Locomotor patterns in cerebellar ataxia

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Martino G, Ivanenko YP, Serrao M, Ranavolo A, d’Avella A, Draicchio F, Conte C, Casali C, Lacquaniti F. Locomotor patterns in cerebellar ataxia. J Neurophysiol 112: 2810–2821, 2014. First published September 3, 2014; doi:10.1152/jn.00275.2014.—Several studies have demonstrated how cerebellar ataxia (CA) affects gait, resulting in deficits in multijoint coordination and stability. Nevertheless, how lesions of cerebellum influence the locomotor muscle pattern generation is still unclear. To better understand the effects of CA on locomotor output, here we investigated the idiosyncratic features of the spatiotemporal structure of leg muscle activity and impairments in the biomechanics of CA gait. To this end, we recorded the electromyographic (EMG) activity of 12 unilateral lower limb muscles and analyzed kinematic and kinetic parameters of 19 ataxic patients and 20 age-matched healthy subjects during overground walking. Neuromuscular control of gait in CA was characterized by a considerable widening of EMG bursts and significant temporal shifts in the center of activity due to overall enhanced muscle activation between late swing and mid-stance. Patients also demonstrated significant changes in the intersegmental coordination, an abnormal transient in the vertical ground reaction force and instability of limb loading at heel strike. The observed abnormalities in EMG patterns and foot loading correlated with the severity of pathology [International Cooperative Ataxia Rating Scale (ICARS), a clinical ataxia scale] and the changes in the biomechanical output. The findings provide new insights into the physiological role of cerebellum in optimizing the duration of muscle activity bursts and the control of appropriate foot loading during locomotion. In humans, the gait impairment characterizing cerebellar ataxia (CA) is often clinically described as “drunken gait,” as the clinical features typically observed include a widened base of support and an irregular gait pattern (Holmes 1939). Several studies investigated the biomechanical characteristics of patients with CA, finding these to consist of decreases in step length, gait speed, and ankle torques; increased step width; impaired interjoint coordination; and marked variability of all global and segmental gait parameter values (Palliyath et al. 1998; Mitoma et al. 2000; Earhart and Bastian 2001; Stolze et al. 2002; Morton and Bastian 2003; Ilg et al. 2007; Serrao et al. 2012; Wuehr et al. 2013). All these gait abnormalities, reflecting a lack of limb coordination and impaired balance, greatly restrict these patients in their daily life activities and predispose them to falls (Van de Warrenburg et al. 2005b; Nardone and Schieppati 2010).

No studies have yet been performed to provide a detailed analysis of muscle activity patterns during locomotion in patients with CA. Furthermore, no information on the relationship between the observed kinematic and kinetic abnormalities and the related muscle activity has been provided so far. Therefore, the specific contribution of the cerebellum to the production of locomotor muscle pattern behaviors in humans is still unclear. Impaired processing of sensorimotor information in the cerebellum about foot kinematics and kinetics (Bosco et al. 2006) may also disturb the limb loading and placement. Previous findings suggest that the cerebellum helps in modulating sensorimotor interactions, integrates both feedforward and feedback control of balance, and plays a functional role in motor learning and adaptation (Horak and Diener 1994; Morton and Bastian 2004; Konczak and Timmann 2007; Bastian 2011; Goodworth et al. 2012; Ilg and Timmann 2013). Thus lesions of the cerebellum may induce abnormalities in the spatial and temporal pattern of muscle activation resulting in specific gait impairments.

The aim of this study was to provide a wider characterization of ataxic gait by exploring the muscle activation patterns of patients affected by CA and correlating them with the kinematics, kinetics, and degree of severity of the pathology. The first objective was to test the hypothesis that subjects with cerebellar damage show abnormalities in switching and scaling individual muscles resulting in prolonged activity, as it occurs during upper limb movements in CA (Hallett et al. 1975) or during early development of locomotion (Dominici et al. 2011) when the cerebellum is still immature (Vasudevan et al. 2011). As a secondary objective, we studied the kinematic and kinetic

CEREBELLUM IS KNOWN TO PLAY a critical role in the production of locomotor behavior (Lennard and Stein 1977; Grillner et al. 1995; Roberts et al. 1995; Rossignol et al. 1998). Several physiological studies on animals, in fact, have described how lesions at different regions of cerebellum are responsible for different deficits in locomotion (Thach and Bastian 2004). The medial cerebellar region plays a primary role in static and dynamic balance control and in modulating the rhythmic flexor and extensor muscle activity. The intermediate and lateral cerebellar regions appear to be more important for directing limb placement and fine adjustments to the normal locomotor pattern in novel or complex circumstances or when strong visual guidance is required (Morton and Bastian 2007).

