Distinct multi-joint control strategies in spastic diplegia associated with prematurity or Angelman syndrome

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Abstract

Spastic diplegia is commonly due to periventricular leucomalacia associated with premature birth. It is also a feature of Angelman syndrome (AS), a neurogenetic disorder with developmental delay, absent speech and mirthful behaviour. We studied the kinematics and kinetics of the squatting movement and associated electromyographic (EMG) activities in 20 children with spastic diplegia associated with periventricular leucomalacia (SDPL) or AS and 18 unimpaired children. While movement of normal subjects consisted of vertical translation of most body segments, the movement of SDPL children was operated around the fixed knee with backward shift of the hip, and AS children performed a forward flexion of the trunk over the thigh. Trunk stability was correlated with movement velocity in both pathological groups. In normal subjects, anticipatory EMG pattern consisted of silencing of hamstring muscle tonic activity prior to movement onset. This deactivation was not present in spastic diplegia. In SDPL, anticipatory overactivation of ankle joint actuators was recorded and tonic co-contraction persisted throughout the movement. In AS, rhythmic EMG bursting was seen during the movement. Shoulder, hip and knee trajectories in the sagittal plane showed marked within-group stereotypies in orientation, shape and length. The patterns in both pathological groups were therefore distinctive. We speculate that they reflect corticospinal impairment in SDPL and combined corticospinal and cerebellar dysfunction in AS. © 2001 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Movement; Posture; Cerebral palsy; Spastic diplegia; Angelman syndrome

1. Introduction

Cerebral palsy is a clinical syndrome characterised by abnormal movement and posture secondary to non-progressive pathological processes affecting the immature brain, with no reference to aetiology or histopathology. In spastic diplegia, the most prevalent type affecting 0.09% of the population, the motor syndrome is pyramidal, bilateral and predominates in the lower limbs (Minear, 1956). Since Freud (1893) coined the term diplegia, it has been used universally to designate a self-contained entity despite the clinical heterogeneity such a basic descriptor is expected to cover. This may be related to an epidemiological bias, as spastic diplegia is most commonly due to perinatal hypoxic–ischaemic insult in premature neonates causing lesions in the white matter adjacent to the lateral ventricles of the brain, or periventricular leucomalacia. However, a number of unrelated conditions may present within this clinical framework. Angelman syndrome (AS) (Angelman, 1965) is among these. AS is a neurogenetic disorder with developmental delay, virtually absent speech, motor impairment and a remarkable behavioural phenotype, associated with genetic or epigenetic abnormalities of chromosome 15q11-13 (Williams et al., 1995) (Table 1). It has an estimated prevalence of 0.008% (Steffenburg et al., 1996) but is thought to be largely under-diagnosed (Therasse et al., 1997). AS and spastic diplegia associated with periventricular leucomalacia (SDPL) share some features such as limb hypertonia, which is more marked distally, predominates in the lower limbs and increases with active mobilisation, hyperactive jerks, extensor plantar responses and varying degrees of trunk hypotonia. Despite major advances in genetics and clinical neurophysiology (Boyd et al., 1988) for AS and neuroimaging for SDPL, the diagnosis of both conditions is ultimately based on clinical elements including motor impairment.

Although motor impairment is present in all the patients with AS (Williams et al., 1995), no systematic studies of movement have been conducted in this condition. In the

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Table 1
Clinical characteristics of AS (adapted from Williams et al., 1995)

Consistent features (100%)
Functionally severe developmental delay
Speech impairment
Movement or balance disorder
Behavioural uniqueness: frequent laughter, happy demeanour, hyperactivity, short attention span

Frequent features (>80%)
Delayed growth in head circumference
Seizures
Characteristic electroencephalographic pattern (see Boyd et al., 1988)

Associated features (20–80%)
Flat occiput, occipital groove
Protruding tongue, sucking and swallowing disorders
Feeding problems during infancy
Prognathism, wide mouth, wide-spaced teeth
Frequent drooling
Excessive chewing and mouthing behaviours
Strabismus
Hypopigmented skin, hair and eyes
Hyperactive lower limb myotatic reflexes
Uplifted, flexed arms, especially during ambulation
Increased sensitivity to heat
Sleep disturbance
Attraction to water

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present work, we aimed to compare movement organisation in normal children, SDPL and AS in order to assist the clinical approach to spastic diplegia, and bring insights into the pathophysiology of the movement disorder in SDPL and AS. There has been a growing body of evidence that the study of multi-joint, whole-body movements involving change in posture can identify specific strategies of motor control (Stapley et al., 1998; Dan and Cheron, 2000a). We therefore focused on the kinematics and lower limb electromyographic (EMG) activities associated with the movement of squatting, which has been studied previously in different populations (Cheron et al., 1997; Dan et al., 1999; Dan and Cheron, 2000b; Dan et al., 2000a).

