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Toward new sensitive measures to evaluate gait stability in focal cerebellar lesion patients

Wouter Hoogkamer [a,*], Sjoerd M. Bruijn [a,b,c], Stefan Sunaert [d,e], Stephan P. Swinnen [a], Frank Van Calenbergh [f], Jacques Duysens [a,g]

[a] Movement Control and Neuroplasticity Research Group, Department of Kinesiology, KU Leuven, Belgium
[b] Department of Orthopedics, First Affiliated Hospital of Fujian Medical University, PR China
[c] MOVE Research Institute, VU University Amsterdam, The Netherlands
[d] Department of Radiology, University Hospitals Leuven, Belgium
[e] Department of Imaging & Pathology, KU Leuven, Belgium
[f] Department of Neurosurgery, University Hospitals Leuven, Belgium
[g] Department of Research, Development & Education, St. Maartenskliniek Nijmegen, The Netherlands

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ABSTRACT

The evident ataxic characteristics of gait in patients with cerebellar damage suggest that the cerebellum plays an important role in the neural control of gait. Ataxic features, such as increased gait variability and increased step width, are often related to gait stability. However, the link between these measures and gait stability is not straightforward. Therefore, to gain more insights into relations between gait stability, gait variability and gait ataxia, we quantified gait stability using the short-term maximum Lyapunov exponent. This is a more valid measure of gait stability, derived from dynamical systems theory. Eighteen patients with focal cerebellar lesions after tumor resection walked on an instrumented treadmill at 1.0 m/s for 3 min. The patients displayed relatively mild functional deficits (ICARS = 6.9 ± 6.4, range 0–20) and had a lower overground walking speed as compared to healthy controls (1.12 m/s versus 1.31 m/s). During treadmill walking, the short-term maximum Lyapunov exponent was higher in cerebellar patients, indicating reduced gait stability. Furthermore, step width was increased in the patient group while other spatio-temporal gait parameters were similar. Patients with the largest lesions in the vermis displayed the least stable gait pattern. These observations imply that the short-term maximum Lyapunov exponent is a sensitive measure of gait deficits in mildly ataxic cerebellar patients.

1. Introduction

The evident ataxic characteristics of gait in patients with cerebellar damage suggest that the cerebellum plays an important role in the neural control of gait (for review, see [1]). Prominent ataxic gait features include increased gait variability [2–10] and an increased step width [2,3,5,8,9]. Increased gait variability is often used to infer reduced gait stability (for review [11]) and, similarly, step width has been used as a measure of gait stability, for instance in cerebellar lesion patients [3]. In this group increased step length variability has been associated with damage in specific areas in the cerebellum, partially different from cerebellar areas related to increased lateral sway and step width [3,4]. These observations are important since the individual contributions of balance and limb-coordination deficits to ataxic gait are still under debate [2,12]. Furthermore, increased gait variability, specifically during slow walking, has been linked to fall risk in cerebellar ataxia patients [7].

However, the link between gait variability and gait stability is not straightforward. From a biomechanical perspective, increased variability itself does not necessarily imply decreased stability, since stability depends on both the constraints and the control strategy of a system (for discussion, see [11]). This notion is important since in cerebellar patients increased gait variability could be related to cerebellar deficits in intra-limb coordination [2], rather than to gait stability.

Likewise, step width is also not an ideal measure to quantify gait stability. In order not to fall, the center of mass needs to be

* Corresponding author at: Movement Control and Neuroplasticity Research Group, Department of Kinesiology, KU Leuven, Tervuursevest 101 bus 1501, 3001 Leuven, Belgium. Tel.: +32 16 32 90 65; fax: +32 16 32 91 97.
E-mail address: wouter.hoogkamer@faber.kuleuven.be (W. Hoogkamer).

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controlled such that it stays over the base of support. For dynamic conditions, such as gait, this is best assessed using the extrapolated center of mass concept [13]. The extrapolated center of mass combines center of mass position and velocity, and it should be within the base of support [11,13]. Because the distance between the extrapolated center of mass and the boundary of the base of support (the 'margin of stability'), is not only affected by step width but also by movements of the rest of the body, it is clear that an increased step width does not necessarily imply more stability.

A more valid [11] measure for gait stability is the short-term maximum Lyapunov exponent [14], derived from dynamical systems theory. This measure quantifies the ability to recover from small perturbations. It has a valid theoretical basis and has been shown to have a high predictive validity with respect to falling in both modeling and observational studies (for review, see [11]). While this measure has been used to evaluate gait stability in many different populations such as elderly [15,16], amputees [17,18] and patients with knee osteoarthritis [19], anterior cruciate ligament deficiency [20] and peripheral neuropathy [21], so far it has, to the best of our knowledge, not been used to evaluate gait stability in cerebellar ataxia patients.