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behavior of whole lower limb by analyzing the multiple joint coordination as well as the ground reaction force (GRF) during loading response. Particularly, we sought to investigate whether the loading response in CA is impaired during weight acceptance, representing the most demanding task to guarantee the initial limb stability and the preservation of progression (Perry 1992). To assess the coordination deficits, we used the methods developed earlier for normal gait (Borghese et al. 1996; Lacquaniti et al. 2002) and we expected that applying this analysis technique to CA patients may highlight specific alterations in the planar covariation of limb segment elevation angles (Dominici et al. 2010; MacLellan et al. 2011; Leurs et al. 2012). To this end we investigated a sample of patients with primary degenerative pancerebellar diseases. These cerebellar disorders may represent an appropriate model to investigate the role of cerebellum as a whole in locomotor pattern generation.

MATERIALS AND METHODS

Participants

Nineteen patients [5 females and 14 males; age range: 32–65 yr, weight: 68 ± 8 kg (means ± SD), and leg length: 0.78 ± 0.06 m] affected by inherited CA, and twenty-age-matched healthy subjects (HS; 7 females and 13 males; age range: 34–70 yr, weight: 70 ± 14 kg, and leg length: 0.80 ± 0.05 m) were studied. The characteristics of patients are described in Table 1. Eleven patients had a diagnosis of autosomal dominant ataxia (spinocerebellar ataxia, 7 pts with SCA1 and 4 pts with SCA2), while the other eight had sporadic adult onset ataxia of unknown etiology (SAOA). Even if extracerebellar involvement is common in both SCA1 and 2, none of our patients was found to have clinically significant signs other than cerebellar ones. In particular, they did not show extrapyramidal or pyramidal signs nor signs of peripheral nerve or muscle deficits, which tend to be overt over the course of the disease. All patients were at a relatively early stage of disease as demonstrated by the low International Cooperative Ataxia Rating Scale (ICARS) (Table 1), so that within the limits of clinical ascertainment methods they can be regarded as relatively “pure” cerebellar patients. All patients underwent a complete neurological assessment that included the following: 1) cognitive evaluation [Mini-Mental State Examination (MMSE) scale]; 2) cranial nerves evaluation; 3) muscle tone evaluation; 4) muscle strength evaluation; 5) joint coordination evaluation; 6) sensory examination; 7) tendon reflex elicitation; and 8) disease severity measured by ICARS (Trouillas et al. 1997). Particularly, sensation was tested clinically for light touch, pain, joint position, and vibration, starting from the toes and moving proximally; touch was tested by a wisp of cotton, pain by a sharp pin, and vibration by a 128-Hz tuning fork; and proprioception was investigated by asking five times the blinded patient to describe the position of the second toe and the ankle, which were passively moved upward or downward by the examiner, avoiding end-of-range-of-motion position (DeMyer 2003). In each of these three sensory tests, we assessed whether sensation was normal, reduced, or absent, specifying the region of the body. All the patients were evaluated by two experienced neurologists (C. Casali and M. Serra).

No patient had any kind of visual impairment, in particular no optic atrophy or retinitis pigmentosa were revealed. On the other hand, almost all patients had oculomotor abnormalities such as gaze nystagmus or square waves during pursuit movements, which are common in cerebellar disorders with no obvious impairment of visual acuity. No patient showed clinical features of spasticity, strength deficit, sensory deficit, and/or cognitive impairment (MMSE >26). Furthermore, no relevant interlimb asymmetries in terms of dysmetria, ataxia, and hypotonia and limb kinetic ICARS scores were found between right and left side. All patients showed (at MRI) pancerebellar degenerations with significant atrophy of the cerebellar vermis. Patients enrolled in our study were undergoing physical therapy, which included upper and lower limb exercises, balance, and gait training. All participants were capable of walking independently on a level surface, and they provided informed written consent before taking part in the study, which complied with the Helsinki Declaration and had local ethics committee approval.