2. Methods

2.1. Patients with periventricular leucomalacia

Ten patients with SDPL aged between 6 and 13 years (mean 9.0 ± 2.3) participated in the study. All were born premature (30.2 ± 3.8 weeks gestation). Magnetic resonance imaging showed features of periventricular leucomalacia in all patients, with cystic lesions in the anterior periventricular white matter in two. Motor milestones were attained late in all children, namely, absence of head lag when pulled to sitting from 7 to 21 months (mean 11.5 ± 3.4); independent sitting from 8 to 19 months (mean 13.2 ± 4.5); independent walking from 21 to 40 months (mean 31.8 ± 5.2). In order to compare the functional limitations of SDPL and AS patients, gross motor

function measure (GMFM) scores were recorded. This validated test of gross motor skills was developed specifically for clinical and research use in children with cerebral palsy (Russell et al., 1989). The 85 items of this test include simple tasks performed while lying, rolling, sitting, creeping, kneeling, standing, walking, running and jumping. Quantification is based on how much of the task the patient can realise independently, without any reference to the quality of the performance. Mean normalised global GMFM scores were 0.78 ± 0.28, corresponding to partial completion of the tasks, with 0.76 ± 0.34 for the items specifically concerning the lower limbs. All patients had Bobath-type physiotherapy (1–3 times per week, started in the first year of life in all but one patient).

2.2. Patients with AS

Ten patients with AS aged between 7 and 13 years (mean 9.5 ± 2.1) participated in the study. All met the diagnostic criteria for AS (Williams et al., 1995). A deletion of chromosome 15q11-13 was found in 6 patients using fluorescence in situ hybridisation with GABR3 and SNRPN probes. Methylation studies at the D15S63 (PW71) locus of patients and their parents, using PW71b probe on Hind III + HpaII blots, were consistent with paternal uniparental disomy in one patient and imprinting centre deficiency in another patient. No genetic abnormalities were found in two patients, for whom a search for UBE3A gene mutations is underway. All these patients were born at term and had normal magnetic resonance imaging of the brain. Motor milestones achievement did not differ significantly from SDPL children: absence of head lag when pulled to sitting from 8 to 13 months (mean 12.8 ± 4.1); independent sitting from 10 to 25 months (mean 15.6 ± 5.1); independent walking from 22 to 48 months (mean 35.7 ± 8.4). GMFM scores were similar to SDPL patients: global scores 0.72 ± 0.26; 0.70 ± 0.39 for the lower limb items, implying that the two groups could not be discriminated on the basis of gross motor skills. All patients had physiotherapy of various types (one–two times per week, started in the first year of life in all but two patients).

2.3. Normal children

The normal group consisted of 18 children aged 6–13 years (mean 9.2 ± 2.2) with normal development and no disabilities.

2.4. Task

The studied movement consisted of self-paced rapid squatting from a stationary standing position. Prior to the movement, the subject stood quietly with the arms extended forward horizontally. Following a verbal instruction and an illustration performed by the observer, the subject was asked to realise a flexion of the lower limbs as fast as possible, and to maintain the final flexed position. In order not to

interfere with the initiation of the voluntary movement by some reaction time requirements, the subject was instructed to decide when to produce the movement. Each subject performed 10 trials. Ten trials were recorded in each child.

