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**Title: Anticipatory postural adjustments in a bimanual load-lifting task in children with Duchenne Muscular Dystrophy**

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## **Keywords**

Anticipatory postural adjustment, bimanual coordination, EMG, Duchenne muscular dystrophy, children

## **Abstract**

We investigated the consequences of a progressive damage to the muscular system on the organization of Anticipatory Postural Adjustments (APA) in children with Duchenne Muscular Dystrophy (DMD). We used a bimanual load-lifting task requiring the stabilization of the forearm position despite its voluntary or imposed unloading. Eight children with DMD from 4 to 11 years of age were compared to 8 typically developing (TD) children. Elbow angle and multiple surface EMGs were recorded and assessed the use of APA. The muscle weakness did not impair (1) the proprioceptive afference and the motor efference constituting the unloading reflex and (2) the use of an anticipatory function in children with DMD. However, APA used for the forearm stabilization were less efficient in the group of children with DMD. We conclude that in DMD, the muscular weakness could be a restraint to the efficiency of APA with respect to TD children.

## **Introduction**

Anticipatory postural adjustments (APA) consist in muscular activities which occur before the onset of a voluntary movement. They usually occur in association with voluntary movements, but they can also be observed when imposed disturbance is recurrent. Their functions are to prevent a forthcoming disturbance of posture and to assist the movement during its execution [18]. The acquisition of APA relies on the transformation of a feedback postural correction into a feedforward control associated with the voluntary movement that causes the postural disturbance [19]. Thus, APA involve a nervous system that can efficiently monitor, integrate and store sensorimotor information into a representation used to parameterize and coordinate a movement and its associated APA. Yet, APA rely on an efficient system, from central to peripheral nervous and muscular structures [20].

During childhood, previous studies suggest that the feedforward control of posture does not appear consistently until 4-5 years of age [2;12-14;17;24;28]. Schmitz and collaborators [29] studied the development of APA in a bimanual load-lifting task between 4 and 8 years. They showed that the postural stabilization enabled by the use of APA gradually develops during childhood, and is not yet fully efficient at 8 years of age as seen by the lower stability performance as compared to adults still at this age. The developmental sequence in the acquisition of APA consists in first the selection of an efficient electromyographic (EMG) pattern underlying the forearm stabilization and second the mastering of the timing adjustment of the muscular activities.

Duchenne Muscular Dystrophy (DMD) is due to a genetic lack of dystrophin which induces an increasing muscular weakness [3;15;32]. DMD is characterized by a decrease in the number of muscle fibres which are progressively replaced by fibro-adipose tissue. The progression of these changes grows from the lower to the upper segments and in a proximal to distal direction [1;7]. Despite the existence of studies exploring the muscle and joint elastic

properties [4;5], the consequences of the muscular weakness on postural and motor efficiency have rarely been explored in DMD patients [1], except for clinical evaluation [10;21]. Furthermore, since DMD induces an increasing muscle weakness at a time when the muscular patterns underlying the APA are normally selected, consolidated, and stabilized, the changes in the muscle properties might have an influence on the development of APA in DMD.

This study mainly focused on the expression of a feedforward control in children with DMD as compared to typically developing (TD) children during a bimanual load-lifting task. Our hypothesis was that the developmental processes of the feed-forward mode of control would not be impaired but that the muscular weakness would hinder the function of APA, that is, the stabilization.

### **Materials and Methods**

Eight right-handed boys with DMD with age ranged from 3 years 11 months to 10 years 11 months participated in this experiment (mean  $\pm$  SD, 7,6  $\pm$  2,4). All of them were contacted in the neurology care unit of Marseille's main hospital and were selected from those who had a progressive DMD. A clinical evaluation (ambulatory status, orthopedic evaluation, global and manual motor functions...) was conducted prior to their participation. Children participated only if their manual abilities were considered to be normal by a trained paediatrician. All children had normal growth and normal compulsory schooling, supposing no mental retardation. Eight right-handed age matched boys with age ranged from 3 years 9 months to 11 years 2 months and with a typical development constituted the control group (mean  $\pm$  SD, 7,6  $\pm$  2,4). All control children were at school and presented, at each age, a normal range of motor capacities for their upper extremities in their every day life. Parents, and also children when they were able to, gave their informed consent prior to the experiment, which obtained the approval of the local ethics committee (CCPPRB Marseille 1).

