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ORIGINAL ARTICLE/ARTICLE ORIGINAL

Evaluation of neuromuscular tone phenotypes in children with autism spectrum disorder: An exploratory study

Évaluation du tonus musculaire chez les enfants avec un trouble du spectre de l'autisme : étude exploratoire

Aude Paquet[a,b,c,d,*], Bertrand Olliac[c,e], Bernard Golse[a,b,f], Laurence Vaivre-Douret[a,b,f,g,h]

[a] *Faculty of medicine, university of Paris Descartes, Paris, France*
[b] *Inserm 1018, CESP, university Paris-Sud, UVSQ, university of Paris-Saclay, Paris, France*
[c] *Department of child and adolescent psychiatry, Esquirol hospital, Limoges, France*
[d] *Research and neurostimulation unit, research federation for psychiatry and innovation at Limousin, Esquirol hospital, Limoges, France*
[e] *UMR 1094, university of Limoges, Limoges, France*
[f] *Department of child psychiatry, Necker—Enfants-Malades university hospital, Paris, France*
[g] *Department of paediatrics, child development, Cochin-Port Royal university hospitals of Paris center, Paris, France*
[h] *Endocrinology laboratory, Imagine instituts, Paris, France*

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KEYWORDS
Autism spectrum disorder;
Children;
Muscular tone;
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Summary

Objective. — Motor disorders are known in autism spectrum disorder (ASD), but muscle tone assessments are rarely performed. Muscle tone underpins movement. We investigated muscle tone in 34 ASD children using a standardized neuro-developmental battery, which uses the French norms for muscular tone in children.

Methods. — Dangling and extensibility were used to examine passive muscle tone in the upper and lower limbs and the body axis. A comparison between muscles of the right and left sides enabled the determination of tonic laterality.

Results. — We found a disharmonious tonic typology, with a tonic component for the muscles of the trunk and the proximal muscles of the lower limbs and a laxity component for the ankles and the proximal and distal muscles of the upper limbs (wrists and shoulders). No establishment of tonic laterality was found in the upper limbs in 61% of ASD children ($P < 0.001$).

* Corresponding author at: unité de recherche et de neurostimulation, centre hospitalier Esquirol, 15, rue du Dr-Marcland, 87000 Limoges, France.
E-mail address: audepaquet@gmail.com (A. Paquet).

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Conclusion. — The disturbed tonic organization influenced by subcortical structures, such as the cerebellum, may partially explain the motor disorders, and indefinite tonic laterality may also be linked to low hemispheric brain dominance described in autism. This preliminary examination is necessary before any gross motor assessments to understand the nature of movement disorders, explore typologies and highlight possible soft neuro-motor signs.

MOTS CLÉS
Enfants ;
Évaluation neurodéveloppementale standardisée ;
Tonus musculaire ;
Trouble du spectre de l'autisme

Résumé
Objectifs. — Les troubles moteurs sont connus dans le trouble du spectre de l'autisme (TSA), mais l'évaluation du tonus musculaire est rarement réalisée. Pourtant le tonus musculaire sous-tend le mouvement. Nous avons étudié le tonus musculaire chez 34 enfants avec TSA à partir d'une batterie neurodéveloppementale standardisée, qui utilise les normes françaises chez l'enfant pour le tonus musculaire.
Méthodes. — Le ballant et l'extensibilité ont été utilisés pour examiner le tonus musculaire passif au niveau des membres supérieurs et inférieurs puis de l'axe du corps. Une comparaison entre les muscles des côtés droit et gauche a permis la détermination d'une latéralité tonique.
Résultats. — Nous avons trouvé une typologie tonique dysharmonique, avec une composante d'hypertonie au niveau des muscles du tronc et des muscles proximaux des membres inférieurs et une composante d'hyperlaxité pour les chevilles et les muscles proximaux et distal des membres supérieurs (poignets et épaules). Une absence de prédominance tonique au niveau des membres supérieurs a été trouvé chez 61 % des enfants atteints de TSA ($p < 0,001$).
Conclusion. — L'organisation tonique perturbée influencée par les structures sous-corticales, comme le cervelet, pourrait expliquer en partie les troubles moteurs décrits dans les TSA, de plus, la latéralité tonique indéterminée pourrait également être liée à une dominance cérébrale hémisphérique absente ou peu dominante décrite dans l'autisme. Cet examen préliminaire est nécessaire avant toute évaluation de la motricité globale pour comprendre la nature des troubles du mouvement, explorer les typologies et mettre en évidence des signes neurologiques doux.

Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental disorder with a multifactorial origin that affects a child's development at an early stage and persists into adulthood. Children are characterized by pervasive impairments in several areas of development associated with restricted patterns of behavior and interests, which affects social functioning and communication. Recent literature indicates movement and coordination disorders and impairment in gross motor skills in autism, but no systematic and standardized approach has been used despite the increased performance of motor assessments [22]. Muscle tone assessment is a difficult examination in children with ASD because it requires physical contact and access to voluntary muscle relaxation. Few studies have reported neurological examination or investigations of walking in people with autism, nor data regarding muscular tone [11,18]. Moreover, tone data are often derived from imprecise muscular tone exploration methodologies without any reference to standards in children. Passive or active muscular tone is not explored in a standardized manner. Shetreak-Klein et al. [29], measured joint angles and found evidence of greater ligament laxity in distal limbs in children with ASD compared to a control group. Hypotonia was also reported in several observational clinical studies. Adrien et al. [1] retrospectively analyzed video of young children later diagnosed with autism and noted a ''passivity'' in these children that was characterized by a lack of initiative, hypoactivity and hypotonia (i.e., low tone and no tonic reactions to stimuli). Ming et al. [18] performed physical examinations of children aged 2 to 18 years and highlighted reduced resistance to passive movement in the limbs. These authors found a high prevalence of mild to moderate hypotonia in approximately 63% of the 2—6-year old children, and the prevalence in 7—18-year olds was only 38%. Another study demonstrated minor neurological dysfunctions using assessments of soft signs with the Touwen examination in children with ASD; this study mentioned dysfunctional muscle tone without specifying the nature or localization of the dysfunction [8]. Other studies used the Physical and Neurological Examination for Soft Signs (PANESS) but provided no information on muscle tone [13,17]. No current studies have specifically examined muscle tone in children with ASD. However, according to Bergès [6], muscle tone is the foundation on which movement emerges and is elaborated. The examination of muscle tone is an essential prerequisite to any examination of motor skills that account for neuromuscular maturation, subject typology (e.g. hyperlaxity and hypertonicity), tonic lateral dominance and possible neurological or neuromuscular disorders. Most studies have assessed gross motor skills in children with ASD using global batteries of movement without developmental references. However, these tools do not elucidate our understanding of the nature of dysfunction, specific functions that are affected or delayed, underlying pathological mechanisms or subtle neurological abnormalities. However, motor disorders in neuro-developmental disorders are often associated with soft signs [9,12] that reflect the existence of a mild brain dysfunction, and which may help explain the etiology of these disorders. Knowledge of the motor phenotype in children with ASD from detailed information of neuro-psychomotor functions, such as muscle tone, laterality, postural control or manual and digital praxis, is important to enable the identification of the intact and altered functions and understand the nature of the failures in the motor function of these children.

A complete examination of muscle tone in children and its semiology was developed in 1946 by Saint-Anne Dargassies, who was a pioneer for tone examination in newborn and premature babies [2]. Thomas and de Ajuriaguerra [3] and Bergès [6] developed similar tests for children. These authors developed methods for the examination of muscular tone and interpreted its role in different disturbances and organic and pathological damage. Several studies reported data regarding newborns and infants [4,30,32] and focused their research on the maturation of the central nervous system (CNS) or the detection of anomalies due to CNS lesions.

