

Upper Limb Training with Dynamic Arm Support in Boys with Duchenne Muscular Dystrophy: A Feasibility Study

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Abstract

Patients with Duchenne Muscular Dystrophy (DMD) develop progressive loss of arm function. Regular moderate-intensity activities are recommended to prevent disuse atrophy, but conventional resistance exercises are often too strenuous. We conducted a feasibility study to investigate the feasibility and safety of upper limb training with dynamic arm support. Eight boys with DMD who were unable to lift their arms against gravity (age 12-20 years) performed reaching movements with their non-dominant arm for 24 weeks. Participants played a virtual reality computer game and performed activities of daily living while using dynamic arm support. The dominant (untrained) arm of each participant served as a reference. Six of the eight participants completed the entire training program without any adverse events. The trained arm retained more motor function than the untrained arm in 4/6 participants. The findings indicate that boys with DMD can safely train their arms with dynamic arm support.

Keywords: Upper limb; Muscular dystrophy; Rehabilitation

Abbreviations

ADL: Activities of Daily Living; ARAT: Action Research Arm Test; DAS: Dynamic Arm Support; DMD: Duchenne Muscular Dystrophy; Jebsen Test: Jebsen Taylor Hand Function Test; MFM D3: Motor Function Measure Dimension 3 Distal Motor Function; NMD: Neuromuscular Disorder; 9HPT: Nine-Hole Peg Test

Introduction

Duchenne muscular dystrophy (DMD) is the most common childhood neuromuscular disorder (NMD), affecting 4.78 in 100,000 live male births [1]. DMD is caused by a loss of the dystrophin protein, which causes progressive muscle fibrosis, loss of muscle strength and loss of muscle function [2]. Although there is currently no cure, improved symptomatic treatments have increased the mean life expectancy of patients with DMD to the early thirties [3]. As a result of this increased life expectancy, there is now a growing population of older, wheelchair-dependent patients with severely impaired arm function and associated limitations in activities of daily living (ADLs) such as grooming and dressing.

The decline in arm function in patients with DMD is primarily a result of the disease; wasting of the shoulder muscles causes an inability to lift the arms by the age of 13-15 years [4]. This inability to lift the arms limits the patients to reaching forward and sideward only. This decline in arm function can also be accelerated by environmental and behavioral factors. For example, using an electric wheelchair with a top blade and central operating joystick allows the patient to

function within the confines of the wheelchair only. This can cause a discrepancy between the patient's true capacity and their performance (i.e., disuse), which can reduce the level of physical activity for the upper limb and reduce arm function even further. The negative consequence of disuse is underscored by the increasing difference in strength and motor function between the dominant and non-dominant hands over time-specifically, the non-dominant hand is used less and becomes less useful than the dominant hand [5,6]. From this point of view, the adage "use it or lose it" clearly applies to patients with DMD.

The current international guidelines regarding physical activity for DMD patients recommend regular gentle, functional activity in order to avoid secondary complications due to physical inactivity [7]. However, these recommendations are based on only a limited amount of evidence. Although three non-controlled trials found that low-resistance exercises were safe for ambulatory boys with DMD, these exercises had only a limited positive effect on muscle strength and function [8-10]. Another limitation of resistance exercises is that they are often impractical for wheelchair-dependent boys, as even the lowest resistance level can be too heavy to sustain or can rapidly exhaust their weak muscles [11]. Finally, strenuous high-resistance exercises and eccentric exercises can cause myofibrillar disruption in patients with DMD [12].

A recent randomized controlled trial found that assisted bicycle training is both feasible and safe for ambulatory and recently wheelchair-dependent patients with DMD [13]. Moreover, this training program prevented 6.3% of the functional deterioration that occurred without this intervention. In this study, boys trained their legs and arms using a mobility trainer with electrical motor support. Although assisted training provides training opportunities to patients

with DMD who have been confined to a wheelchair for several years, arm cranking may not be possible for patients who cannot lift their arms. We hypothesized that training with dynamic arm support (DAS) may be a viable solution for these patients. DAS provides horizontal and vertical external mechanical support for weak muscles via non-powered (e.g., counterweights) or powered components and increases the active range of motion for joints [14].

The aim of this study was to investigate whether DAS-assisted upper limb training is feasible and safe for wheelchair-dependent patients with DMD who are unable to lift their arms against gravity. We expected that patients would be able to practice reaching movements, which have high priority in patients with a neuromuscular disorder [15], with a DAS without causing harm. Because no previously published study has used DAS to train upper limb function in patients with DMD, and because the safety is a concern with exercise in DMD patients, we elected to perform a feasibility study with a multiple N=1 design. The goal of this study was to determine whether this type of assisted training is safe and can help patients with DMD. In addition, we measured-albeit to a limited extent-the effect of DAS-assisted upper limb training on motor function.