Procedures and Data Recording

Subjects were asked to walk barefoot along a walkway, ~7 m in length, while looking forward. They walked at comfortable self-selected speeds but were encouraged to walk also at the fastest speed.
at which they still felt safe, resulting in a range of different speeds across the recorded trials. Given that typical walking speeds were on the slow side in patients, we instructed the healthy control subjects to also walk barefoot at low comfortable speeds (~30–50% slower than self-selected speed) to roughly match the walking speed in the two groups of subjects. Before the recording session, subjects practiced for a few minutes to familiarize with the procedure. To ensure safe walking conditions, an assistant walked alongside the patients during the trials when necessary. To avoid muscle fatigue, groups of three walking conditions, an assistant walked alongside the patients during a few minutes to familiarize with the procedure. To ensure safe groups of subjects. Before the recording session, subjects practiced for also walk barefoot at low comfortable speeds (~30–50% slower than self-selected speed) to roughly match the walking speed in the two groups of subjects. Before the recording session, subjects practiced for a few minutes to familiarize with the procedure. To ensure safe walking conditions, an assistant walked alongside the patients during the trials when necessary. To avoid muscle fatigue, groups of three walking conditions, an assistant walked alongside the patients during a few minutes to familiarize with the procedure. To ensure safe groups of subjects. Before the recording session, subjects practiced for

The following general gait parameters were calculated for each subject: walking speed, cycle duration, relative stance duration, stride length, and stride width. The stride length and width were normalized to the limb length (thigh + shank) of each subject. We computed both the anatomical joint angles and the elevation angles of the limb segments relative to the vertical for the right lower limb (Borghese et al. 1996), as well as the pitch and roll angles for the trunk. From these variables, we derived the range of angular motion (RoM). The kinematic data were time interpolated over individual gait cycles to fit a normalized 200-point time base. We also assessed the interstride angular variability by calculating the mean standard deviation (SD) of the joint and trunk orientation angles.

Most coordination analyses of gait in CA (Earhart and Bastian 2001; Stolze et al. 2002; Morton and Bastian 2003; Ilg et al. 2007) involved the use of angle-angle plots and thus examined movement at two joints at a time. We used a more advanced analysis technique, termed the planar law of intersegmental coordination, which allows us to examine movement coordination at the thigh, shank, and foot segments simultaneously (Borghese et al. 1996; Lacquaniti et al. 2002). Briefly, the temporal changes of the elevation angles at the thigh, shank, and foot covary during walking. When these angles are plotted in three dimensions (3D), they describe a loop that can be least-squares fitted to a plane over each gait cycle (Borghese et al. 1996). A principal component analysis was applied to the group of three segment elevation angle trajectories to determine covariance loop planarity, width, and orientation. To this end, we computed the covariance matrix of the ensemble of time-varying elevation angles over each gait cycle. The first two eigenvectors $u_1$ and $u_2$ lie on the best-fitting plane of angular covariation, and the third eigenvector ($u_3$) is normal to the plane and thus defines the plane orientation. The planarity of the trajectories was quantified by the percentage of total variation ($PV_1$) accounted for by the third eigenvector of the data covariance matrix (for ideal plane rotation $PV_1 = 0\%$). Covariance loop width was determined using the percent variance ($PV_2$) explained by the second eigenvector $u_2$ since it is oriented in the direction of the minor axis of the loop formed by the elevation angles (if $PV_2$ is small, the thigh-shank-foot loop tends to be a line; Ivanenko et al. 2008). Covariance plane orientation was quantified using the direction cosine between the third principal axis and the positive semi-axis of the thigh segment ($\alpha_{th}$), which was found to vary depending on walking conditions (Bianchi et al. 1998; Ivanenko et al. 2008) or gait pathology (Grasso et al. 1999, 2004; MacLellan et al. 2011; Leurs et al. 2012). For each subject, the parameters of planar covariation ($\alpha_{th}$, $PV_1$, $PV_2$, and $PV_3$) were averaged across strides.