The present study presents the profile of muscular tone in children with ASD using the first properly standardized neuro-developmental battery, which uses the French norms for muscular tone in children from the age of 4.

Methods

Subjects

Children with ASD aged 4 to 11 years, regardless of their level of intellectual ability, were recruited following consultations for the diagnosis of autism in three French centers for autism diagnosis between October 2013 and April 2015. All children complied with the criteria for the diagnosis of Pervasive Developmental Disorders according to DSM-TR-4 and the Autism Diagnostic Interview-Revised (ADI-R [16]) criteria. A child psychiatrist who specialized in autism diagnosis administered both tests. Thirty-four children were included in the study (31 boys and 3 girls, mean age 89 ± 28 months). Eighteen of these children were diagnosed with Autism Disorder (AD) (aged 81 ± 29 months), nine children were diagnosed with Pervasive Developmental Disorder not otherwise specified (PDD NOS) (aged 106 ± 26 months), and seven children were diagnosed with Asperger's Syndrome (AS) (aged 88 ± 22 months). Fifteen children had intellectual disabilities (intelligence quotient [IQ] < 70): 10 children with AD (56%) and 5 children with PDD NOS (56%). The new classification proposed by the DSM-5 [5] and new records review were followed. All children recruited satisfied the criteria for ASD under the new nosographic classification, which does not separate AD, PDD NOS and AS. Children with motor disabilities of lesional or accidental origin or with a proven genetic disease or a confirmed neurological disease were not included. All parents were informed of the study and provided their written consent to participate. The agreement of all children was obtained. An ethics committee approved the study (CPP-AC15-007).

Evaluation from NP-MOT battery

Specific data for muscular tone was derived from assessments of the neuro-psychomotor functioning of the children using a specific standardized evaluation of muscular tone in children, the NP-MOT battery (Batterie d'évaluations des fonctions neuro-psychomotrices de l'enfant) [23,33,34]. The NP-MOT was normalized from a group of 446 French elementary school children with average-range IQs and school achievement. The NP-MOT exhibits good test-retest reliability ranging from 70 to 98%. The calibration group for the NP-MOT battery was composed of 446 French children with typical development (i.e., without motor or sensory disorders), aged 48 months to 101 months, including 218 boys and 228 girls. All children in the calibration group were born full term, and they had a height-weight development that corresponded to the normal average according to the standards proposed by Sempé, Pédron and Roy-Pernot [28]. The sample for calibration was divided into 5 age groups using the normal Gaussian distribution, and the mean and standard deviation were calculated for each group [34].

We compared the results of muscle tone assessments of children with ASD with the NP-MOT norms, i.e., a comparison of the distribution of the results of each ASD child with the results of children of the same age group in the NP-MOT calibration group. The battery is normalized until 8.5 years with a maximum notation in this 8.5-year old subgroup. Therefore, we compared the older children (8.5 to 11 years) to the 8.5-year old calibration group.

Examinations of passive muscular tone were conducted via the observation of ''dangling'' (i.e., the degree of fluidity of movement of a body segment) and ''extensibility'' (i.e., the degree of mechanical stretching of a muscle and the opening of a joint angle) in the distal and proximal limbs (ankles, wrists, shoulders). Each task is explained in the Appendix 1. Dangling and extensibility were examined in both upper limbs (Fig. 1) and both lower limbs from the measurement of joint angles (wrist, ankle, popliteal, adductors and ear-heel) (Fig. 2). The resistant side of the body (i.e., the most tonic side) was noted to enable comparisons between the two sides of the body. This comparison between muscles on the right and left sides was used to determine the most resistant side to muscle stretching. The comparison of muscular resistance in the right/left body parts determines the more tonic side of the body. The predominance of one side of the body over the other determines the dominant side of the body and neurological tonic laterality. The tonic laterality of the upper or lower limbs is determined when stretching resistance is present in the same side of the body for three muscular tone tests of the upper limbs (dangling wrist, extensibility of the wrist and extensibility of shoulder) or three muscular tone tests of the lower limbs (dangling foot, extensibility of the foot with legs bent and low thrust test) [24].