Methods

Design

This study was a feasibility study with a multiple N=1 design. Each participant acted as his own internal control (i.e., the participant's untrained arm served as the reference for the trained arm). A detailed description of the study protocol has been published previously [16]. The study was approved by the regional Medical Ethics Committee. The participants and/or legal guardians provided written informed consent. The study was registered with the Netherlands Trial Register (trial number 1631).

Participants

Wheelchair-dependent boys with DMD who were unable to touch the top of their head with at least one hand but were still able to use their hands for tabletop activities such as writing were eligible for this study. At the start of recruitment, an estimated 120 boys with DMD within the Netherlands were in this stage of the disease. Boys were excluded if they were unable to touch their nose while using the DAS, as this movement was required for several daily activities, including feeding, which was part of the intervention. In addition, boys who had previously used DAS were excluded. Boys were recruited from the Dutch Duchenne Parent Project database. Recruitment started 1 January, 2009 and ended 31 December 2009.

Procedure

After an eight-week period (T0-T2; Figure 1) in which baseline information was collected regarding the stability of the patient's disease course, each participant was provided with a powered or non-powered DAS device (Dynamic Arm Support Top/Help, non-powered or powered versions, Focal Meditech BV, Tilburg, the Netherlands) for their non-dominant arm. At baseline (T2), the participants began a 24-week training program for their non-dominant arm using DAS. Participants performed forward and sideward reaching movements by playing a computer game and by performing regular daily activities such as eating. For this study, we chose to train the non-dominant

arm, as this arm is often used less than the dominant arm in daily activities and thus may experience more disuse than the dominant arm; thus, we expected any potential training effects to be more pronounced. Efficacy was assessed after 12 weeks (T3) and at the primary endpoint of 24 weeks of training (T4). A final follow-up assessment was performed 12 weeks after the end of the training (T5). For the complete timeline of the study (Figure 1).

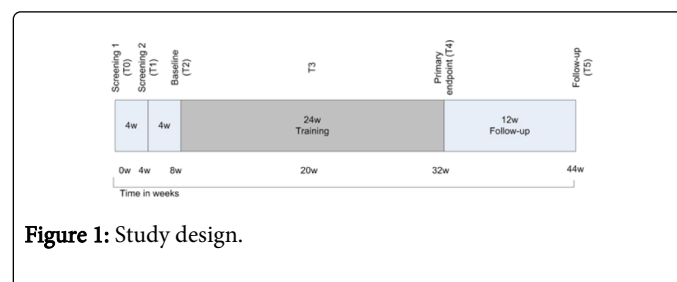


Figure 1: Study design.

Dynamic Arm support (DAS)

The DAS Top/Help device has originally been developed to be an assistive device. It has a weight-bearing construction mounted beneath the user's arm (Figure 2). The device aims to provide an active range of motion-assisting movements in the horizontal and vertical planes. The "Top" part of the DAS device consists of an axis with several rotation points, a forearm fitting, and a connection to the wheelchair. The "Help" part of the DAS device uses a mechanical spring mechanism (mechanical arm support) or an electric actuator (electric arm support) to facilitate vertical displacements. Participants who were unable to touch their nose with the help of a mechanical arm support received an electric arm support.

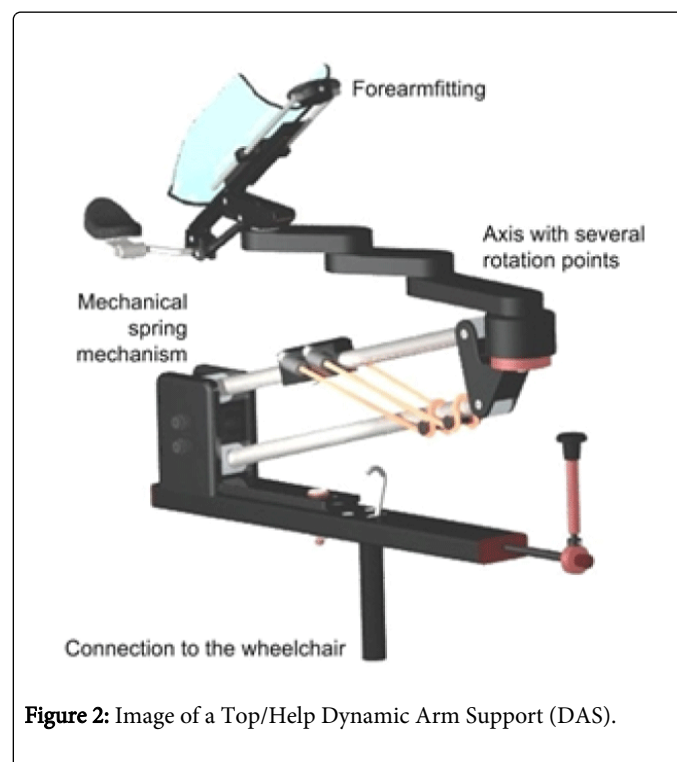


Figure 2: Image of a Top/Help Dynamic Arm Support (DAS).