Here, we aimed to gain more insight into relations between gait stability, gait variability and gait ataxia. Therefore, we assessed gait stability and variability in a group of patients with focal cerebellar lesions after tumor resection. We specifically focused on stability in the medio-lateral direction in these mildly ataxic cerebellar patients, inspired by the commonly observed increased step width in cerebellar ataxia. We quantified gait stability using the short-term maximum Lyapunov exponent [11,14] and we evaluated the margin of stability based on the extrapolated center of mass [13]. We hypothesized that patients would walk with a less stable gait pattern and with a reduced margin of stability. Specifically, we expected that the short-term maximum Lyapunov exponent would make an important contribution to the description of gait deficits in this mildly ataxic patient group.

2. Materials and methods

2.1. Participants & protocol

Eighteen cerebellar patients (age: 24.4 ± 7.3 yrs; mean ± SD; 13 female, 5 male) and fourteen healthy participants (24.4 ± 3.5 yrs; 11 female, 3 male) participated in the study. All patients displayed chronic focal lesions after cerebellar tumor resection (various types, see Table 1). Nine patients received radiation therapy and four of them chemotherapy (Table 1). Lesion sizes are summarized in Table 1 (more details on lesion locations and on magnetic resonance imaging data acquisition and analysis procedures can be found in the supplementary materials). All patients were in a stable condition (>2 years post-op; range 4.8–30.2 yrs; Table 1). Severity of ataxia was rated using the International Cooperative Ataxia Rating Scale (ICARS [22]). All participants gave written informed consent, as approved by the local ethics committee and in accordance with the Declaration of Helsinki.

Participants performed three trials of overground walking at self-selected speed over a distance of 6 m [23], followed by 3 min of treadmill walking at 1.0 m/s. In daily life none of the participants employed walking aids and all testing was performed without walking aids or holding the hand rail of the treadmill. We recorded three-dimensional kinematics at 100 samples/s (Vicon Nexus, Oxford Metrics, Oxford, UK) using a marker cluster placed at the pelvis. During treadmill walking 3D ground reaction forces were collected at 1000 samples/s (custom built instrumented treadmill, Forcelink, Culemborg, The Netherlands).

2.2. Data analysis

We calculated overground walking speed as the mean forward velocity of the pelvis marker cluster during the three overground walking trials. We calculated gait stability for the treadmill walking trials. Heel strike and toe-off events were extracted from the center of pressure trajectory [24]. Gait parameters were based on 150 strides for each participant. Step width was defined as the medio-lateral distance between the average center of pressure locations during subsequent single stance phases. The coefficient of variance of stride time was calculated to assess stride time variability.

Gait stability was addressed by calculating the short-term maximum Lyapunov exponent (λ_S) from the medio-lateral displacement of pelvis marker cluster, following Bruijn's protocol [25]. In short, the Euclidean distance between each data point in state space and its nearest neighbor was tracked over time. A divergence curve was constructed by taking the mean of the log of all these time-distance curves. The short-term maximum Lyapunov

Table 1
All patients had stable focal lesions after cerebellar tumor resection.

#	Age	Time	Sex	Diagnosis	Lesion	Vermal Lesion	ICARS			Adjuvant therapies	
	(years)	Post-op (years)			Volume (cm^3)	Volume (cm^3)	Total/100	P&G/34	Kin Fun/52	Radiation	Chemo
1	28.8	13.9	f	Lhermitte Duclos Disease	58.0	–	3	1	1	–	–
2	20.2	8.7	f	Pilocytic Astrocytoma	8.2	–	3	0	0	–	–
3	18.1	6.5	f	Pilocytic Astrocytoma	4.5	–	1	0	1	–	–
4	19.6	11.8	m	Pilocytic Astrocytoma	1.7	1.1	6	3	2	–	–
5	20.5	4.8	f	Pilocytic Astrocytoma	47.3	5.6	3	1	1	–	–
6	20.5	13.1	f	Pilocytic Astrocytoma	36.3	–	2	1	0	–	–
7	19.0	13.2	m	Pilocytic Astrocytoma	15.7	–	7	2	5	–	–
8	41.2	28.1	f	Pilocytic Astrocytoma	20.2	4.9	20	6	10	Y	–
9	26.9	24.9	f	Pilocytic Astrocytoma	58.4	–	5	1	1	Y	–
10	22.0	18.7	m	Astrocytoma grade II	2.0	0.7	1	0	1	–	–
11	21.6	19.5	f	Astrocytoma grade II	7.1	2.1	0	0	0	Y	–
12	31.4	19.7	f	Astrocytoma grade III	8.6	0.4	11	5	4	Y	–
13	22.3	17.7	m	Medulloblastoma	22.0	3.3	13	6	2	Y	–
14	18.6	13.6	m	Medulloblastoma	6.3	2.5	19	5	10	Y	Y
15	18.4	15.5	f	Medulloblastoma	5.4	2.2	5	1	3	Y	Y
16	31.3	18.2	f	Medulloblastoma	14.2	4.0	17	10	4	Y	Y
17	18.5	10.0	f	Medulloblastoma	22.6	5.2	2	1	1	Y	Y
18	39.9	30.2	f	Hemangioblastoma	No MRI	No MRI	6	4	2	–	–

For patient 18 no MRI data was acquired. ICARS = International Cooperative Ataxia Rating Scale [24]; P&G = Posture & Gait sub-score; Kin Fin = Kinetic Functions sub-score; f = female, m = male; Y = yes.