The influence of visual and tactile perception on hand control in children with Duchenne muscular dystrophy

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Duchenne muscular dystrophy (DMD) is the most common and severe neuromuscular disease and the second most prevalent genetic disorder in children. Dystrophin synthesis impairment causes progressive and irreversible muscular weakness, leading to loss of ambulation by adolescence. New treatment approaches have enhanced the survival of individuals with DMD to the third decade of life. This has increased the need to identify functional outcomes in DMD in order to evaluate the efficacy of existing therapeutic interventions.

As a result of the proximal-to-distal progression of muscular weakness, upper limb assessment is possible in almost all patients and may represent an important functional outcome at different stages of the disease. However, as has been described in the past few years, reach and grasp control can also be affected by altered brain function.

Morphological and functional changes in sensorimotor areas of the cerebral cortex seem to be related to diminished manual dexterity in children with DMD. In addition, reductions in glucose metabolism in the post-central gyrus and cerebellum have also been reported in these patients. The hypometabolism in these brain regions may interfere with the integration of somatosensory inputs, particularly the tactile afferent inputs of the hands, which are required for adjusting prehension force, velocity, and dexterity. Color vision impairment or other visual problems, caused by lack of dystrophin in the retina and decreased visual-spatial attention, could also have an influence on visuomotor coordination. It seems plausible to hypothesize, therefore, that motor skills in males with DMD may be influenced by both motor impairment and/or the sensory loss of visual and somatic systems.

To our knowledge, the possible influence of tactile perception and visual feedback in manual dexterity has not been previously investigated in DMD. In this study, therefore, we investigated tactile perception and manual dexterity with and without visual feedback in males with DMD. The outcomes of this study may contribute to the planning of specific rehabilitation approaches and assessment tools in order to improve upper limb function in males with DMD.
**METHOD**

**Participants**

Forty males aged between 5 and 14 years (mean age 9y 8mo, SD 2y 3mo; 35 were right-handed), diagnosed with DMD by genetic tests and other clinical features of the disease, including elevated serum levels of creatine phosphokinase and a myopathic pattern on muscular biopsy, were recruited from the teaching hospital of the School of Medicine of the University of São Paulo. The comparison group was composed of 49 healthy males aged between 5 years and 11 years (mean 8y 2mo, SD 1y 11mo), with typical motor development, who were recruited from the Meninó Jesus Socio-Educational Center, São Paulo, Brazil. The eligibility criteria for the group of males with DMD were the ability to walk (stages ‘1’ to ‘6’ according to Vignos’ classification), to actively move their upper limbs were the ability to walk (stages ‘1’ to ‘6’ according to Vignos’ classification), and the absence of any other neurological or musculoskeletal disorder. All children were enrolled in school at the appropriate level for their age. Data of children who exhibited difficulties in either understanding or cooperating during the tests were excluded from the study.

The present study was approved by the ethics committee for analysis of research projects of the School of Medicine of the University of São Paulo (Protocol no. 0377/09). The parents or legal representatives of the children gave written informed consent allowing their child to participate in the study.

**Procedures**

From August 2009 to September 2010 the participants were individually assessed sitting in a comfortable position close to a table. The height of the chair and table were adjusted such that their feet could touch the floor and their hands rested on the table. The hand used to write and draw was considered the dominant hand.

Tactile perception was evaluated using the two-point discrimination and stereognosis tests.

The two-point discrimination test was employed to evaluate the minimal distance necessary for the participant to distinguish between two tactile punctual stimuli applied simultaneously to the skin. The body regions tested included the index fingertip, the tip of the thumb, and the centre of the palm (determined by the intersection of two lines, one from the third finger to the medial border of the thenar region, and the other from the head of the first metacarpus to the pisiform bone) in both hands. During this test the participants kept their hands on the table, with the forearm in a supine position and the eyes covered by a mask. Using the method of limits and a caliper rule adapted with two rods, each measuring 0.25mm in diameter, the examiner systematically varied the distance between the rods using steps of 0.5mm in an either increasing or decreasing sequence, and touched the skin perpendicularly to the surface with both rods. Stimulation was such that a slight skin deformation was produced over 3 seconds. When using an increasing sequence, the distance between the rods was so small that the participants initially reported only one stimulation point. In contrast, when using a decreasing sequence the distance between the rods was such that the participants initially reported two stimulation points. The measure for two-point discrimination corresponded to the moment the participants changed their perception from one to two points in increasing sequences and from two to one point in decreasing sequences. Each body region was tested ten times, five using an increasing sequence randomly interspersed with another five using a decreasing sequence.