Computer-assisted training

The participants practiced DAS-assisted forward and sideward reaching movements five days per week by playing the virtual-reality computer game “FurballHunt”¹ without becoming overexerted (as assessed using the OMNI scale). FurballHunt is controlled by motion capture technology using a webcam to detect gross arm movements [17].

Functional training

The participants were also instructed to eat at least two meals per week while using the DAS device. In addition, they were instructed to use DAS as much as possible while performing daily activities that involved reaching movements of the arms (for example, turning on the lights).

Feasibility and safety assessments

We monitored whether participants were able to complete the entire training program in accordance with the protocol, without any signs of overexertion. This was assessed via a questionnaire completed once every two weeks and home visits by the primary investigator (MJ) after 2 and 12 weeks of training. The participants recorded their training sessions in a journal and kept written records of the primary activities that they performed with the DAS device. The questionnaire regarding overexertion focused on excessive muscle pain, a feeling of severe discomfort, and exhaustion (OMNI score >6) [18].

Outcome measures on effectiveness

All assessments were performed by the primary investigator (MJ) either at the hospital (for assessments in T2 and T4) or at the participant’s home (for the other assessments). Both the dominant (untrained) and non-dominant (trained) arms were assessed. The non-dominant arm was assessed without DAS; in addition, to gain information regarding the benefits of training with the device, the non-dominant arm was assisted with DAS at baseline (T2).

The primary outcome was the Action Research Arm Test (ARAT), a standardized tool for assessing arm motor function and capacity in stroke patients [19,20]. At the time of the study, no validated arm motor function test for assessing boys with DMD was available. We calculated the total ARAT score (range 0-57) as well as the score of subscale D (gross arm movements, range 0-9), with a higher score indicating better function. An adjustable-height table is needed to properly administer the test execution, and because such a table was usually not available in the participant’s home, the total ARAT was measured at T0, T2 and T4.

The secondary outcome measures were Dimension 3 (distal motor function) of the Motor Function Measure (MFM D3) to assess motor function [21], the Nine-Hole Peg Test (9HPT) to assess finger dexterity [22], and the Jebsen Taylor Hand Function Test (referred to here as the Jebsen Test) to assess hand function [23]; these measures were collected at T2 and T4. Although the 9HPT and Jebsen Test assess primarily hand function, both tests force participants to lift and/or reach with their arms. At the end of the training period (T4), the participants also received a questionnaire designed to collect information regarding their DAS training experiences.

Statistical analysis

This was a feasibility study with a multiple N=1 design; therefore, the feasibility, safety and effectiveness of the DAS training program are described separately for each participant. The effectiveness of training was measured by calculating the change in the untrained and trained arms from T2 to T4; assessment T2 was chosen as our baseline value because T2 was closest to the time in which the participants received their DAS device and began training. In addition, the immediate effectiveness of using the DAS was assessed by comparing the results of the non-dominant arm without and with DAS at baseline (T2).

Results

Participants

Thirteen boys were initially assessed for eligibility. Five were excluded because they were unable to touch their nose even with the use of DAS. Thus, eight boys (age 12-20 years, with wheelchair dependence for 3-10 years) were first assessed for their baseline parameters and then provided with a DAS, after which they began training. The participants’ score on the Brooke scale [24] ranged from 3 (cannot raise hands above the head, but can raise an 8-ounce glass of water to the mouth) to 5 (able to use the hands for some daily activities only). A full overview of the participants’ characteristics is presented in Table 1.

| ID | Age (years) | Years wheelchair - dependent | Cortico-steroids | Brooke (range 0-6) | DAS | Compliance |
|----|-------------|------------------------------|------------------|--------------------|------------|-------------|
| 1 | 12.1 | 3 | Yes | 3 | Mechanical | 5x p/w |
| 2 | 15.4 | 5 | Yes | 5 | Electrical | 4x p/w |
| 3 | 12.1 | 4 | No | 4 | Electrical | Inadequate* |
| 4 | 20.0 | 7 | No | 5 | Electrical | 3x p/w |
| 5 | 14.1 | 3.5 | Yes | 3 | Mechanical | 4x p/w |
| 6 | 15.9 | 7 | Yes | 3 | Electrical | 3x p/w |
| 7 | 18.9 | 10 | No | 5 | Electrical | Inadequate† |
| 8 | 15.0 | 4 | Yes | 3 | Electrical | Inadequate‡ |

*Social support was limited, and the computer broke during the study.
 †Unexpected trip for 3 months; lost to follow-up.
 ‡New wheelchair without DAS; lost to follow-up.
 DAS, Dynamic Arm Support; p/w, per week

Table 1: Characteristics of the participants (N=8).

