J Neurophysiol 110: 2337–2349, 2013.
First published August 21, 2013; doi:10.1152/jn.00062.2013.

Effects of cerebellar lesions on working memory interacting with motor tasks of different complexities

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Submitted 25 January 2013; accepted in final form 21 August 2013

Ilg W, Christensen A, Mueller OM, Goericke SL, Giese MA, Timmann D. Effects of cerebellar lesions on working memory interacting with motor tasks of different complexities. *J Neurophysiol* 110: 2337–2349, 2013. First published August 21, 2013; doi:10.1152/jn.00062.2013.—We examined the influence of focal cerebellar lesions on working memory (*n*-back task), gait, and the interaction between working memory and different gait tasks in a dual-task paradigm. The analysis included 17 young patients with chronic focal lesions after cerebellar tumor resection and 17 age-matched controls. Patients have shown mild to moderate ataxia. Lesion sites were examined on the basis of structural magnetic resonance imaging. *N*-back tasks were executed with different levels of difficulty ($n = 1–4$) during sitting (baseline), treadmill walking, and treadmill tandem walking (dual-task conditions). Patients exhibited decreased *n*-back performance particularly at difficult *n*-back levels and in dual-task conditions. Voxel-based lesion-symptom mapping revealed that decreased baseline *n*-back performance was associated with lesions of the posterolateral cerebellar hemisphere and the dentate nucleus. By contrast, decreased *n*-back performance in dual-task conditions was more associated with motor-related areas including dorsal portions of the dentate and the interposed nucleus, suggesting a prioritization of the motor task. During baseline walking, increased gait variability was associated with lesions in medial and intermediate regions, whereas for baseline tandem gait, lesions in the posterolateral hemispheres and the dentate nucleus became important. Posterolateral regions overlapped with regions related to baseline *n*-back performance. Consistently, we observed increased tandem gait variability with growing *n*-back difficulty in the dual-task condition. These findings suggest that dual-task effects in cerebellar patients are at least partially caused by a common involvement of posterolateral cerebellar regions in working memory and complex motor tasks.

cerebellum; lesion-symptom mapping; dual task; working memory; gait

STUDIES COMBINING MOTOR and cognitive tasks in dual-task paradigms reveal interactive influences on both modalities. Cognitive performance can even increase with motion in young people but substantially decreases for the elderly (Lindenberger et al. 2000; Srygley et al. 2009; Verrel et al. 2009), and in particular for patients with neurological movement disorders (e.g., Haggard et al. 2000).

Similarly, gait disorders in neurological patients are often accentuated when the patients perform concurrent cognitive tasks during walking (for reviews see Al-Yahya et al. 2011; Woollacott and Shumway-Cook 2002). This has been extensively examined, for instance. in Parkinson's disease (Bloem et al. 2001; Yogev-Seligmann et al. 2008; Yogev et al. 2005). Today, there exist very few dual-task studies in cerebellar patients. Two studies indicated that cerebellar patients are impaired in shifting motor performance with practice from an attentionally demanding to a more automatic state (Doyon et al. 1998; Lang and Bastian 2002). In the study by Lang and Bastian, cerebellar patients practiced to make figure-8 arm movements. Unlike in healthy controls, the performance of cerebellar patients deteriorated to pre-practice level when attention was distracted by an auditory vigilance task (Lang and Bastian 2002). As yet, dual-task performance in cerebellar patients during gait has not been investigated. Cerebellar disorders are well known to induce ataxic gait characterized by an instable, stumbling walking path, high movement variability (Diener and Dichgans 1996; Holmes 1939; Ilg and Timmann, in press; Morton and Bastian 2004), and a high risk of falling, in particular when attention is distracted from walking (e.g., van de Warrenburg et al. 2005).

The medial region of the cerebellum is well known to play a strong role in the control of balance in locomotion, whereas the lateral cerebellum is particularly involved when precise limb placement is necessary (intermediate zone) or when strong reliance on visual information is required (lateral zone) (for reviews see Cerminara et al. 2005; Ilg and Timmann, in press; Morton and Bastian 2004; Stein and Glickstein 1992; Thach and Bastian 2004).