2.5. Movement recording and analysis

We used the opto-electronic ELITE system (BTS, Milan, Italy) for electromyography-coupled tridimensional analysis of motor patterns involved in this movement. The ELITE system consisted of two infrared light-emitting digital cameras that detect reflective markers at a sampling rate of 100 Hz. The markers were 10 adhesive plastic spheres (∅15 mm) placed on the child's skin overlying the following bony landmarks: (1) the lateral aspect of the nose at the height of the infra-orbital edge, (2) the ear tragus, (3) the upper limit of the acromion, (4) the lateral epicondyle of the elbow, (5) the styloid process of the wrist, (6) the antero-superior iliac spine, (7) the greater trochanter, (8) the lateral condyle of the knee, (9) the lateral malleolus and (10) the distal end of the fifth metatarsal. Computerised integration of the signals was then used for tridimensional reconstruction of the markers movements. Tridimensional reconstruction was complete in 342 of the 380 recorded movements. Angles were computed as follows: *head orientation* as the angle of the (1)-(2) segment relative to the horizontal; *arm orientation* as the (3)-(5) segment relative to the horizontal; *trunk orientation* as the (3)-(7) segment relative to the vertical; *hip* as the (6)-(7)-(8) angle; *knee* as the (7)-(8)-(9) angle; and *ankle* as the (8)-(9)-(10) angle. The final position of the head relative to the body stature was measured as the ratio between the vertical displacement of ear marker (2) from the onset and to the end of movement, and the length of the vertical projection of ear-foot (2)-(9) distance at the onset of movement. Surface EMG activity was recorded at a sampling rate of 1000 Hz using a telemetry system and adhesive silver–silver chloride surface electrodes placed over the right anterior, vastus lateralis, biceps femoris, semi-membranous, tibialis anterior, lateral gastrocnemius and soleus muscles.

2.6. Statistical analysis

Analysis of variance (ANOVA) between sets of data and linear regression were computed using the Statistica Software (StatSoft, Tulsa, OK, USA).

2.7. Ethical aspects

This project has been approved by the local Ethics Committee of the University Children's Hospital Queen Fabiola (Université Libre de Bruxelles). Informed consent was obtained from the parents and (as much as possible) patients after the nature of the procedure had been fully explained.

3. Results

3.1. Kinematics

As illustrated in Fig. 1A, normal children kept their trunk practically erect throughout the movement. Head and arm orientation was maintained throughout the movement, realising dissociated flexion of the lower limbs with preserved extension of the upper part of the body. In contrast, children with SDPL (Fig. 1B) and AS (Fig. 1C) demonstrated less dissociation in the movement, with loss of head and arm orientation and trunk verticality as lower limbs flexion was performed. The loss of trunk verticality was more marked in AS than SDPL. The ankle joint movement was minimal in both pathological groups. Whereas the normal children's movement consisted of vertical translation of most body segments, the movement of SDPL children was operated around the fixed knee, with backward shift of the hip, and children with AS chiefly performed a
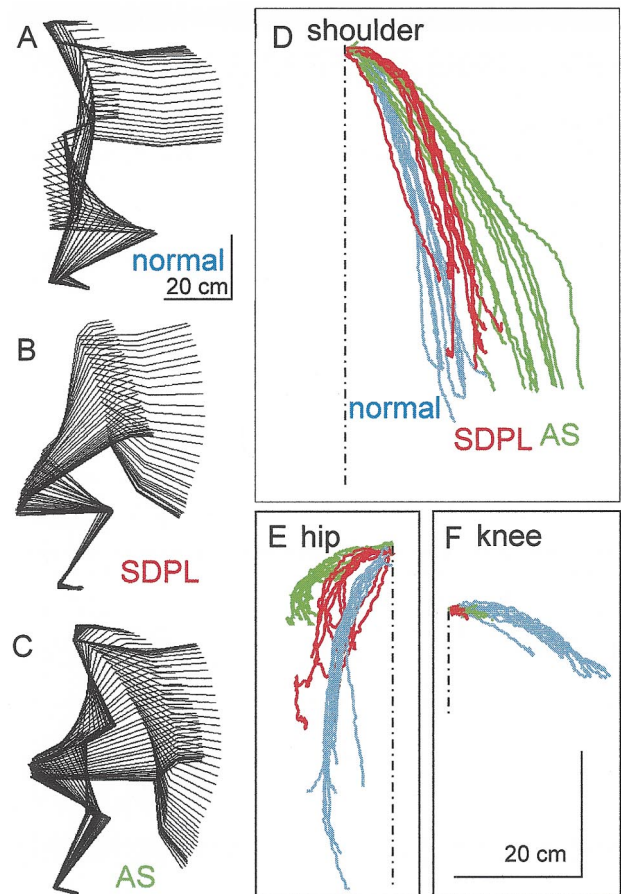