The experimental set up was the same as the one described in previous studies [27-30]. The subjects were seated on a hard-back chair. Their left forearm, placed in a support, was horizontal and semi-prone during the entire session. A bracelet, placed near the wrist, was equipped with a strain gauge and supported a platform on which a load could be placed either below or onto the forearm. The angular displacement of the forearm was measured by a potentiometer situated along the elbow joint axis. During the imposed unloading situation, the load suspended below the forearm was released by the experimenter switching off the electromagnet circuit. During the voluntary unloading situation, the subjects lifted with their right hand the load from a platform resting on the left forearm. As with previous studies in children [27;29] the weight of the load was chosen to maintain a constant ratio between the body weight and the load weight in each age group (0,7% of the body weight). The mean weight of TD and DMD children being similar for the ages studied [11], in the two groups the 4 to 6 year-old children used a 300 g load, 7 to 8 year-old children a 350 g load and the 9 to 11 year-old children a 400 g load. The general procedure was as follows: first a session of 10 imposed unloadings, then a session of 15 voluntary unloadings. Five training trials were offered so that the experimenter was sure that the task was correctly performed. There was a 10 min rest period between each situation. Force and angular elbow displacement signals were recorded, digitised and stored on a computer disk (sampling rate: 500 Hz) along with EMG signals for analysis. Each trial was viewed offline on a monitor screen. The onset of unloading ( $t_0$ ) was given by the first visible deflection of the force signal given by the gauge (see Fig. 1). The upward movement of the postural forearm was quantified by means of the maximal angular amplitude (MA) and the maximal angular velocity (MV), calculated starting from the derivative of the postural forearm displacement. Their latencies were also measured. During the session of voluntary unloading, MA and MV were expressed for each child in percentages of the mean value obtained in the imposed unloading. Bipolar surface electrodes

(integration surfaces: 2.5 mm<sup>2</sup>) were placed over the surface of two muscles implied in the forearm postural stabilisation: one flexor (*Biceps brachii*) and one extensor (*Triceps brachii*). EMG were amplified, filtered (10 Hz - 200 Hz band pass), rectified and integrated with a 10 ms time constant. During the imposed unloading situation, latency and duration of the unloading reflex were measured on the flexor by means of averaged trials for each subject. During voluntary unloading, two main EMG patterns were previously identified in children [29]: a simultaneous increase of activity on the flexor and extensor muscles (co-contraction), and a reduction of activity on the flexor while the extensor stayed silent or shown an increase of activity (flexor inhibition). We calculated for each subject the rate of co-contraction pattern and the rate of inhibition pattern. However, in this study, we chose to focus on the flexor inhibition pattern. Thus, in each trial where a decreasing activity was defined on the flexor, the latency and the duration of the inhibition were determined. The latency was measured as the time-interval between the onset of unloading and the onset of the reduction of activity, and the duration was measured between the onset and the end of the reduction of activity. Non parametric tests were used for inter group (Mann-Whitney U-tests) and within subject (Wilcoxon signed-rank tests) comparisons. Comparisons between the rates of EMG patterns in the two groups were made by means of a Chi2 test. Differences with a *P* value < 0.05 were considered to be statistically significant.

INSERT FIGURE 1 ABOUT HERE

Examples of force, elbow rotation and EMG traces are shown in Fig. 1 on one trial obtained in a 8 year-old child with DMD during both an imposed and a voluntary unloading trial. The MA reached 16.9° in the imposed situation (*left*) and 2.1° in the voluntary situation (*right*), indicating an effective stabilization of the postural forearm in the last situation. During the imposed situation, the *biceps brachii* showed a decrease of EMG activity with a latency of

50 ms which corresponds to the unloading reflex. During the voluntary situation, a decrease of the *biceps brachii* activity was observable before the unloading onset (-18 ms).