The stereognosis test was used to evaluate active tactile perception, which depends on the participants’ ability to manipulate and name objects relying on tactile information (see Krumlinde Sundholm and Eliasson). Six objects (an eraser, a Lego block, a coin, a shirt button, a wooden ball, and a marble) were randomly shown, named by the researcher and individually offered to the child, who was asked to look at them, manipulate them, and name them. The child's eyes were then occluded and each object was again offered randomly for unilateral manipulation. The time taken by the child to name the six objects, even if incorrectly, was recorded. In addition, the number of objects correctly identified was also recorded. The test with the eyes covered was first performed with the preferred hand and then repeated with the other hand.

Manual dexterity assessment involved the Pick-Up test, which provides information about visuomotor coordination when performed with the eyes open and motor coordination without visual information, when performed with the eyes closed. Briefly, in each trial a flat box measuring 128 × 128 × 15mm containing ten wooden cubes, each measuring 10mm on each side, was made available to the child, who was asked to transfer the cubes, one at a time, as quickly as possible, to another box measuring 120 × 120 × 40mm. This test was performed three times with the eyes open and using the preferred hand. Then, the child was asked to perform the task another three times, still with the eyes open, using the other hand. Finally, the eyes were occluded and the same procedure was repeated, that is three times using the preferred hand and another three times with the other hand. The time taken to perform each test was recorded in seconds.

**Statistical analysis**

The sample size required to achieve 80% power at a significance level of 5% in the DMD group was 37 participants. For ethical reasons, the evaluations were...
offered to all males, both DMD and comparison participants, resulting in a larger sample.

The two-point discrimination results were analyzed using repeated measures analysis of variance (ANOVA) with Group (two levels, DMD and comparison participants) as the between-participants factor, and Hand (two levels, dominant and non-dominant hand) as the within-participants factor. Separate ANOVAs were used for the index finger, thumb, and palm of the hand data.

The stereognosis test data were analyzed using ANOVA with Group as the between and Hand (either the dominant or non-dominant) as the within-participants factors. Separate ANOVAs were used for the time spent identifying the six objects and for the number of correct identifications.

The Pick-Up test included three tests under each of the following combined conditions: eyes either open or closed, using either the dominant or the non-dominant hand. Mean trial scores were calculated for each condition. These data were then analyzed using ANOVA having Group as the between-participants factor, and Visual feedback (eyes either open or closed) and Hand (either the dominant or the non-dominant) as the within-participant factors.

Each of these analyses was preceded by a Kolmogorov–Smirnov normality test (D). In order to meet test assumptions for ANOVA (normally distributed data and homogeneity of variances), data were log transformed after adding one and then the resulting scores were subjected to ANOVA. All tests were two-tailed.

Post-hoc analysis, when required, was run using Scheffe’s multiple range test. Differences were considered significant when the p values were less than 0.05.

All statistical analyses were performed using SAS software (SAS Institute Inc., Cary, NC, USA).

RESULTS

Summary measures (median and interquartile range) calculated from scores obtained during the tests are shown in Table I.

The ANOVAs, including two-point discrimination scores for the three investigated body regions (Fig. 1), revealed no significant Group (F1,87=0.85–1.20, p=0.27) or Hand (F1,87=0.09–0.90, p=0.34) main effects, and no significant Group versus Hand interaction effects (F1,87=0.02–0.37, p=0.54). These data indicate that tactile perception of males with DMD, as evaluated by the two-point discrimination test, is not impaired relative to that of the comparison participants without DMD.

Tactile perception was also evaluated by recognition of six objects using stereognosis. In relation to the time spent identifying six objects (Fig. 2a), the ANOVA revealed a significant Group main effect (F1,87=29.32, p<0.001), but lack of a significant Hand main effect (F1,87=0.17, p=0.68) and Group versus Hand interaction effect (F1,87=1.34, p=0.25). In contrast, in relation to the number of objects correctly identified (Fig. 2b), ANOVA revealed a lack of significant Group (F1,87=0.10, p=0.74) and Hand (F1,87=0.001, p=0.94) main effects, and a lack of significant Group versus Hand interaction effect (F1,87=0.53, p=0.46). These results show that even though males with DMD are slower when performing the stereognosis test, they are as accurate as comparison participants in naming the six objects.

The scores obtained in the Pick-Up test (Fig. 3) allowed for an evaluation of manual dexterity using each hand, either with or without visual feedback. The ANOVA revealed significant Group (F1,87=22.10, p<0.001) and Visual feedback (F1,87=283.43, p<0.001) main effects, and a significant Group versus Visual feedback (F1,87=20.28, p<0.001) interaction effect. In addition, ANOVA revealed a lack of significant Hand main effect (F1,87=1.43, p=0.23), and Group versus Hand (F1,87=0.51, p=0.69), Hand versus Visual feedback (F1,87=1.14, p=0.28) and Group versus Visual feedback (F1,87=1.32, p=0.25) interaction effects. The post hoc Scheffe’s test revealed, in addition, that males with DMD were significantly slower than comparison participants when using the non-dominant hand with the eyes open (p<0.05). As Figure 3 shows, the performance of males with DMD was poorer than that of comparison participants, particularly when the task was performed without visual feedback.