Fig. 1. Sagittal kinogram of the squatting movement. Kinograms represent the superimposition of the sagittal projections of the segments defined by the markers every 40 ms from the standing posture to the squatting posture in a normal child (A), a child with SDPL (B) and a child with AS (C). Trajectories of the shoulder (D), hip (E) and knee (F) during one movement trial performed by 10 children from each group are represented superimposed (blue, normal group; red, periventricular leucomalacia, SDPL; green, Angelman syndrome, AS).

flexion of the trunk over the thigh. Differential angles between the onset and the end of the movement in the sagittal field are presented in Table 2 for the head, trunk and arm orientation, and hip, knee and ankle joints. Except for the hip angular variation, all showed significant differences between the normal and pathological groups. There were no statistical differences between the final position of the head recorded in the 3 groups, as it corresponded to a descent by $44.23 \pm 7.85\%$ relative to the body stature for normal children, $44.84 \pm 6.88\%$ for SDPL and $45.34 \pm 7.12\%$ for AS. However, examination of the shoulder, hip and knee trajectories in the sagittal plane revealed marked within-group stereotypies in orientation, shape and length, and a clear dissociation of the 3 groups of children (Fig. 1D). In normal subjects, the orientation of the shoulder and hip trajectories was relatively straight with a downward–forward and downward–backward direction, respectively. This was quantified by calculating the angle of the regression line of these trajectories with respect to the vertical, giving values of 16.92 ± 2.61 and $-18.45 \pm 5.95°$, respectively. The knee trajectory of normal subjects presented a much greater horizontal component (with an angle of linear regression of $63.39 \pm 6.51°$ with respect to the vertical). By contrast, the SDPL children displayed more curved shoulder and hip trajectories with respective orientation angles of 23.62 ± 6.87 and $-40.47 \pm 11.07°$ that differed significantly from normal values ($F = 143.80$ and 46.90, respectively, $P < 0.001$) and virtually no movement of the knee marker. In AS children, shoulder and hip trajectories diverged even more from normal ones (34.15 ± 11.15 and $-63.72 \pm 17.99°$), being significantly different from SDPL ($F = 34.18$ and 43.12, respectively, $P < 0.001$). In particular, the initial part of the hip trajectory was close to the horizontal. As in SDPL, the knee remained fixed in space. Whereas both pathological groups showed marked deviations of shoulder and hip trajectories from the vertical, distinctive features between SDPL and AS were greater length of hip trajectory in the former and of shoulder trajectory in the latter.

The time interval between the onset and the end of knee flexion was significantly higher in AS (mean 2246 ± 648 ms) than in SDPL (mean 1199 ± 433 ms) and normal chil-

dren (mean 817 ± 232 ms) ($P < 0.05$). No correlation was found between the extent of white matter lesions and kinematic results in SDPL nor between the mode of inheritance and kinematic results in AS patients.

In normal children, the profile of angular velocity of the knee showed a short, single-peaked ascending phase and a longer descending phase with an inconsistent number of subcomponents (Fig. 2A, top trace) reflecting unrestrained postural unloading followed by braking action. In SDPL and AS children, the standing posture preceding the movement was relatively unstable, as evidenced by small oscillations in the angular velocity of the knee (Fig. 2B,C, top trace). During the movement, the ascending phase of this velocity profile was prolonged and showed multiple peaks, reflecting early braking action. The maximal amplitude of the velocity was significantly higher in normal (mean $223.29 \pm 47.30°$ s^{-1}) than in SDPL children ($132.45 \pm 59.61°$ s^{-1}; $P < 0.01$), and significantly higher in SDPL than in AS ($109.97 \pm 44.50°$ s^{-1}; $P < 0.05$). Fig. 2 shows the relationship between trunk excursion and peak knee angular velocity for each group. No significant correlation was found in normal children (Fig. 2A, $r = 0.50$), but there was an inverse significant correlation between trunk angular deviation and knee velocity in SDPL (Fig. 2B, $r = 0.67$) and AS (Fig. 2C, $r = 0.76$).