During imposed unloading, the kinematics data show that the sudden change in force was followed by an upward rotation of the postural forearm elbow. No difference was found between the two groups concerning the absolute values and latencies of MA and MV. The EMG activity measured on the postural forearm decreased in the *Biceps Brachii* after imposed unloading (table 1). The latency and duration of the EMG inhibition were not significantly different between the two groups of children.

INSERT TABLE 1 ABOUT HERE

In TD children, the elbow flexion following the voluntary unloading was reduced as compared to the one obtained during imposed unloading: the median value of MA (figure 2 a) and MV were notably reduced during voluntary unloading as compared to the median value obtained during the imposed unloading (MA :  $T=0$ ,  $p<0.05$ ; MV :  $T=0$ ,  $p<0.05$ ). This was also the case for children with DMD (MA :  $T=0$ ,  $p<0.05$ ; MV :  $T=0$ ,  $p<0.05$ ).

INSERT FIGURE 2 ABOUT HERE

Nevertheless, the forearm stabilization was impaired in the group of children with DMD. During voluntary unloading, the median of the MA expressed in percentages was significantly larger in the group of children with DMD than in the group of TD children (figure 2 b;  $U=11$ ,  $p<0.05$ ). The same result was significant for MV expressed in percentage ( $U=13$ ,  $p<0.05$ ). Concerning the MA latency, there was no difference between the two groups (figure 2 c). However, the MV latency was markedly increased in the group of DMD children. The late appearance of the MV reflects a delayed intervention of the voluntary control aiming at stabilizing the forearm.

The EMG activity measured on the flexor decreased before the voluntary unloading in both groups of children (table 1). The latency and duration of the inhibitions did not differ between



TD children and children with DMD during voluntary unloading. Finally, the preferential use of one or the other pattern of muscular activity did not significantly differ between the two groups of children: the inhibition pattern appeared with a higher rate in both group (96.1% in DMD children, and 93.1% in TD children).

Both kinematic and EMG data indicated that during imposed unloading, the reflex was the same in the two groups. Other studies using this paradigm found an integrity of the unloading reflex in Parkinson disease [20] and in autism [30] but not in a deafferented patient [9]. In the group of children with DMD, the properties of the unloading reflex were not impaired by the progressive muscular dystrophy. Interestingly enough, a study of Lazzaro and colleagues using transcranial magnetic stimulation showed that the nervous conduction is not impaired in DMD children [6]. Taken together, these results suggest that the peripheral muscular disability characterizing the DMD disease does not impair the proprioceptive afference and the motor efference constituting the unloading reflex.

The decrease of the maximal amplitude of the elbow flexion during voluntary unloading assesses the intervention of a postural control in children with DMD [23]. Furthermore, the latencies of the EMG inhibition measured on the flexor muscle belonged to a temporal window compatible with APA. These results indicate that our group of children with DMD used APA during this bimanual task.

However, despite a significant reduction of the elbow rotation during voluntary unloading, the kinematic data also indicated that the postural stabilization was less efficient in the group of children with DMD as compared to the group of control children. The latency of MV is an important landmark for the intervention of the control which slows down the elbow flexion until the forearm is stabilized [23]. Our results indicate that despite the fact that the nervous commands were sent on time, as assessed by EMG latencies, this control was translated late in terms of changes in the forearm trajectory in the group of children with DMD. As we did not