**Ground reaction forces.** The steps in which only the right foot stepped onto one of the force plates were analyzed. The vertical GRF was calculated and normalized to the body mass (Winter 1991). In addition, because the lower limb can undergo an impulsive load, the heel strike transient (Verdini et al. 2006) during the weight-acceptance period was evaluated by calculating the peak-to-peak change between the transient maximum and the following local minimum in the GRF ($\Delta_1$, see Fig. 4A). If this transient was absent, the change was considered equal to zero. Since the transient may also be related to limb instability or to small oscillations of the limb during the heel strike, we evaluated the corresponding kinematics correlates: the peak-to-peak change between maximum and minimum values of the vertical velocity of three markers placed on the greater trochanter (hip), lateral femur epicondyle (knee), and lateral malleolus (ankle) during the 0–10% interval of the stance phase ($\Delta_2$, Fig. 4B).

**Assessment of EMGs.** The raw EMG signals were band-pass filtered using a zero-lag third-order Butterworth filter (20–450 Hz), rectified, and low-pass filtered with a zero-lag fourth-order Butterworth filter (10 Hz). The time scale was normalized by interpolating individual gait cycles over 200 points. For each individual, the EMG signal from each muscle was normalized to its peak value across all trials.

To characterize differences in the amplitude and timing of EMG activity between CA and HS groups, we computed the following parameters: mean and maximum EMG activity (in $\mu$V), antagonist...
coactivation index (CI), center of activity (CoA), and full width at half maximum (FWHM). EMG parameters were calculated over individual strides and then averaged across cycles.

The CI was assessed between the thigh (mean activity of quadriceps RF-FL-VM vs hamstrings BF-ST) and calf (mean activity of triceps MG-LG vs TA) antagonist muscle groups using the following formula (Rudolph et al. 2000; Mari et al. 2014):

$$CI = \frac{\sum_{j=1}^{200} \left( [EMG_{H}(j) + EMG_{L}(j)]/2 \right) \times [EMG_{H}(j)/EMG_{H}(j)]}{200}$$

where $EMG_{H}$ and $EMG_{L}$ represent the highest and the lowest activity between the antagonist muscle pairs. To have a global measure of the coactivity level, the CI was then averaged over the entire gait cycle ($j = 1:200$). This method provided a sample-by-sample estimate of the relative activation of the pair of muscles as well as the magnitude of the cocontraction over the entire cycle. With the use of this equation, high cocontraction values represent a high level of activation of both muscles across a large time interval, whereas low cocontraction values indicate either low level activation of both muscles or a high level activation of one muscle along with low level activation of the other muscle in the pair (Rudolph et al. 2000).

The CoA during the gait cycle was calculated using circular statistics (Batschelet 1981) and plotted in polar coordinates (polar musculature). The CoA of the EMG waveform was calculated as the angle of the vector (1st trigonometric moment) that points to the center of mass of that circular distribution using the following formulas:

$$A = \sum_{j=1}^{200} (\cos \theta \times EMG_{j})$$

$$B = \sum_{j=1}^{200} (\sin \theta \times EMG_{j})$$

$$CoA = \tan^{-1}(B/A)$$

The CoA was chosen because it was impractical to reliably identify a single peak of activity in the majority of muscles, especially in pathological subjects. It can only be considered as a qualitative parameter, because averaging between distinct foci of activity may lead to misleading activity in the intermediate zone. Nevertheless, it can be helpful to understand if the distribution of muscular activity remains unaltered across different groups and muscles.

The FWHM for each EMG waveform was calculated as the sum of the durations of the intervals in which the EMG activity (after subtracting the minimum throughout the gait cycle) exceeded the half of its maximum.

**Statistics**

Between groups differences in the spatiotemporal gait parameters, intersegmental coordination, interstride variability, and FWHM were assessed by performing unpaired two-sample t-tests. The analysis of CoA was performed using the Watson-Williams test for circular data (Watson and Williams 1956). The correlation between kinematics, kinetics, muscle activation patterns, and clinical scores was performed using Spearman’s rank correlation coefficient. The correlation coefficients used in the regression plots were corrected for multiple samples from the same participants. Descriptive statistics included means ± SD, and significance level was set at $P < 0.05$. All statistical analysis were performed using Statistica (v7.0) and custom software written in Matlab (v8.1).