Effectiveness of the dynamic arm support (DAS)

All eight participants were provided with a DAS device for their non-dominant (left) arm. Six participants received an electrical arm support, and two participants (who had only been fully wheelchair-dependent for 3 to 3.5 years) received a mechanical arm support (Table 1).

¹ “Furballhunt is developed by Roessingh Research and Development.

At baseline (T2), when using the DAS, the total ARAT score increased by 11-17 points for four of the eight participants, whereas the total ARAT score was either unchanged or decreased by up to 14 points for the other four participants. We found that the configuration of the ARAT testing board interfered with the use of the DAS device. This effect was most pronounced for the participants who scored relatively high (>20) without using the DAS. With respect to subscale D, this score increased by 1-4 points for six of the eight participants. The score decreased by 2 points for the eighth participant; this participant was unable to touch the top of his head with DAS, although he was able to touch the top of his head without DAS. Thus, the DAS device hindered this movement for this participant. The scores for all eight participants are summarized in Table 2.

| | ARAT | Scal e D (range 0-57) | MFM , D3 (%) | 9HPT (sec) | Jebs en (sec) | J1 | J2 | J3 | J4 | J5 | J6 |
|-------------|------|-----------------------|--------------|------------|---------------|-------|-------|------|------|------|------|
| ID 1 | | | | | | | | | | | |
| Without DAS | 19 | 3 | 66.7 | 28.7 | ND | ND | ND | ND | ND | ND | ND |
| With DAS | 31 | 7 | 71.4 | 32.1 | ND | ND | ND | ND | ND | ND | ND |
| Difference | 12 | 4 | 4.8 | 3.3 | NA | NA | NA | NA | NA | NA | NA |
| ID 2 | | | | | | | | | | | |
| Without DAS | 9 | 3 | 66.7 | 49.1 | 8.4 | U | U | 6.8 | 13.2 | U | U |
| With DAS | 20 | 4 | 66.7 | 49.8 | 21.6 | 28.7 | 67.0 | 6.2 | 12.2 | U | U |
| Difference | 11 | 1 | 0 | 0.7 | 13.2 | NA | NA | -0.6 | -1.0 | NA | NA |
| ID 3 | | | | | | | | | | | |
| Without DAS | 24 | 3 | 71.4 | 40.6 | 13.6 | 20.2 | 41.3 | 7.5 | 5.3 | 9.0 | 9.0 |
| With DAS | 23 | 4 | 76.2 | 32.0 | 23.6 | 18.6 | 44.2 | 6.7 | 10.9 | 15.1 | 15.1 |
| Difference | -1 | 1 | 4.8 | -8.6 | 10.0 | -1.7 | 2.9 | -0.8 | 5.6 | 6.2 | 6.2 |
| ID 4 | | | | | | | | | | | |
| Without DAS | 21 | 4 | 66.7 | 83.0 | 42.6 | 54.6 | 37.9 | 7.8 | 26.7 | 39.8 | 39.8 |
| With DAS | 21 | 5 | 61.9 | 47.6 | 22.7 | 21.8 | 24.3 | 6.3 | 23.5 | 33.5 | 33.5 |
| Difference | 0 | 1 | -4.8 | 35.4 | -19.9 | -32.9 | -13.7 | -1.4 | -3.3 | -6.3 | -6.3 |
| ID 5 | | | | | | | | | | | |
| Without DAS | 54 | 7 | 66.7 | 21.8 | 5.7 | 8.2 | 24.3 | 3.8 | 4.9 | 8.3 | 8.3 |
| With DAS | 40 | 5 | 76.2 | 25.1 | 7.3 | 9.2 | 24.4 | 6.9 | 4.4 | 7.5 | 7.5 |
| Difference | -14 | -2 | 9.5 | 3.2 | 1.6 | 1.0 | 0.1 | 3.1 | -0.6 | -0.8 | -0.8 |
| ID 6 | | | | | | | | | | | |

| | | | | | | | | | | | |
|-------------|----|---|------|------|------|------|------|-----|------|------|------|
| Without DAS | 20 | 4 | 66.7 | 35.6 | 8.4 | 15.8 | 47.0 | 4.5 | 8.4 | 20.0 | 20.0 |
| With DAS | 19 | 4 | 76.2 | 41.7 | 14.2 | 14.5 | U | 5.2 | 6.7 | 6.7 | 6.7 |
| Difference | -1 | 0 | 9.5 | 6.0 | 5.8 | -1.3 | NA | 0.7 | -1.7 | -1.3 | -1.3 |
| ID 7 | | | | | | | | | | | |
| Without DAS | 2 | 0 | 57.1 | 164 | U | U | 79.0 | U | U | U | U |
| With DAS | 19 | 3 | 62.0 | ND | ND | ND | ND | ND | ND | ND | ND |
| Difference | 17 | 3 | 4.8 | NA | NA | NA | NA | NA | NA | NA | NA |
| ID 8 | | | | | | | | | | | |
| Without DAS | 8 | 0 | 62.0 | 41.3 | 8.5 | 28.5 | 35.4 | 4.1 | 5.5 | 8.7 | 8.7 |
| With DAS | 19 | 4 | 66.7 | 36.3 | 19.7 | 23.9 | 80.0 | 5.3 | 11.7 | 16.6 | 16.6 |
| Difference | 11 | 4 | 4.7 | -5.0 | 11.1 | -4.6 | 54.6 | 1.2 | 6.2 | 7.9 | 7.9 |