DISCUSSION

The results of the present study provide evidence that males with DMD (1) exhibit disturbances in object manipulation that seem not to be related to tactile perception, as revealed by the accuracy seen in both the two-point discrimination and stereognosis tests; (2) exhibit a slight but significant disruption of manual dexterity with the non-dominant hand when compared with the dominant hand, in the presence of visual feedback; and (3) are more dependent on visual feedback during hand control than children with typical development.

Both the passive and active accuracy of tactile perception seem to be intact in males with DMD, as revealed by the
unaffected spatial resolution in the two-point discrimination test and by the number of objects correctly identified in the stereognosis test. In contrast, males with DMD were slower when compared with comparison participants during the stereognosis test.

Earlier studies have shown that individuals with DMD exhibit lower motor cortex excitability and reduced glucose metabolism in the sensorimotor cortex and the cerebellum. As these brain areas are responsible for hand control during manipulation, it seems plausible to hypothesize that the slower performance in the stereognosis test observed in the present study may be related to neural impairment during sensorimotor integration. Even though no males included in this study exhibited any movement impairment in the upper limbs, as evaluated by Brooke's Scale, the hypothesis that muscular weakness could have influenced the speed of their performance in the stereognosis test cannot be discarded. Taken together, these data suggest that slowness during object manipulation is related to either a disruption in central processing or a muscular weakness, or both, rather than to the accuracy of tactile perception.

An impairment of neural processing could also explain the slightly poorer dexterity of the non-dominant hand of males with DMD in the Pick-Up test performed with the eyes open. Cotton et al. suggested the existence of an asymmetric functional deficit in males with DMD, related to dysfunctions in the right cerebral hemisphere. A
hypometabolism restricted to the right hemisphere was also detected in the temporal cortex, postcentral gyrus, and hippocampus. In fact, as 35 out of 40 of our children were right-handed, these findings suggest that the neural control of the non-dominant hand could be worse when compared with that of the dominant hand. This hypothesis does not conflict with the observation that there were no significant differences between the groups in manual dexterity when using the dominant hand and with the eyes open. This relatively better performance of males with DMD when using the dominant hand and with the eyes open could also be related to the fact that this is the hand most frequently used in daily activities; therefore, it is more exposed to such training when compared with the non-dominant hand.

More interestingly, the present results revealed a dramatic disruption of manual dexterity in DMD when the task was performed with the eyes closed, and with the dominant and non-dominant hands. Therefore, despite color vision impairment or other visual problems possibly caused by a lack of dystrophin in the retina, and decreased visual-spatial attention, the poorer performance with the eyes closed suggests that children with DMD are more dependent on visual feedback. The predominant use of visual information for hand control is typical of children who are younger than the ones who were enrolled in this study, suggesting that this dependence on visual feedback could be related to delayed motor development in children with DMD.

There have been proposals that muscle spindle primary endings and skin receptors contribute to both the sense of limb position and the sense of limb movement. Ribot-Ciscar et al. showed that muscle spindle proprioceptive functions are not impaired by muscular dystrophies. Although our results suggest that males with DMD have no disturbance in tactile perception in the glabrous skin of the hands, the sense of limb movement depends on skin stretch receptors around the joints, which were not assessed in this study. Therefore, the present data do not clarify if there is a disruption in multimodal perception that would interfere with the performance in the Pick-Up test when visual feedback is eliminated (Fig. 3). In favor of this interpretation, neuroimaging studies have shown that both the cerebellum and the parietal cortex are involved in the multisensory integration of visual, auditory, somatosensory, and vestibular information required for performing fine motor skills. Further, Lee et al. reported changes in cerebellar and somesthesic cortex metabolism related to cognitive disruption and manual dexterity losses in DMD.

The present findings suggesting specific features of the neural control and development of males with DMD strengthen the hypothesis that these males have motor problems that are not restricted to muscular impairment. In particular, their dependence on the use of visual information for hand control may contribute to difficulties during some daily living activities. In this sense, the present work reinforces the proposal of Mazzone et al. to include items to assess upper limb control in the existing scales, especially in the absence of vision, or to develop new assessment devices.

Treatment strategies, as well, should include tasks related to dexterity and proprioceptive feedback.

In this study, we evaluated males in the early stages of DMD. Therefore, additional work is necessary to verify the progression of the impairment in manual dexterity and perception. Other studies are also necessary to evaluate skin sensitivity in other body regions besides the hands in order to better understand sensory integration in males with DMD.

CONFLICTS OF INTEREST
The authors have stated that they had no interests that might be perceived as posing a conflict or bias.