3.2. EMG activities

Whereas minimal activity was recorded in most muscles in normal and AS children in the standing position (Fig. 3A,C EMG traces prior to the onset of movement marked by the dotted line), SDPL children had generalised tonic activity (Fig. 3B, EMG traces prior to the movement marked by the dotted line). If a normal child had a postural tonic activity in the semi-membranous muscle, this was deactivated 130–200 ms before the onset of the movement (Fig. 3A, arrow). Such a deactivation was neither found in SDPL nor in AS. On the contrary, in 40–80% of trials in 5 SDPL children, an anticipatory burst of EMG activity was recorded in the soleus muscle (Fig. 3B, arrow). The latter contributed, together with the tibialis anterior muscle, to locking the ankle as a postural preparation for the move-

Table 2
Kinematic data of normal children, children with periventricular leucomalacia and with AS[a]

	Normal children	Periventricular leucomalacia	AS	
Head orientation	$0.96 \pm 7.94°$	$-15.86 \pm 16.18°$	$-12.70 \pm 23.17°$	N > SDPL,AS
Trunk orientation	$-39.00 \pm 8.86°$	$-49.14 \pm 12.44°$	$-79.62 \pm 19.02°$	N,SDPL > AS
Arm orientation	$-15.48 \pm 16.22°$	$-51.38 \pm 27.52°$	$-59.83 \pm 21.66°$	N > SDPL,AS
Hip	$96.12 \pm 17.71°$	$68.98 \pm 28.33°$	$82.24 \pm 24.66°$	N,SDPL,AS
Knee	$109.81 \pm 19.61°$	$68.36 \pm 23.68°$	$65.83 \pm 20.90°$	N > SDPL,AS
Ankle	$25.93 \pm 7.83°$	$0.46 \pm 4.09°$	$4.55 \pm 7.96°$	N > AS > SDPL

[a] Mean differential angles ($\pm$standard deviation) between the initial and final orientation of the head, trunk and arm, and maximal angular variation of the hip, knee and ankle in the sagittal field are shown. The last column shows statistically significant differences ($P < 0.05$) between sets of values. (Key – N, normal children; SDPL, spastic diplegia associated with periventricular leucomalacia; AS, Angelman syndrome; >, significantly greater than; ',', not statistically different from.)
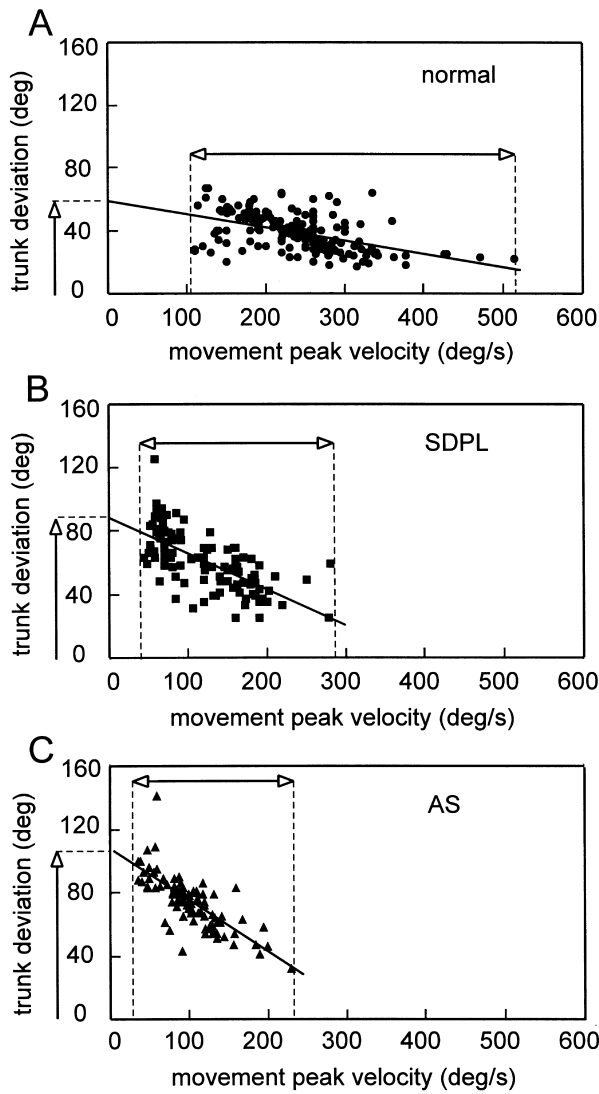
Fig. 2. Relationship between trunk forward excursion and peak angular velocity of the knee. (A) In the normal children. (B) In the children with SDPL. (C) In the children with AS. Horizontal arrows index the range of movement velocities for each group. Vertical arrows index the projection of the regression line of trunk deviation at zero-velocity.

profile. After the end of the movement, virtually no EMG activity was recorded in normal and AS children, but patients with SDPL retained tonic activity in most recorded muscles.