Table 2: Function test scores with and without dynamic arm support at baseline (T2). The immediate effectiveness of the DAS is described separately for each participant (ID 1-8). Efficacy parameters are the ARAT, MFM D3, 9HPT and the Jebsen test. Differences are individual results of the non-dominant (trained) arm with DAS minus those of the same arm without DAS at baseline (T2). For the ARAT and MFM D3, a positive difference indicates an improved motor function by using the DAS. A negative difference on the 9HPT and Jebsen tests indicates a decreased time necessary to perform the task by using the DAS. DAS: Dynamic arm support; ARAT: Action Research Arm Test; MFM: Motor Function Measure; 9HPT: Nine-Hole Peg Test; Jebsen: Jebsen Taylor Hand Function Test; J1: Turning cards; J2: Small objects; J3: Feeding; J4: Stacking; J5: Light objects; J6: Heavy objects; ND: Not determined; U: Unable to perform; NA: Not applicable.

Similar to changes in the ARAT scores, the baseline (T2) MFM D3 and 9HPT scores were also improved with DAS (Table 2). On the other hand, the Jebsen Test scores did not improve with the DAS (with the exception of one item-the time required to pick up and drop small common objects) (Table 2). As occurred when performing the ARAT, the Jebsen Test board interfered with the DAS device, and maximum elbow extension was restricted by the mechanical construction of the device. This effect was most pronounced for the items that required reaching movements (for example, turning cards and moving objects).

Feasibility and safety of the DAS-assisted training program

Of the eight participants who began training, two did not complete the program; one boy had an unexpected three-month stay abroad, and the other boy obtained a new wheelchair (without the DAS installed). The remaining six participants finished the training program and practiced computer-assisted training 3-5 times per week. One boy had fewer training sessions because his computer broke, and he was unable to play during the first eight weeks. In addition to the computer-assisted training sessions, use of the DAS ranged from seldom to 2 hours a day for the following activities: eating and drinking (7/8 participants), horizontal and vertical reaching activities such as turning on the computer or a light (1 participant), and using a pin-card (1 participant). The use of DAS by the participants is summarized in Table 1.

No signs of serious overexertion were reported by the participants. One participant reported pain in his shoulder during the training; he

reported that his shoulder was painful when he reached forward and moved his arm above 90° of ante flexion. When we adjusted this participant's training program (the participant was instructed not to raise his arm above shoulder height), the pain disappeared and he completed the training program.

Effects of the DAS-assisted training program

Of the six participants who completed the program, four had a larger decrease in ARAT score in the untrained arm compared to the

trained arm; for the other two participants, the untrained arm scores decreased slightly less than the trained arm after 24 weeks of training (T4). This more pronounced decrease in the untrained arm was particularly pronounced for the participant who was still able to raise a glass to his mouth at baseline; similar results were obtained for subscale D of the ARAT for this participant. The remaining five participants had no differences between their trained and untrained arm with respect to subscale D at T3 or T4. These scores are summarized in Table 3.

| | ARAT | | MFM, D3 (%) | 9HPT (sec) | Jebsonm(sec) | | | | | |
|-----------|-------|---------|-------------|------------|--------------|---------|---------|-------|-------|---------|
| | Total | Scale D | | | J1 | J2 | J3 | J4 | J5 | J6 |
| ID 1 | | | | | | | | | | |
| Trained | 6 | 1 | 4.8 | 5.6 | ND T2 | ND T2 | ND T2 | ND T2 | ND T2 | ND T2 |
| Untrained | -16 | -4 | -4.8 | 2.4 | ND T4 | ND T4 | ND T4 | ND T4 | ND T4 | ND T4 |
| ID 2 | | | | | | | | | | |
| Trained | -2 | -2 | 0 | 0.4 | U T4 | U T2/T4 | U T2/T4 | -1.8 | U T4 | U T2/T4 |
| Untrained | -4 | -2 | -9.5 | -17.0 | 2.5 | 10.3 | U T2/T4 | -1.7 | -2.3 | U T2/T4 |
| ID 3 | | | | | | | | | | |
| Trained | -13 | -2 | 0 | -7.2 | -3.3 | 0.8 | U T4 | -1.7 | 5.4 | 2.3 |
| Untrained | -21 | -2 | -4.8 | 1.1 | -0.7 | U T4 | U T4 | -3.3 | 1.3 | 2.0 |
| ID 4 | | | | | | | | | | |
| Trained | 0 | 0 | 0 | -8.0 | 19.9 | -21.6 | U T4 | -0.7 | U T4 | U T4 |
| Untrained | -9 | 0 | 0 | -4 | -4.9 | U T4 | U T4 | -2.6 | U T4 | -10.7 |
| ID 5 | | | | | | | | | | |
| Trained | -14 | -1 | 4.8 | -4.8 | -0.6 | -1.7 | -7.5 | -2.0 | -0.4 | -2.8 |
| Untrained | -8 | -1 | 0 | -10 | 0.8 | -4.0 | -1.9 | -4.4 | -1.6 | -1.1 |
| ID 6 | | | | | | | | | | |
| Trained | -2 | 0 | 0 | -4.1 | -0.6 | -0.5 | 9.5 | 0.8 | 0.6 | U T4 |
| Untrained | 2 | 0 | -4.8 | 14.4 | -4.8 | 1.3 | U T4 | 0.8 | -5.1 | U T4 |

