaviour and motor experience (54, 55). The brain produces new neurons in the olfactory bulb and dentate gyrus of the hippocampus throughout life. Increasing evidence indicates that this process has a very importance role in learning and memory. The new cells are preferentially activated during learning tasks (49). Researcher found that an increase in neurogenesis is associated with improved cognition and the strongest neurogenesis stimulus is exercise (63). Kronenberg and colleagues (2006) showed that the onset of the effect of running on cell genesis is rapid. Cell genesis peaks at three days. After 32 days of running the pro-proliferative effect has returned to baseline but the number of immature neurons continues to increase at this time-point (50). Moreover, in mice that started running exercise in middle age new neuron number was elevated (51). Physical activity also accelerates the maturation of dendritic spines in new born neurons (52) and regulates hippocampal neurogenesis, synaptic plasticity, and learning (53). This change in synaptic plasticity seems to be specific for the dentate gyrus, indicating that neurogenesis might be important (63). Thus, an exercise- increase in highly plastic cells in the dentate gyrus might explain, in part, the profound effect of physical activity on memory function (49).

In this research analysis of results showed that from five comparative analyses (four sub-scales in the second part and the scores of third section of this questionnaire) only two comparisons show significant differences. The first questionnaire subscales that assess memory disorders and confusion and includes 18 questions (known as the most important indicators for measuring dementia) in the experimental group between pre and post-test shows a significant change (P=0.028). It means that our training has led to significant decreases in the incidence of dementia symptoms in memory disorders and confusion in experimental group. However in this subscale we cannot find significant changes in the control group (P=0.0487). So we can conclude that these changes in the experimental group scores were caused by the selected exercise training. Based on previous research, we found that combined exercise training includes strength, aerobic, balance and endurance training can be useful for patients with Down syndrome

(66, 67, 68-70). The results of this study show that combined exercise training with the use of various useful techniques by Kashi practices can reduce initially symptoms of dementia in adults with Down syndrome. These training primarily improved memory and confusion. These two factors are the first signs of dementia in Down syndrome peoples. Therefore it can be concluded that this type of training could successfully be preventive from early signs of dementia.

The second significant comparison in this study is the third part of questionnaire. It includes 10 questions and provides information about the individual skills, social withdrawal, physical symptoms and speech abnormalities. Analysis of results showed that the variable scores in post-test of experimental group were significantly lower than pre-test scores (P=0.047) and this change is not significant in the control group (P= 0.165). So we can conclude that these changes in the experimental group scores were caused by selected exercise training. Another important factor in improving people's physical and mental health has improved in fitness. What that after training in the experimental group caused changed in questionnaire scores were increase in physical activity which caregivers who responded negatively to questions such as: Seems generally more tired, appears generally slower, Appears lazier, lost some skills and the result of post-test decreased in compare with pre-test. Results of several studies on people with Down syndrome have shown that these individuals are less active physically than other people (11, 18, 55, and 64). One reason for this problem is failure in brain development and muscle hypotonia during early development and makes these individuals different from early childhood with other children (18). It is clear that the physical activities improve health and relieve some of the medical problems of Down syndrome peoples, and also improves musculoskeletal system Status (87). In recent years for the treatment of these patients, physicians only have used medication practices. A few researchers effort to identify ways for prevents dementia. Whereas established that early identification and treatment of Alzheimer disease could reverse the functional decline frequently associated with these disorders (88). Given the high rates of early-onset age-related this disorders among adults with Down syndrome, programmatic screening, monitoring, and preventive interventions are required to limit secondary disabilities and premature mortality. Gonzalez-Aguero et al. (2010) mentioned that many of the training programs carried out in children and adolescents with DS did not yield the desired responses, and more research is needed to clarify the issue (89).

Conclusion

Recent researches demonstrated that this type of training could successfully be preventive from early signs of dementia. It is clear that physical activity enhances body composition, skeletal health, and several aspects of psychological, psychological and neurological health including in Down's syndrome peoples. Exercise programs appear to have potential to positively affect the overall health of adults with DS, thereby increasing the quality of life and years of healthy life for these individuals. This research showed that physical activities can be helpful in reducing symptoms of dementia in adults with Down syndrome.

As a conclusion it can be affirmed that all these changes shown in our research had positive impact on reducing symptoms of dementia and improving general health in people with Down syndrome. Major challenge to reach these changes was the establishment of the correct training plan. Since, to choose a correct training program has the main role in the design of rehabilitation exercises.

Therefore trainers, parents and caregivers should take great care to select appropriate training for these people.

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Declaration of interest

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