Extensibility of the trunk was also sought through the assessment of dorsal and ventral curvatures of children lying on their side (Fig. 3). The amplitudes of extension and flexion of trunk were compared to give information on nature of muscular tone (hypotonia, hypertonia).

A preliminary study was used to select the most objective tests for the evaluation of muscular tone. The standard

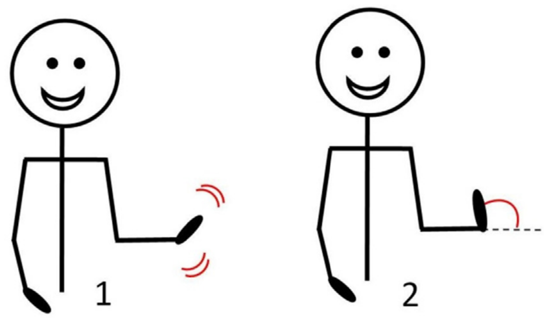

Figure 1 Passive tone of the upper limbs: 1: dangling wrist. 2: extensibility wrist 3: extensibility of shoulder.

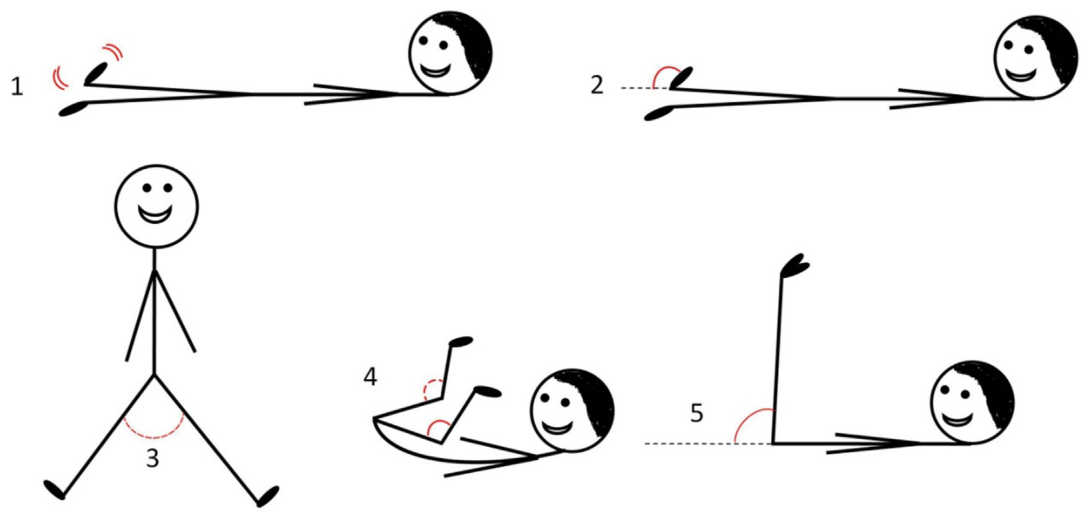

Figure 2 Passive tone of the lower limbs: 1: dangling ankles. 2: extensibility ankles 3: adductor angle. 4: popliteal angles. 5: ear-heel angle.

deviations that remained the most stable and most reduced and the best inter-examiner correlations in each age group were selected for the NP-MOT battery [34].

Procedure

A qualified and trained psychomotor therapist administered the NP-MOT battery. The evaluation of muscle tone requires only a gymnastics mat to mobilize the child in a lying position. Test instructions were given verbally, but pictures were provided with instructions for the muscular tone tests to facilitate an understanding about positioning in children with comprehension difficulties.