**RESULTS**

**General Gait Parameters and Kinematics**

At matched walking speeds, cerebellar patients showed a significant increase in the stride width, reduction in the cycle duration and stride length compared with healthy controls (Fig. 1A). Instead, the relative stance duration was not significantly different in the two groups. These results are consistent with previous studies (Palliyath et al. 1998; Mitoma et al. 2000; Serra et al. 2012). Figure 1B shows the ensemble-averaged kinematic patterns. The time course of changes of hip and knee joint angles of CA patients was very similar to that of HS. In contrast, a substantial reduction of the ankle joint excursion ($P < 0.00004$) and consistently larger oscillations in the trunk roll and pitch angles ($P < 0.0009$) were observed in CA relative to HS (Fig. 1C).

Figure 2A illustrates the stride-averaged (±SD) thigh, shank, and foot elevation angles and corresponding gait loops plotted in 3D for one representative HS (left) and one CA patient (right). In both groups, the temporal changes of the elevation angles covary during walking, describing a characteristic loop over each stride that is best-fitted by a plane (PV$_3$ < 1%; Fig. 2B). The percentage of variance accounted for by the second eigenvector (PV$_2$) was significantly greater in CA ($P < 0.002$) indicating a wider gait loop (Fig. 2B). The orientation of the covariance plane (u$_3$) was also significantly different between the two groups ($P < 0.0002$).

The stride-by-stride variability in gait kinematics was consistently larger in CA. Figure 3A illustrates superimposed plots of the hip, knee, ankle, and trunk pitch and roll angles during individual gait cycles in one control subject and one CA patient. On average, the interstride variability in the angles, estimated as the mean SD over the gait cycle, was ~50% greater in CA patients (Fig. 3B).

**Ground Reaction Forces**

Figure 4A illustrates the vertical component ($F_v$) of the GRF for both individual strides in single subjects (top) and averaged curves for all subjects (bottom). Both groups showed the typical two-peaked profile, with a first maximum during the initial stance phase (~25% of stance phase) and the second one at the end of stance (~80% of stance phase). A small additional peak during weight acceptance, at ~10% of stance, could also be observed (Fig. 4A), consistent with previous studies in HS (Borghese et al. 1996; Verdin et al. 2006). This peak was prominent in all CA patients, while it was seen only in a few control subjects at these slow to moderate speeds. We quantified the heel strike transient by calculating the $\Delta_1$ parameter (Fig. 4A): $\Delta_1$ was significantly larger ($P < 0.00004$) in CA compared to HS (Fig. 4C). The horizontal shear forces did not show systematic differences between the two groups and are not reported.

We also examined whether the augmented transient in the vertical GRF in CA (Fig. 4A) correlates with kinematic parameters. To this end, we computed the difference between maximum and minimum values of the vertical velocity of the markers located on the hip, knee, and ankle, measured at the beginning of stance (0–10% of the stance phase; $\Delta_2$ in Fig. 4B). Examples of velocity traces in one control subject and one CA patient are illustrated in Fig. 4B. The $\Delta_2$ parameter was
significantly larger \((P < 0.0001)\) for the knee and hip markers in patients (Fig. 4C), consistent with a greater instability of limb loading in CA as shown by the prominent transient in vertical force (Δ1, Fig. 4A).

**EMG Envelopes**

We recorded EMG signals from 12 muscles of the right lower limb. Figure 5A illustrates EMG traces in one HS and one CA patient during two consecutive strides. In both groups, EMG activity during walking tended to occur in bursts that were temporally related to specific kinematic/kinetic events: weight acceptance (VM, VL, RF, TFL, and GM), limb loading/propulsion (SOL, MG, LG, and PL), foot lift (TA), and heel strike (ST and BF). The normalized and ensemble-averaged EMGs for the two groups of subjects are illustrated in Fig. 5B. We noticed that the EMG profiles in CA patients often differed relative to those in HS in two main features. First, the major bursts tended to be wider (more prolonged) for most muscles. Second, EMG profiles of CA could show some extra bursts, presumably related to gait instability (Fig. 5A). For instance, the activity of hamstring muscles (BF and ST) in patients started earlier (at ~80% of gait cycle) and was prolonged till...
and FWHM (Fig. 6) activity between HS and CA groups, we computed the CoA of antagonist muscles (Fig. 5). The CoA analysis did not reveal any significant correlation between FWHM (expressed in %gait cycle) and walking speed in both groups. Although large interindividual variability was observed (in part due to the individual differences in skin impedance), on average the mean and the maximum amplitude was observed (in part due to the individual differences in skin impedance), on average the mean and the maximum amplitude increased activity in CA was found in both proximal and distal muscles.