Table 3: Effects of 24 weeks of training with dynamic arm support (N=6). Data are individual differences in scores between T2 (start of training) and T4 (primary endpoint) for the trained and untrained arms. ARAT: Action Research Arm Test; MFM: Motor Function Measure; 9HPT: Nine-Hole Peg Test; Jebson: Jebson Taylor Hand Function Test; J1: Turning cards; J2: Small objects; J3: Feeding; J4: Stacking; J5: Light objects; J6: Heavy objects; ND: Not determined at the indicated assessment(s); U: Unable to perform at the indicated assessment(s).

With respect to the secondary outcomes, none of the participants had a decrease in MFM D3 score for the trained arm after 24 weeks of training (T4). For the untrained arm, however, four participants had a decrease in MFM D3 score (the change in score for these four participants ranged from -4.8 to -9.5%); the other two participants had no change. The 9HPT score decreased for the trained arm for two participants and decreased for the untrained arm for three participants. Finally, the Jebson Test revealed no notable differences between the trained and untrained arms, with the exception of the

item in which the participants had to pick up and drop small common objects-at T4, two participants lost the ability to pick up the objects with their untrained arm, although they retained the ability with their trained arm. The secondary outcomes are summarized in Table 3.

Follow-up 12 weeks after the end of the training

Of the six participants who completed the training program, five participants were followed until 12 weeks after the end of the training program (T5), and two of the participants had continued to use the DAS device, but without specific training. The sixth participant was lost to follow-up due to a scoliosis surgery. Twelve weeks after training, Dimension 3 of the ARAT had not decreased for any of the participants for either the trained or untrained arm. Similar results were obtained for the MFM D3 and 9HPT tests at T5. The follow-up data are summarized in Table 4.

Participants' experiences

The participants reported that they found DAS useful for the following activities and movements: lifting their arm, scratching their face, moving their arm beyond the tray of the wheelchair, and feeding themselves. However, the DAS limited their ability to reaching down and to open a door. In addition, eating with a fork or spoon was challenging, as the DAS device did not allow the full range of supination movements. Sitting at a table while using the DAS device was also problematic because of interference between the device and the table. Nevertheless, six of the eight participants requested to keep the DAS at the end of the study; these six participants were the patients who were unable to lift their arms against gravity without DAS and had received electrical support. Although all of the participants liked the computer-assisted training at the start of the training, none of the participants found the game attractive after 24 weeks of training.

| Test/ ID | ARAT | | MFM, (%) | D3 | 9HPT (sec) |
|-------------|-------|---------|-------------|----|---------------|
| | Total | Scale D | | | |
| ID 1 | | | | | |
| Trained | ND | 0 | 0 | | -3.1 |
| Untrained | ND | 0 | 4.8 | | -4.2 |
| ID 2 | | | | | |
| Trained | ND | 0 | -9.5 | | 11.5 |
| Untrained | ND | 0 | 4.8 | | 20.6 |
| ID 3 | | | | | |
| Trained | ND | 0 | 0 | | 12.1 |
| Untrained | ND | 0 | 9.5 | | -2.1 |
| ID 4 | | | | | |
| Trained | ND | M | 0 | | -13.0 |
| Untrained | ND | 0 | -4.8 | | 3.0 |
| ID 5 | | | | | |
| Trained | ND | 0 | 4.7 | | 4.8 |
| Untrained | ND | 0 | 0 | | 6.0 |
| ID 6 | | | | | |
| Trained | ND | M | M | | M |
| Untrained | ND | M | M | | M |

Table 4: Follow-up after the end of the training. Data are individual changes between T4 (primary endpoint) and T5 (follow-up) for the trained and the untrained arm. ARAT: Action Research Arm Test; MFM: Motor Function Measure; 9HPT: Nine-Hole Pegtest; M: Missing; ND: Not determined (assessment was conducted at home).