On the other hand, there exist various pieces of evidence for the involvement of the lateral cerebellum in cognitive processes (for reviews see Ito 2008; Stoodley and Schmahmann 2010; Strick et al. 2009; Timmann and Daum 2007, 2010). One of the best-examined cognitive tasks is verbal working memory, for which neuroimaging studies have identified the involvement of different brain areas including premotor cortex, prefrontal cortex, and posterior parietal cortex (see meta-analysis for the *n*-back task in Owen et al. 2005), as well as the lateral cerebellum (Hautzel et al. 2009; Marvel and Desmond 2011; Stoodley and Schmahmann 2009, 2010). Verbal working memory dysfunction has been observed in patients with cerebellar disease, although deficits are generally mild in standard tests (Cooper et al. 2012; Ravizza et al. 2006; Tedesco et al. 2011; Timmann and Daum 2010).

We examined a dual-task paradigm consisting of a verbal working memory task and gait tasks with different complexi-

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ties (treadmill walking, treadmill tandem walking) in young cerebellar patients with focal lesions. Advanced methods of lesion symptom mapping (Rorden et al. 2007; Timmann et al. 2009) were used to identify cerebellar areas associated with performance changes in both single-task (working memory, walking) and dual-task conditions.

Although divided attention (not primarily influenced by the cerebellum) and prioritization of the motor task for security reasons (Springer et al. 2006; Woollacott and Shumway-Cook 2002; Yogev-Seligmann et al. 2008) are possible explanations of expected dual-task effects, decrease of performances due to the involvement of overlapping regions in both tasks may play a specific role. We hypothesize that the latter will be observed in the more difficult tandem gait, since precise, visually guided leg movements likely involve lateral regions of the cerebellum, as does the cognitive working memory task. Hence, we expect to find dual-task interaction effects caused by the involvement of overlapping regions in the lateral cerebellum for both the cognitive and the tandem walking task.

METHODS

Subjects

We analyzed 17 patients (CP1–CP17) with chronic focal lesions after cerebellar tumor resection (age range 18–45 yr, mean 27.4 yr; 10 women, 7 men) and an age-matched control group (age range 18–45 yr, mean 27.2 yr; 10 women, 7 men). All patients suffered from benign cerebellar tumors (pilocystic astrocytoma WHO grade I, 10 patients; astrocytoma WHO grade II, 1 patient; hemangioblastoma, 5 patients; or angioma, 1 patient). None of the patients received adjuvant radio- or chemotherapy (see Table 1 and APPENDIX A).

Severity of ataxia was rated using the International Cooperative Ataxia Rating Scale (ICARS) (Trouillas et al. 1997). All patients showed mild symptoms of ataxia and were able to walk without aid (ICARS score: mean 6.3, SD 7.3; see Table 1). Each subject was examined by an experienced neurologist (DT). All patients and control subjects gave informed written consent before participation. The study was approved by the local institutional ethical review boards in Tübingen and Essen.

N-Back Task

The *n*-back task (Dobbs and Rule 1989) is a working memory task in which participants have to monitor a sequence of numerical digits and indicate whenever the currently presented digit coincides with the one that was given *n* steps earlier in the sequence. For instance, in the 2-back condition, participants have to respond when the current digit is the same as the one presented two steps before, as in the sequence 36<u>7</u>1<u>7</u>82<u>9</u>6<u>9</u>.

In the present study responses were given verbally, specifying the digits "seven" and "nine" in the given example immediately after appearance of the target pair. In our implementation of the *n*-back task, a sequence of 30 digits was presented auditorily via wireless headphones, with interstimulus intervals jittered between 2.85 and 3.15 s. Trials in all conditions included seven targets. *N*-back performance was determined as follows: performance (%) = 100 × (true positives − false positives)/number of targets.