4. Discussion

This study describes the motor strategy for squatting observed in normal children and patients with spastic diplegia of two different aetiologies, namely perinatal white matter injury of prematurity and AS. Kinematic analysis revealed differences in multi-joint control. Normal children performed the movement using the motor strategy recently described for children of 3–12 years (Dan et al., 1999) and adults (Cheron et al., 1997). It consists of coordinated hip, knee and ankle flexion resulting in quasi-rectilinear trajec-
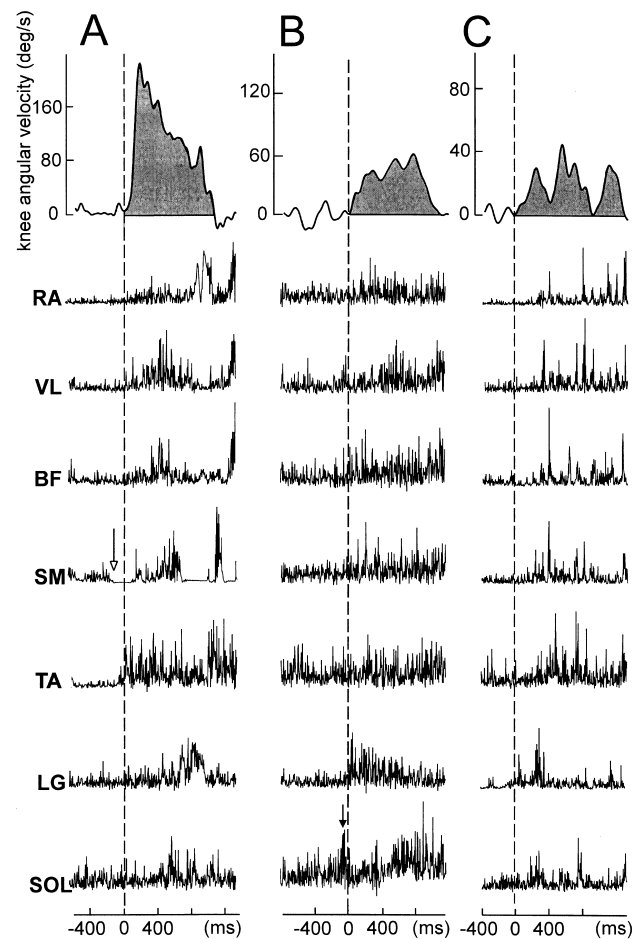

Fig. 3. Knee angular velocity and muscle activities during the squatting movement. (A) In a normal child. (B) In a child with SDPL. (C) In a child with AS. EMG signals are rectified. RA, rectus anterior muscle; VL, vastus lateralis muscle; BF, biceps femoris muscle; SM, semi-membranous muscle; TA, tibialis anterior muscle; LG, lateral gastrocnemius muscle; SOL, soleus muscle. The dotted line indexes the onset of movement. The open-headed arrow marks the anticipatory deactivation of the SM in the normal child. The black-headed arrow shows the anticipatory burst of SOL activity in the child with periventricular leucomalacia.

ment. No consistent anticipatory changes in muscle activity were detected in the patients with AS. During the movement, no clear braking activities were observed in normal children until the maximal peak of knee angular velocity, except for the tibialis anterior muscle, which became active from the outset of the movement. After the maximal peak of velocity, braking activities consisted of EMG bursts in most recorded muscles. In contrast, children with SDPL had phasic co-contraction activities in the quadriceps, biceps femoris, semi-membranous and lateral gastrocnemius muscles from the outset of the movement. Patients with AS showed early rhythmic bursts of activity in all recorded muscles before the maximal peak of knee angular velocity, but this consistently occurred after the movement had started, corresponding to the subcomponents of the velocity