EMG envelopes in Fig. 5B were normalized to the maximum value across all trials, but we also quantified the absolute mean activity and the extent of modulation of activity of leg muscles over the gait cycle. Although large interindividual variability was observed (in part due to the individual differences in skin impedance), on average the mean and the maximum amplitude of muscle activity over the gait cycle was about twice greater in CA patients than in HS patients (means SD: estimated as the mean SD of angular waveforms across strides averaged over all time points of the gait cycle) in HS and ataxic patients (means SD). *Significant group difference (P < 0.05).

CA patients showed significantly higher CI values throughout the gait cycle both for RF-VL-VM vs. ST-BF (11.7 ± 2.8 for CA and 9.3 ± 2.1 for HS; P < 0.01) and MG-LG vs. TA (15.5 ± 3.5 for CA and 8.7 ± 2.1 for HS; P < 0.00001) pairs of antagonist muscles (Fig. 5D).

To characterize differences in timing and duration of EMG activity between HS and CA groups, we computed the CoA and FWHM (Fig. 6A). The CoA was similar for many muscles for the two groups of subjects, although it shifted to slightly later phases of the gait cycle (counterclockwise in the polar plots) in proximal muscles (VL, ST, and BF), and to earlier phases (clockwise in the polar plots) in distal muscles (SOL, MG, LG, and PL) in CA patients with respect to HS (P < 0.00001; Fig. 6D). The analysis of FWHM allowed us to quantify the duration of activity of each muscle.

Figure 6B shows that most muscles (TA, hamstrings, and distal extensors) significantly increased their FWHM in CA patients compared with HS. The mean FWHM (across all muscles) in HS and CA was 20 and 29% of the gait cycle, respectively. Also, we verified whether the FWHM depended on velocity in the range of analyzed walking speeds (3–4.5 km/h). The analysis did not reveal any significant correlation between FWHM (expressed in %gait cycle) and walking speed in both HS and CA patients.
The FWHM was similar among different forms of CA: 29.2 clinical ICARS measures (see also Ilg et al. 2007; Serrao et al. increased stride-by-stride variability in CA patients and the HS (Fig. 3), there was no simple relationship between the stride variability in the kinematic parameters between CA and SAOA. While there were significant differences in the inter-

Correlations Between EMGs Activation Patterns, Clinical Scores, and Gait Parameters in CA

Figure 7A illustrates significant correlations between muscle activation pattern characteristics and kinematic and kinetic parameters in CA patients. We observed significant relationships ($P < 0.02$) among mean FWHM (averaged across all muscles) and cycle duration, stride length, and stride width of CA patients (Fig. 7A). For the intersegmental coordination and angular motion, we found a significant ($P < 0.01$) correlation of FWHM only with PV2 (Fig. 7A).

Figure 7, B–D, shows the relationship between clinical ICARS measures and gait parameters (which were significantly different between HS and CA). The following parameters correlated significantly with the ICARS score: cycle duration ($P = 0.04$), stride length ($P = 0.04$), stride width ($P = 0.03$), PV2 ($P = 0.02$; Fig. 7B), $\Delta_1$ of the GRF ($P = 0.02$), $\Delta_2$ of the hip and knee ($P = 0.01$ and $P < 0.001$, respectively; Fig. 7C), and mean FWHM of EMG envelopes ($P = 0.002$; Fig. 7D). The FWHM was similar among different forms of CA: 29.2 ± 8.9% for SCA1, 28.9 ± 7.1% for SCA2, and 28.3 ± 5.7% for SAOA. While there were significant differences in the inter-stride variability in the kinematic parameters between CA and HS (Fig. 3), there was no simple relationship between the increased stride-by-stride variability in CA patients and the clinical ICARS measures (see also Ilg et al. 2007; Serrao et al. 2012). Thus a large number of gait and muscle pattern parameters that were significantly different between CA and HS gaits (Figs. 1, 2, 4, and 6) correlated with the severity of pathology (ICARS score).