Case narratives

ID 1: Participant 1 was a 12-year-old boy who had been fully wheelchair-dependent for three years at the start of the study. He was still able to raise a glass of water to his mouth, and he was provided with a mechanical DAS device. The DAS increased his arm and hand motor function as assessed with the ARAT, MFM and 9HPT tests. He

completed the entire training program with good compliance (i.e., he performed the computer-assisted training an average of 4-5 times per week). He reported that the DAS device hindered his ability to reaching the table surface because of interference between the device and the table. Opening a door and reaching down were difficult as well because his arm fell out of the forearm support. Nevertheless, he ate once a week with DAS, and he reported that scratching his face and lifting objects (such as a glass) were easier with DAS. After 24 weeks of training, his ARAT and MFM D3 scores were either unchanged or increased; in contrast, the scores for his untrained arm had decreased considerably, particularly with respect to the ARAT.

ID 2: Participant 2 was 15-year-old boy who had been confined to an electric wheelchair for five years at the start of the study. This patient only had function remaining in his hands and was provided with an electric DAS device. The device increased his gross arm movements as assessed with the ARAT, and it allowed him to complete the feeding and lifting small objects tasks of the Jebsen Test (which were not possible without support). He completed the training program and performed the computer game four times per week. In addition, he ate once every two weeks with his DAS, but reported that it was difficult to eat with his non-dominant hand (the trained arm). After 24 weeks of training, his MFM D3 score decreased for the untrained arm, but not the trained arm. At the end of the study, the participant requested to keep the DAS device to use for his dominant arm, but he did not wish to continue using the computer game.

ID 3: Participant 3 was a 12-year-old boy who had been fully wheelchair-dependent for four years at the start of the study. He was able to raise his hand-but not a glass-to his mouth. He was provided with an electric arm support, which increased his hand function as assessed with the MFM and 9HPT, but hindered his gross arm movements. Thus, the DAS device interfered with the board required to perform the ARAT and 9HPT tests. In addition, the DAS limited his elbow extension (which was needed to perform the reaching tasks of the Jebsen Test), thereby increased the time needed to complete the tasks. The participant completed the training program, but with moderate compliance during the first eight weeks of training due to technical problems with his computer. Nevertheless, he ate once a week with the DAS-which was difficult for him-with his non-dominant (trained) hand. The participant lost the ability to perform the feeding and lifting small objects tasks of the Jebsen Test with his untrained arm, whereas he was still able to complete these tasks test with his trained arm.

ID 4: Participant 4 was a 20-year old male (the oldest participant) who had been wheelchair-dependent for seven years at the start of the study. He was unable to bring his hands to his mouth. The DAS helped him lift his hand, which was reflected in the decreased time needed to perform the Jebsen Test tasks "Turning cards", "Feeding", and "Small objects". The participant used the DAS approximately two hours per day for eating, drinking, and other reaching and lifting activities such as turning on the light. We found no clear differences in arm function between the trained and untrained arms after 24 weeks of training; however, his scores were already low at baseline.

ID 5: Participant 5 was a 15-year-old boy who had been wheelchair-dependent for 3.5 years at the start of the study. He was still able to lift a glass to his mouth. He was provided with a mechanical arm support, which limited his gross arm movements. In fact, his own compensatory movements were more helpful in terms of performing the clinical assessments than the DAS device. The participant performed the computer-assisted training an average of four times per

week, but he rarely used the DAS to perform functional activities. After 24 weeks of training, there were no clear differences between his trained and untrained arms with respect to change in arm function.

ID 6: Participant 6 was nearly 16 years of age at the start of the study. Although he was still able to lift a glass to his mouth, this effort exhausted him, and he was provided with an electric arm support. Although the DAS device hindered his gross arm movements, the device made eating easier, and he used the DAS device every day for eating. Furthermore, he performed the computer-assisted training with DAS approximately three times per week. After 24 weeks of training, he lost the ability to perform the feeding task of the Jebsen Test with his untrained arm, whereas he was still able to perform this task with his trained arm.

ID 7: Participant 7 was an 18-year-old boy who had been confined to a wheelchair for ten years at the start of the study. He had useful hand function, but he was unable to lift his hand to his mouth. He was provided with an electric arm support that was on a moveable frame, as the corridor in his house was too small to enable him to maneuver his wheelchair when the device was attached. The DAS increased his arm function considerable as assessed with the ARAT. The participant did not complete the training program, and he was lost to follow-up because he went on an unexpected trip for three months.