tories of the body segments with conservative postural adjustment for trunk, head and arm orientation. Although the required movement accuracy was low, the trajectories were remarkably reproducible, suggesting a control of eventual deviations as proposed in the minimum-variance model (Harris and Wolpert, 1998). The peak velocity was high, in accordance with the task instruction, reflecting high pulse magnitude of the command signals, which imply high biological noise in the final control signals. This control signal-associated noise should cause trajectories to deviate, leading to variability in the trajectory paths, unless specific control reduces the effect of noise on the actual trajectory, as reflected in the complex deceleration profile (Fig. 3). The oscillation in the deceleration profile suggests a feed-back regulation process. This would require a stable frame of reference for collecting and integrating information from directional and orientation sensors, which may account for the high stability ensured to head angular orientation throughout the movements. Furthermore, feed-forward control is suggested by anticipatory deactivation of anti-gravity muscles, as previously described for various upper limb (Hufschmidt and Hufschmidt, 1954; Hoffman and Strick, 1995) and lower limb movements (Cheron et al., 1997; Dan et al., 1999; Dan and Cheron, 2000b). This phenomenon ensures interruption of posture controlled by the antagonist muscles, facilitating prompt initiation of movement by a brisk activation of agonist muscles. It is thought to be mediated by the primary motor cortex (Hoffman and Strick, 1995). Taking advantage of gravity, the ankle joint leads the movement with isolated tibialis anterior contraction consistent with a reciprocal command, which may be viewed as an optimal strategy developed for an unimpaired system.

The two groups with diplegia had distinct and consistent strategies that were different from that of the normal children, being neither simplified nor truncated forms of it. The main similarities between SDPL and AS performance were lower extremity stiffening, agonist–antagonist muscle co-activation patterns and non-conservative postural reactions of trunk, head and arms. Using lower extremities co-contraction for locking the ankle joint can be a solution to ensure greater stability in a context, where selective movements cannot be realised, whether over basal hypertonia, as in SDPL (Galli et al., 1999), hemiplegic cerebral palsy (Galli et al., 1999) or hereditary spastic paraplegia (Dan and Cheron, 2000b; Dan et al. 2000b), or hypotonia, as in Down syndrome (Aruin et al., 1996). This reflects non-selective, non-variable coordination of muscle contraction as shown for other tasks in SDPL (Nashner et al., 1983; Woollacott et al., 1998) and AS (Dan et al. 2000c). As for other aspects of motor control in cerebral palsy, it may not result from perturbed monosynaptic stretch reflex, but from interaction between multiple spinal and supra-spinal systems which do not crucially depend on afferent information about the environment, the position of the body and the interaction between the environment and the body (Woolla-

cott et al., 1998; Dietz, 1999). Nashner et al. (1983) showed that equilibrium challenges imposed on the distal part of the lower limbs result in a proximal-to-distal sequence of muscle activation in children with hemiplegic, spastic diplegic and ataxic cerebral palsy. In our study, the equilibrium challenge, primarily affecting the proximal part of the lower limbs, was followed by distal-to-proximal stiffening, resulting in shorter trajectories of the knee and hip as compared with normal subjects. This was more marked in AS than in SDPL. Therefore, the former essentially realised the movement by bending the trunk forwards, whereas SDPL patients operated a backward rotation of the body around the knee. The concurrent loss of head and trunk is consistent with Magnus's and de Kleijn's (1912) classic observation of altered extensor muscle tone in cats with retro-rubral transection when the head position is changed. It is also reminiscent of the Landau reflex in newborn infants, which consists of hip, knee and elbow flexion in response to head flexion.