Experimental Paradigm

The *n*-back tasks were performed in three conditions: *1*) during sitting (baseline condition), *2*) during normal walking on a treadmill, and *3*) during a more demanding gait task, walking on a virtual line on the treadmill (tandem gait; see *Walking task*).

Although the baseline condition for the *n*-back task (sitting) is actually also a motor task requiring balance control, we assumed that the *n*-back performance in this condition is not influenced predominantly by this elementary motor task. This assumption is supported by the facts that *1*) our patients have shown mild to moderate impairments not influencing sitting position (absence of truncal ataxia, which is no point in the ICARS sitting subscore; Table 1) and *2*) there was no correlation between ataxia severity and the *n*-back performance (see RESULTS).

N-back task sessions were always performed in the same sequence: baseline, walking, tandem walking. This strict order ensures that identified decreases in *n*-back performance for the walking conditions can be interpreted as dual-task effects. No instructions were given to the participants to prioritize one task over the other.

Within each session, subjects started with 1-back and continued to increasing *n*. To familiarize themselves with the *n*-back tasks, subject practiced at the beginning of one trial for each *n* in the sitting condition before performing the actual experiment.

Table 1. *Cerebellar subject information*

				ICARS			
Patient	Age, yr	Time Post-op, yr	Diagnosis	Kinetic (max. 52)	Gait and posture (max. 34)	Speech (max. 8)	Total (max. 100)
CP1	24	14	Pilocytic astrocytoma	7	2.5	0	13.5
CP2	45	4.5	Pilocytic astrocytoma	1	1.5	0	2.5
CP3	44	6	Hemangioblastoma	4.5	2.5	1	8
CP4	28	3	Hemangioblastoma	0	0	0	0
CP5	21	1.5	Angioma	13.5	7	2	28.5
CP6	22	5	Polocytic astrocytoma	0	1	0	1.5
CP7	32	6	Hemangioblastoma	0	0	0	0
CP8	19	16	Pilocytic astrocytoma	4.5	3	0	13.5
CP9	26	10	Astrocytoma grade II	1	3	0	4
CP10	25	16	Pilocytic astrocytoma	1.5	2	0	3.5
CP11	18	13	Pilocytic astrocytoma	3.5	3	0	6.5
CP12	36	5	Pilocytic astrocytoma	0	0	0	0
CP13	20	4	Pilocytic astrocytoma	5	3.5	0	11.5
CP14	23	14	Pilocytic astrocytoma	5	4	0	9
CP15	21	12	Pilocytic astrocytoma	2	3	0	6
CP16	39	3	Hemangioblastoma	1	0	0	1
CP17	23	8	Pilocytic astrocytoma	0	0	0	0

Clinical scores were rated using the ICARS score (Trouillas et al. 1997). Total ICARS scores and the relevant subscores for limb kinetics, gait and posture, and speech. Higher scores indicate more severe ataxia. Maximum (max.) scores are indicated in parentheses.

Walking Tasks

During normal treadmill walking, subjects walked on a treadmill at a velocity of 1 m/s. In the second motor task condition, the treadmill tandem walking, subjects were instructed to go on a virtual line on the treadmill at 0.3 m/s by placing one foot in front of the other with a distance of ~5 cm. The second task is considerably more challenging with higher demands on balance control and goal-directed leg movements.

For each condition, subjects had a 3-min familiarization phase before capturing the baseline movements without the *n*-back task. During the *n*-back tasks on the treadmill, each subject walked 10 s on the treadmill before starting the working memory task and capturing the movements. Single-task recordings of walking and tandem walking (as baseline conditions for gait movements) had the same durations as dual-task recordings. In both conditions, participants did not hold onto treadmill bars.

Gait Measures

Previous studies have shown that measures of spatial and temporal variability (e.g., variability in step length and step cycle time) are especially suitable for describing ataxic gait (Ilg et al. 2007, 2008; Morton and Bastian 2003; Schniepp et al. 2012; Stolze et al. 2002). In addition, existing research on dual-task walking revealed that both temporal and spatial variability in gait are also increased in dual-task walking conditions, particularly for patients with neurological disorders (Verrel et al. 2009; Woollacott and Shumway-Cook 2002; Yogev-Seligmann et al. 2010). Thus we focused on the analysis of these variability measures for both walking conditions.