The primary difficulty in children with ASD is that they must tolerate touch and mobilization of the body, and they must have access to adequate relaxation. The examiner used playful verbal and expressive accompaniments during the tone examination (e.g., ''Oh, you're floppy as when you are asleep'', ''Put your legs like a rag doll'', ''Oh! Your leg is going beddy-bye'', ''This little foot is all relaxed, what about the other one?''). The assessment time was variable and dependent on the availability of children. The average time was approximately 10 minutes.

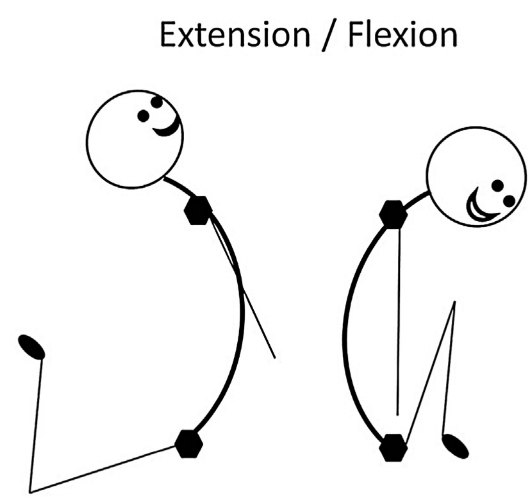

Figure 3 Extensibility of the trunk: comparison flexion/extension.

Data analysis

Results of muscle tone assessments in children with ASD were compared to the NP-MOT standards established from the muscle tone assessment of 446 French children

Table 1 Characteristics of children with Autism Spectrum Disorder (ASD).

	ASD (m ± SD)
Age (months)	89 ± 28
Term (weeks' gestation)	39 ± 2
Sitting position (months)	8 ± 1
Age at first steps (months)	15 ± 7
Gender (M/F)	31/3
Intellectual deficiency (%)	44

without developmental delays. Children of the same age group were compared. Statistical analyses were performed using SPSS® 21 (Statistical Package for Social Science) commercial software for Windows on PC. Comparisons of categorical variables were performed using Fisher's exact tests. The threshold significance level was 5% for all statistical analyses.

Results

Table 1 shows the characteristics of the ASD children.

Muscle tone tests were performed on all children, and 29 children (85%) were assessed in more than 80% of test. The acceptance rate for the full test was 62% (21/34).

The examination of passive tone demonstrated large angular values at the wrists, shoulders, feet and knees (popliteal) in the children in our sample compared to the reference norms (Table 2).

Absence of resistance was observed between the two sides of the body and characterized by distal (wrist) and proximal (shoulder) hypotonia of the upper limbs ($P < 0.001$) and a higher extensibility in the ankles in lower limbs ($P = 0.007$). We found an undetermined neurological tonic laterality in 61% of the ASD children ($n = 19/31$) vs. 28% for the norms for the upper limbs ($P < 0.001$) and 39% of the ASD children ($n = 12/31$) vs. 26% for the norms for the lower limbs (not significant).

However, there was no general hypotonia of the body. Some hypertonia was found in the trunk and proximal muscles of the lower limbs (ear-heel angle).

Subgroup analyses based on the presence or absence of intellectual disability did not reveal any significant differences between the children in our sample with or without mental retardation. We highlighted two cases of distal spasticity in children with intellectual disability during the test for fast extensibility of the feet.

A clinical analysis of the diagnostic subgroups (AD, AS, PDD NOS) revealed a distinction between diagnoses for tonic profiles. The proximal hypertonia found in our sample was not marked in children with AS. Children with AS had significantly less ''medium curvature'' of the trunk than NP-MOT standards (43% vs. 80% $P = 0.035$) but a more ''strong curvature'' (hypotonia) than standards (43% vs. 15%) ($P > 0.05$).

The tonic laterality profile of the upper and lower limbs was similar across the three diagnostic groups. There was no significant difference between the mean age of the children with an affirmed tonic laterality and the mean age of children without established tonic laterality in the upper limbs in 61% of ASD children or with poorly affirmed laterality.