ID 8: Participant 8 was a 15-year-old boy who had been fully wheelchair-dependent for four years at the start of the study. He was able to lift his hand-but not a glass-to his mouth. He was provided with an electric DAS, which increased his gross arm movements. However, he did not use the device for daily activities primarily because the participant did not want to use the DAS at school (he feared that his peers would think it was not "cool"). He did not complete the training program because halfway through the study, he received a new wheelchair that was not equipped with a DAS device (i.e., we would have needed to transfer to the old wheelchair to use the DAS). Surprisingly, the participant requested to keep the DAS at the end of the study, stating that the device allowed him to use an Automated Teller Machine (ATM).

Discussion

This feasibility study revealed that patients with DMD who have impaired arm function can safely participate in assisted training. Thus, patients who are unable to lift their arms against gravity are able to practice reaching forward and sideward movements by playing a virtual reality computer game while using a DAS device. Furthermore, we found indications that assisted training may slow the loss of arm motor functions. Because delaying loss of motor function is important to boys with DMD who wish to maintain their activities of daily living (ADLs), our findings indicate that upper limb training with assistance warrants further research.

The Top/Help DAS device was moderately effective for our training purposes; DAS increased gross arm motor functions (such as the ability to lift the hand to the mouth) in seven out of eight participants and allowed the participants to train without the help of a physiotherapist. This finding is in agreement with previous studies that reported that several ADLs can be improved with DAS [25,26]. The only participant who had a decrease in gross arm motor function after using the DAS was still able to lift a glass to his mouth without the device. The DAS prevented him from placing his hand on his head, an action that he could perform using his own compensatory strategies (i.e., without DAS). This is similar to previous reports that also showed

that stronger children prefer their own compensatory strategies to overcome their limitation [14,27]. In addition, hand function-which is associated with muscle strength and range of motion [28] did not improve using DAS, with the exception of the task in which the participant was required to pick up and drop small objects. This lack of improved hand function is in contrast to previous findings [14], which can be explained by that fact that the DAS device interfered with the equipment required for the hand function test. In addition, some hand functions (such as picking up beans with a spoon) were difficult to perform with the DAS, as the participants found it difficult to stabilize their hand with the device. Finally, the DAS prevented full elbow extension and supination, which are needed to perform the reaching tasks.

The assisted training program was determined to be feasible for six of the eight participants. Two of the participants did not complete the entire training program for practical reasons. The remaining six participants completed the training with moderate compliance (they performed the computer-assisted training 3-5 times per week). Only two of the participants were fully compliant with the functional training program and ate at least one meal twice a week with the DAS device. The other participants used the DAS less frequently, primarily because they found it difficult to use their non-dominant (i.e., the trained) arm to perform ADLs. In addition, the participants who were still able to lift a glass to their mouth without DAS preferred to use their own compensatory strategies, which is similar to previous reports. Compliance might be improved by providing more stimulating computer games and/or by providing a DAS that assists the arm through its entire range of motion. Future clinical trials on functional arm training should also consider to train the dominant arm rather than the non-dominant arm, since it is often not appropriate to train this arm.

Four of the six participants who completed the program had more deterioration of arm motor functions for the untrained arm than for the trained arm as assessed with the ARAT. In addition, none of the participants showed a decline on the distal motor function dimension of the MFM with the trained arm, whereas the untrained arm deteriorated in four participants and remained stable in the other two participants. Previous studies using gentle resistance exercises in DMD patients also found no disease acceleration due to training [8-10], but they reported limited benefits. However, a recent study found that assisted bicycle training for the legs and arms delayed the secondary functional deterioration that can occur due to disuse among ambulatory and recently wheelchair-dependent boys [13]. We hypothesize that training may be less beneficial to older patients, who typically have less remaining muscle mass [29]. Therefore, patients should ideally begin training early in the course of the disease.

Because this was the first study of upper limb training with DAS in patients with DMD, we performed a feasibility study with a multiple N=1 design. Our study had a relatively small sample size (eight patients), and we did not compare our results with a control group. The external validity of our study is therefore limited, and the results should be interpreted with caution [30]. However, boys with DMD show substantial phenotypic variability, and a feasibility study with a multiple N=1 design could be appropriate for this purpose [31]. Larger, controlled trials are needed to expand these results and to further address the question of whether training with DAS can delay loss of arm motor function. These trials should include validated outcome measures of gross arm motor functions that are responsive to small changes over time. The primary outcome measure in our study

(ARAT scores) was not completely compatible with the DAS device used, as the testing kit required for performing the tasks interfered with the device. This forced participants to use an unnatural movement pattern to perform the test when using the DAS. The MFM, a secondary outcome, was compatible with the DAS device, although this test has only a limited number of items for investigating shoulder movements [21]. No other suitable outcome measures of gross arm movements in DMD patients were available at the start of this study [32]. The recently developed Performance of the Upper Limb (PUL) can be useful to evaluate arm function in future clinical trials, since this tool assesses proximal as well as distal arm motor functions [33].

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