DISCUSSION

In this study we investigated muscle activity and the biomechanics of locomotion in a group of patients diagnosed with SCA1, SCA2, and SAOA conditions of CA. We analyzed the characteristics of EMG activity of 12 unilateral lower limb muscles, correlating them with the clinical score and global and segmental parameters extracted from the kinematics and GRFs. Our findings revealed new idiosyncratic features of the CA gait: significant changes in the intersegmental coordination (Figs. 1C and 2), an abnormal transient in the vertical GRF, and instability of limb loading at heel strike (Fig. 4). The marked feature of neuromuscular control of gait in CA was the widening of EMG bursts (Figs. 5 and 6). Below we discuss the relationship between the primary deficits and/or compensatory strategies and adaptive changes in the walking behavior and muscle activity patterns.

Kinematic Features of CA Gait

Several studies have compared the parameters characterizing locomotion of cerebellar patients with that of healthy controls. The results confirmed high variability of spatiotemporal gait parameters (Fig. 3), wide-base support, and reduced cycle
Fig. 5. EMG activity in HS and CA. A: examples of EMG traces in 1 HS (h4, 4.1 km/h) and 1 CA patient (p15, 3.4 km/h) during 2 consecutive strides. The stance phase is evidenced by a shaded region. B: ensemble-averaged (means ± SD) EMG activity patterns of 12 ipsilateral leg muscles recorded from HS and ataxic patients. EMGs were normalized to their maximum value across all trials. C: maximum and mean EMG levels (means ± SD) in microvolts. Note higher level of activity in CA. D: coactivation indexes (CI) of “RF-VL-VM vs. ST-BF” and “MG-LG vs. TA” pairs of antagonist muscles. TA, tibialis anterior; LG, gastrocnemius lateralis; MG, gastrocnemius medialis; SOL, soleus; PL, peroneus longus; VL, vastus lateralis; VM, vastus medialis; RF, rectus femoris; BF, biceps femoris; ST, semitendinosus; TFL, tensor fascia latae; GM, gluteus medium. *Significant group differences (P < 0.05).
duration and stride length (Fig. 1A) that has previously been shown to be distinctive features of ataxic locomotion aimed at compensating the wide oscillations of the center of mass due to poor dynamic balance and stability (Palliyath et al. 1998; Ilg et al. 2007; Serrao et al. 2012; Wuehr et al. 2013). Reduced RoM in the ankle joint in CA could be related to shorter steps (Fig. 1A), impaired intersegmental coordination (wider gait loop, Fig. 2), and/or stiffening of the ankle joint, which would reduce push-off forces necessary to propel the center of mass forward and upward, and thus destabilize the gait (Morton and Bastian 2003). Increased trunk sway (Fig. 1C, right) can be assumed to be related to multidirectional postural instability (Van de Warrenburg et al. 2005a).

The analysis of the intersegmental coordination in CA revealed significant changes in the covariance plane orientation (expressed by $u_2$; Fig. 2, right) and wider gait loop (expressed by the higher values of $PV_2$; Fig. 2). This is a significant finding, because the orientation of the covariance plane reflects a specific tuning of the phase coupling between pairs of limb segments and is related to an ability of the subject to adapt to different walking conditions (Bianchi et al. 1998; Dominici et al. 2010). For instance, in toddlers, the ability to adapt to different terrains is very limited and the maintenance of a roughly constant planar covariance reduces flexibility of the kinematic pattern and thus restricts the manifold of angular segment motion (Dominici et al. 2010). Likewise, it would be of a great interest to study whether there is also a lack of specific adaptation in the planar covariance of limb segments in CA during walking over different terrains (see, for instance, MacLellan et al. 2011).

**Foot Loading in CA**

In cerebellar patients, the vertical GRF demonstrated a prominent transient following the heel strike (Fig. 4), indicating an abnormal control of limb loading, correlated with the severity of the pathology (Fig. 7C). Even though it can be observed in healthy individuals during fast walking (Borghese et al. 1996), normally the intensity of this impact is adjusted by shock-absorbing reactions at the ankle, knee, and hip (Perry 1992) and it is small or absent at low and normal walking speeds (Fig. 4A, left). A similar peak was also found in other pathologies, like osteoarthritis and low back pain (Collins and Whittle 1989), in amputees (Klodd et al. 2010), and in HS during unstable walking on a slippery surface (Cappellini et al. 2009).