Discussion

The passive muscular tone evaluation found high angle values and an absence of differential resistance between the two sides of the body in the proximal and distal upper limbs. However, tonic asymmetry of one side of the body was established in typically developing children from the age of 4 in the upper limb muscles where asymmetry was first established in the proximal muscles, then in the distal muscles [34]. We did not find the expected difference in resistance between the upper limbs for the dangling and extensibility tests for 61% of the children in our sample, which indicates significantly greater undefined tonic laterality (see method) than the reference population ($P < 0.001$). Our results demonstrated disrupted maturational organization of tonic laterality in the upper extremities in children with ASD, with no difference according to age. This lack of asymmetric organization could be a marker for undifferentiated hemispheric lateralization and could explain the high rate of weakly determined or reverse handedness found in children with ASD [24,25] and the language disorders present in autism [27]. There is a strong relationship between well-established cortical lateralization, strong handedness and language skills [14], and disrupted or reverse lateralization is associated with language disorders [10], which are disturbances that are often present in autism. Studies of structural and functional asymmetry in people with autism tried to establish relationships between abnormalities of cortical lateralization and behavioral manifestations of this neurodevelopmental disorder, such as language disorders. The assessment of tonic laterality using the passive muscle tone assessment may provide additional information about the hemispheric organization of the brain. Handedness is a behavioral result of cerebral dominance, and it seems important to identify functional markers, such as laterality, in autistic disorders, given the diagnostic and prognostic role of language disorders in autism [15].

Greater laxity was also found in the distal lower limbs, but the absence of resistance in the distal lower limbs in ASD children did not differ from reference values. Asymmetry in the distal lower extremities appears later in typically developing children because of the neurological maturation in the cephalo-caudal direction. Reduced heel-ear angle extensibility involving the gluteal and hamstring muscles was found in 47% of children with ASD, which may indicate hypertonia in the proximal muscles of the lower limbs and/or low flexion of the hip in these children. The limited extensibility of the gluteal muscles, particularly the gluteus medius, may be involved in stabilizing the pelvis in ASD children. This hypertonia was most markedly observed in children with AD or PDD-NOS. We noted significantly reduced trunk extensibility in children with PDD-NOS or AD, which suggests physiological hypertonia of the flexor and extensor muscles of the trunk. These observations may suggest motor anomalies in the cortico-spinal tract governed by the motor cortex or abnormalities in the median descending pathways from the brain stem, which is responsible for the adjustments of the proximal muscles and posture. Therefore, this could

Table 2 Distribution of success in the passive muscular tone tasks in children with ASD compared to the reference norms from the standardized battery NP-MOT (%; n = number of ASD children/total tested).

Tasks	Sample % (n/total)	Norms % (n^*)	P-value
Passive muscular tone			
Dangling of the upper limbs: wrist			
Angular value > 30	100 (33/33)	75 (336)	0.002
Resistance	33 (11/33)	72 (323)	< 0.001
Dangling of the lower limbs: ankle			
Angular value > 30	97 (33/34)	55 (245)	< 0.001
Resistance	82 (28/34)	81 (362)	0.864
Extensibility of the upper limbs			
Shoulder			
Elbow > above opposite mammary line	100 (31/31)	67 (299)	< 0.001
Resistance	58 (18/31)	87 (389)	< 0.001
Wrist			
]70–110°]	100 (32/32)	78 (346)	0.002
Resistance	34 (11/32)	69 (306)	< 0.001
Extensibility of the lower limbs			
Popliteal angles			
[90–150°]	100 (34/34)	90 (403)	0.023
Adductors angle			
[80–90°[	12 (4/31)	18 (84)	0.001
[90–150°]	88 (29/31)	81 (361)	0.079
Ear-heel angle			
< 80°	9 (3/34)	0 (0)	< 0.001
[80–90°[	38 (13/34)	10 (45)	< 0.001
[90–150°]	53 (18/34)	90 (401)	< 0.001
Ankles, legs extended			
90°	12 (4/33)	69 (308)	< 0.001
[60–90°[	88 (29/33)	65 (290)	0.007
Resistance	76 (26/33)	49 (218)	< 0.001
Ankles, legs bent			
90°	9 (3/33)	20 (88)	0.133
[60–90°[	91 (30/33)	81 (361)	0.154
Resistance	61 (20/33)	72 (323)	0.146
Extensibility of the trunk			
Low curvature	21 (7/34)	5 (21)	0.002
Medium curvature	62 (21/34)	80 (357)	0.012
Strong curvature	18 (6/34)	15 (68)	0.213
Low thrust test (Foix & Thévenard test)			
Contraction of the tibialis anterior tendon under mild pressure	72 (23/32)	90 (404)	0.004