In whole-body movements, the level of trunk stability is a distinctive feature of mature vs. immature (Ledebt et al., 1995; Cheron et al., 2001), skilled vs. unskilled movement (Mouchnino et al., 1992), and treated vs. untreated movement disorder (Grasso et al., 1999). As discussed before, the 'as fast as possible' requirement used in this study implies high signal controls, and therefore a high level of signal-dependent biological noise, which should result in increasing kinetic variation, and therefore postural instability, with increasing speed of movement. However, as suggested by the reproducibility of trajectory paths, movement organisation was consistent with the minimum-variance theory, which predicts an optimised trade-off between movement duration and postural stability (Harris and Wolpert, 1998). Accordingly, the correlation we found in the present study between trunk stability and movement velocity suggests that trunk stability was integrated in the motor organisation as a primary variable representing a quality factor for the task. Therefore, when higher postural stability could be achieved, higher velocities could be developed (Fig. 2). This is consistent with findings in reaching tasks, where displacements of the centre of mass decreased with increasing movement speed (Stapley et al., 1998). Although a similar trend was observed in normal children, the absence of significant correlation between trunk stability and movement velocity could be explained by the fact that in normal subjects, a high level of trunk stability is achieved even in the slower movements, and the increase in movement velocity is likely to reflect the influence of additional factors which can be managed by an unimpaired nervous system.

Although the programme of physical therapy was not the same in all the patients, the homogeneity of motor strategy within each group suggests that the impact of management differences was not determinant. However, the generally lower level of attention and cognition in AS than in SDPL may have a role in the executive differences between these groups. The differences in strategies between SDPL and AS could be explained by differences in neural constraints.

Anatomo-clinical correlations have been extensively studied in SDPL. This condition is due to haemodynamic failure in a context of respiratory immaturity resulting in ischaemia and/or hypoxia in watershed areas between arterial territories, selectively affecting the posterior arm of the internal capsule. The motor impairment is essentially due to corticospinal tract lesion, with lower limb predominance related to the topographic distribution of periventricular descending fibres. In AS, the neural deficit underlying the motor disorder has been much less documented. Cognitive impairment and seizure disorder in AS suggest cortical dysfunction. Pyramidal-like lack of motor selectivity has been noted clinically since the original report, typically exemplified with upper limb posturing during walking (Angelman, 1965), and long tract clinical signs are so common (Hou et al., 1997) that they have been included in the diagnostic criteria (Williams et al., 1995). Similarly, cerebellar dysfunction was already suspected by Angelman (1965). Neuroradiological studies of AS have shown no abnormalities except for some reports of mild to moderate non-specific cerebral atrophy. Available neuropathological studies of AS concern only two cases. One documented cerebellar atrophy, which may have been secondary to anticonvulsant therapy (Jay et al., 1991). In the other one, a few isolated ectopic neurons were seen, including one Purkinje cell heterotopia, the cerebellum being otherwise normal (Kyriakides et al., 1992). The recent identification of a responsible gene for AS and the development of animal models have opened the way to more specific studies. Early results demonstrated selective imprinting of the Ube3a gene in the hippocampus and cerebellum of mice, resulting in reduced expression of the gene in hippocampal neurons and Purkinje cells in animals with the silencing of both alleles due to paternal uniparental disomy (Albrecht et al., 1997). The phenotype of deficient mice resembles human AS (Dan, 2000). Another mouse model is based on the absence of the gene for the β_3-subunit of the γ-aminobutyric acid type A receptor in AS due to 15q11-13 deletion (Homanics et al., 1997). This subunit is widely distributed throughout the brain and has an important role in inhibition mechanisms. Diminished γ-aminobutyric acid in the cerebellum of one autopsied AS patient (Jay et al., 1991) is related likely to the defect of this gene. Lack of movement selectivity observed in AS is consistent with reduced presynaptic inhibition in the spinal cord and cerebral cortex, as well as with recent views on dynamic selection in the cerebellum (Bloedel, 1994). The greater extent of multiple joint stiffening in AS as compared to SDPL may represent an adaptive compensation for the inability to control dynamic interaction forces, which depend on the cerebellum (Bastian et al., 2000).

We conclude that the motor patterns observed in SDPL and AS are different. They reflect individual adaptation to the impairment of the central nervous system characteristic of each condition. Taken phenomenologically, these patterns can contribute to the clinical approach to spastic diplegia. They may also have implications on the management of the motor disorder of affected patients, as understanding of relatively simple but important motor skills such as squatting will likely have an increasing clinical relevance in the context of the development of new therapies to improve motor skills, including pharmacological and surgical procedures directed at neurological disorders with muscle tone impairment. This study stresses the importance of multi-joint movements involving intersegmental interactions for postural control (Cheron et al., 1998). In particular, the present paradigm could be practically applied at a gait and posture laboratory before and following specific treatments (Dan and Cheron, 2000b).

Acknowledgements

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