measure the children's muscle strength, one could argue that this difference might arise from the weight of the load, which could be relatively heavier for the children with DMD than for the TD children. However, Schmitz and Assaiante (personal communication) noted in a previous study that the stabilisation enabled by the use of APA does not depend on the load weight (being lighter or heavier, with a 200g difference) in TD children (4-6 and 7-8 years) and in adults. Thus, changes in muscle properties (weakness, increased elastic stiffness or increased joint stiffness) [5;8] might explain the fact that despite their correct use of APA, children with DMD still lack postural stability. Among these properties, the muscle weakness induces a muscular fatigue in children with DMD. Studies exploring the effect of muscle fatigue on motor efficiency showed that fatigue induces changes and small variations in the developed muscle force [16;25;31]. These fluctuations of force are known to impair the motor and postural output [22;26]. We think that the increased muscle fatigue in children with DMD could explain the discrepancy between a preserved temporal organization of the postural command and the poor forearm stabilisation.

Interestingly, as compared to the youngest TD children, the youngest children with DMD showed a marked preference for the inhibition muscular pattern (data not shown) classically used in older children and adults for the forearm stabilization during voluntary unloading [29]. This pattern is less expensive than a co-contraction in terms of energy and its predominant use in the youngest DMD children could reflect a plasticity of the selection process that enables an adaptation of the motor development to the muscular deficiency. Further investigation focused on the youngest children with DMD (3-5 years of age) should help us to confirm this hypothesis.

Finally, we think that modifications of the efficiency of APA in the unloading task could bring some insights into the efficiency of other postural responses in DMD: APA used in other tasks involving a coordination between posture and movement (locomotion...) but also

postural reactions (to a support displacement for instance...) might be altered as well. The muscular weakness and the changes it induce could yield to a general alteration of the postural function, which plays a crucial role in correcting for the consequences of external disturbances (postural reaction) or enables to anticipate the disturbances generated by a movement (APA), but also accompanies the movement to optimize its efficiency [18]. Thus, besides the alteration of motricity, it might be important to consider the functional aspects of a postural deterioration in DMD to get a more complete view of the neural control regression in DMD.

In conclusion, the building of APA, characterized by the fine tuning of EMG events, is protected from the muscle weakness in children with DMD. However, the muscle fatigue induced by muscle weakness impairs the efficiency of the muscle response to the motor command. Probably the alteration of at least one of the muscle properties in DMD is a restraint to the efficiency of APA with respect to TD children.

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## Figure legends

**Figure 1:** Raw trial recordings of a 8 year-old child with DMD during imposed unloading (*left*) and voluntary unloading (*right*). The parameters recorded are as follows, from *top to bottom*: force, elbow rotation angle, integrated and rectified EMG of the *triceps brachii*, and *biceps brachii*, on the postural forearm. The decrease of the force indicated the onset of unloading (*vertical line*), used as a reference time. During imposed unloading, note the upward elbow rotation. The increased activity on the *triceps brachii* and the decreased activity on the *biceps brachii* correspond to the unloading reflex (see grey arrows). During voluntary unloading, note the reduced elbow rotation. The unloading onset was time-locked with the decreased activity occurring on the *biceps brachii* (see black arrows).

**Figure 2:** a) **Comparison between the two unloading situations in TD children and in children with DMD.** Histograms show medians and quartiles of the MA expressed in degrees during imposed (grey columns) and voluntary (black columns) unloading. \* =  $p < 0.05$ . b) **Group comparison: MA and MV during voluntary unloading expressed in percentage.** Histograms show medians and quartiles of MA (*left*) and MV (*right*) expressed in percentage of the mean value obtained during the imposed situation in TD children (dashed columns) and in children with DMD (white columns) during voluntary unloading. \* =  $p < 0.05$ . c) **Group comparison: latencies of MA and MV during voluntary unloading.** Histograms show medians and quartiles of MA (*left*) and MV (*right*) latencies obtained during the voluntary situation in TD children (dashed columns) and in children with DMD (white columns). \* =  $p < 0.05$ .

**Table 1:** Median and quartile values of the latency and the duration of the *Biceps brachii* inhibitions during the imposed and voluntary unloading situations, in TD children and in children with DMD.