n^*: number of children tested for calibration; resistance: tonic predominance of one side of the body to the other.

explain the puppet-like type of gait, the tendency to walk on tiptoes, postural control disorders and postural regulation disorders described in some ASD children [19–21].

Our findings regarding neuromuscular tone show a tonic typology that was disharmonious, with a tonic component for the muscles of the trunk and the lower limbs (gluteal muscles) and a laxity component for the distal muscles (ankles and wrists) in children with AD and PDD-NOS. A possible retraction of the gluteal muscles may partially explain the hypertonia encountered in the trunk in 21% of the children in our sample. This weak tonic regulation profile was not found in children with SA, in whom no hypertonia was found. There was distal hyperextensibility and proximal hypertonia in a large number of ASD children, which may form a phenotype characteristic of these children.

Therefore, examinations of muscle tone should be encouraged and continued to refine the tonic profile of children with ASD [26]. The DSM-5 does not distinguish PDD-NOS, AD and AS, but our exploratory study demonstrated different profiles between children with ASD that were important to distinguish. More in-depth research of the muscle tone of children with ASD in a larger population could confirm the existence of different profiles and may reveal associations with clinical and motor characteristics in these children.

Conclusion

This study enabled the identification of a tonic base that is disrupted in ASD children between 4 and 11 years of age that was associated with a largely undetermined tonic laterality, which may be related to a particular brain hemispheric organization in these children. No dominance becomes established with neurological maturation in these cases. This tonic disharmony may affect general coordination dynamics (e.g., postural control, tonic and postural adaptation, and praxis), fine motor skills and language, which are often described as disrupted in ASD. The particularities of muscle tone organization that were found in most ASD children in our sample could result from the involvement of the cerebellum, which is affected in autism [31,35]. The cerebellum acts as a control system over movement and muscle tone that affects cortical structures (e.g., premotor, frontal, and association areas). Our study of muscle tone suggests that the motor disorders described in autism may linked to dysfunction of the subcortical structures. Future investigations associating neuroimaging and clinical assessments (for example, muscular tone, laterality, gross motor skills and language) should be considered.

The examination of muscle tone is an essential preliminary examination to assess gross motor skills because it provides information regarding the degrees of neuromuscular maturation, typology, and laterality and the possible underlying neurological or neuromuscular disorders. We found two children with discreet distal spasticity, which had not been noticed in the overall evaluation of motor disorders. It is important to not settle for a global assessment of motor skills because this does not provide a neuromuscular semiology but, instead, an in-depth assessment of each function involved in psychomotor performances.

Examination of muscle tone is an inexpensive method that is particularly interesting because it elucidates the semiology of motor disorders in ASD. The phenotypical characteristics found in our results may be used to improve the screening of the earliest signs in the ASD population. Future genetic investigations in ASD may provide evidence of a close link between the neuromuscular characteristics observed in neurodevelopmental phenotypes and a possible underlying genetic abnormality. Neuromuscular characteristics may be specific, such as the hypotonia in some genetic mutations [7].

Disclosure of interest

The authors declare that they have no competing interest.

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Appendix 1. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.neucli.2017.07.001.

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