Despite its deceiving simplicity, human locomotion incorporating an heel strike and appropriate heel-to-toe rolling pattern during stance is a precise and complex motor task that requires learning (Dominici et al. 2007; Ivanenko et al. 2007). The cause of the impaired loading in CA (Fig. 4) may originate from the unbalanced control and preparation to the foot touchdown. An increase in the impact transient could also be a consequence of leg stiffening in CA patients (Mari et al. 2014).
or reduced push-off of the contralateral limb in late stance (Serrao et al. 2012). For instance, in amputees, the occurrence of the heel strike transient is evident on the sound side while the prosthetic limb exhibits smooth loading, presumably due to a lack of active push-off from the prosthetic feet in late stance and/or reduced energy storage and return from the prosthetic feet (Klodd et al. 2010). Nevertheless, the weakness of distal extensors does not inevitably result in the abnormal GRF transient since it was not observed in peripheral neuropathy (Ivanenko et al. 2013a). Further experiments are needed to understand better its biomechanical nature. Whatever the exact biomechanical reasons for the observed phenomenon, the cerebellum may play an important role in the foot loading control. For instance, cats with unilateral section of the dorsal spino-cerebellar tract cannot walk on a slippery floor (unpublished observations, Poppele RE) as well as cerebellar gait ataxia in humans may result in leg-placement deficit (Morton and Bastian 2003).

Muscle Activation Patterns in CA

Despite that the kinematics and bilateral coordination of leg muscle activity are quite symmetrical in normal HS, in pathological conditions there might be some differences (Perry 1992). We did not find any significant difference in the kinematic parameters and clinical assessment on both sides in CA patients. However, although no relevant clinical and kinematic asymmetry were found in our patients, we cannot exclude subclinical differences in the EMG patterns between left and right sides. The recordings of unilateral muscle activity, nevertheless, revealed distinctive features of EMG bursts in CA with respect to HS (Figs. 5, 6, and 7D).

Although the muscular patterns of CA patients are variable, the analysis of muscle activation patterns showed distinctive features of the CA gait, in particular an increased amplitude (Fig. 5C) and duration (Fig. 6B) of EMG bursts. On average the amplitude of muscle activity over the gait cycle was about twice that in CA patients than in HS (Fig. 5C; see also Mitoma et al. 2000). It is therefore remarkable that significantly larger muscle activation could lead to similar leg movement kinematics and even to smaller angular oscillations in the ankle joint (Figs. 1B and 2A). In addition to a relatively high level of muscle activity in patients (Fig. 5C), the main difference between HS and CA was the duration of the muscle activation periods (Fig. 6B). The enlarged FWHM was observed in all three groups of CA patients (SCA1, SCA2, and SAOA). The widening of EMG bursts was somewhat asymmetric since there were also changes in the CoA (Fig. 6C): the CoA shifted to slightly later phases of the gait cycle in proximal muscles (VL, ST, and BF) and to earlier phases in distal muscles (SOL, MG, LG, and PL).

The increased coactivation observed in the CA patients (Fig. 5D, see also Mari et al. 2014), in part due to EMG widening (Fig. 5), may represent a compensatory strategy useful to provide mechanical stability by stiffening joints. For instance, an abnormal cocontraction pattern has been demonstrated in categories of people who have a great need for active muscular stabilization, such as the elderly (Peterson and Martin 2010), individuals who have undergone knee arthroplasty (Fallah-Yakkhdani et al. 2012), patients with stroke or traumatic brain injury (Chow et al. 2012), and patients with Parkinson’s disease (Meunier et al. 2000). Indeed, compared with HS, ataxic patients needed to activate antagonist muscles more and
Our findings are consistent with the idea that the cerebellum contributes to optimizing the duration of muscle activation patterns during locomotion. It remains to be determined if the abnormalities discussed here are specific for cerebellar deficit. In this regard, it is worth noting that abnormal prolongation of EMG activity was also observed in the upper limb muscles during elbow flexions in patients with cerebellar deficits and thus may represent a general feature of cerebellar dysmetria (Hallett et al. 1975). Future research can be focused on the mechanisms underlying the observed phenomena for understanding cerebellar physiology and for using these abnormalities as diagnostic tools for the documentation of cerebellar deficits.

REFERENCES