Variability measures were calculated using the coefficient of variation (CV = σ/μ), normalizing the standard deviation (σ) with the corresponding mean value (μ) (Winter 1984). Gait analysis was performed using a VICON MX motion capture system (for details see APPENDIX C).

MR Imaging

MR images of all patients were acquired with a 1.5-T Siemens scanner (Espree) using a 12-channel head coil. A three-dimensional (3-D) sagittal volume of the entire brain was made using a T1-weighted, magnetization-prepared rapid acquisition gradient-echo (MPRAGE) sequence (repetition time = 2,400 ms, echo time = 3.63 ms, field of view = 256 mm, 160 slices, voxel size 1.0 × 1.0 × 1.0 mm^3). Three-dimensional fluid attenuation inversion recovery (FLAIR) and 2-D T2-weighted magnetic resonance images (MRI) were acquired at the same time. Images were examined by an experienced neuroradiologist (SLG), and extracerebellar pathology was excluded.

Focal Lesions

Cerebellar lesions of focal patients were manually traced on axial, sagittal, and coronal slices of the nonnormalized 3-D MPRAGE MRI data set and saved as regions of brain injury (RBI) using free MRIcro software (http://www.sph.sc.edu/comd/rorden/mricro.html; see also Donchin et al. 2012 for more detailed information). Probabilistic atlases of the human cerebellum were used in MRIcroN (http://www.mccauslandcenter.sc.edu/mricro/mricron/index.html) to define the affected cerebellar lobules and nuclei (http://www.icn.ucl.ac.uk/motorcontrol/imaging/propatlas.htm; Diedrichsen et al. 2009, 2011). RBIs were normalized by using a spatially unbiased infratentorial template of the cerebellum (SUIT; Diedrichsen 2006) with the SUIT toolbox in SPM5 (http://www.fil.ion.ucl.ac.uk/spm/software/spm5).

At first, the program isolated the cerebellum and created a mask. These masks were manually corrected with the help of CARET software (http://brainvis.wustl.edu/wiki/index.php/Caret:About). The nonlinear deformation was then applied to RBIs from the individual patients. For further analysis all lesions were flipped to the right. Superposition of individual lesions is illustrated in Fig. 1.

Voxelwise lesion-symptom mapping (VLSM) was performed with the use of NPM software (http://www.mccauslandcenter.sc.edu/mricro/npm/). Only voxels damaged in at least 10% of individuals (2 patients) were considered. Associations between cerebellar damage and behavior impairments were obtained using multiple *t*-tests (Bates et al. 2003; Rorden et al. 2007). *T*-tests were conducted at each voxel comparing the behavioral scores of subgroups of patients for whom that voxel was intact and lesioned on the parameters of interest. *P* values <0.05 ($Z = 1.65$) were considered significant.

Statistics

Performance in the *n*-back tasks was analyzed by carrying out a 2 (Group: healthy controls vs. cerebellar patients) × 4 (Task Difficulty: levels $n = 1–4$) × 3 (Movement Condition: sitting, walking, and tandem) mixed-model ANOVA. In case of violations of the sphericity assumption, as indicated by a significant result of Mauchly's test, we report Greenhouse-Geisser corrected statistical data. In cases where an interaction of Group and Movement Condition was present, we ran additional 2 (Group) × 4 (Task Difficulty) mixed-model ANOVAs for each movement condition separately.

Post hoc paired comparisons between the cerebellar group and the control group at individual levels of task difficulty were conducted with more conservative nonparametric statistics using the Mann-Whitney *U*-test at the 5% alpha level of significance. Cutoff levels based on the 10% quantile of *n*-back performance for the healthy control group were determined to analyze whether individual cerebellar patients are impaired in *n*-back performance.

To test for differences between the patient and control groups in their motor behavior, we conducted 2 (Group) × 4 (Task Difficulty)

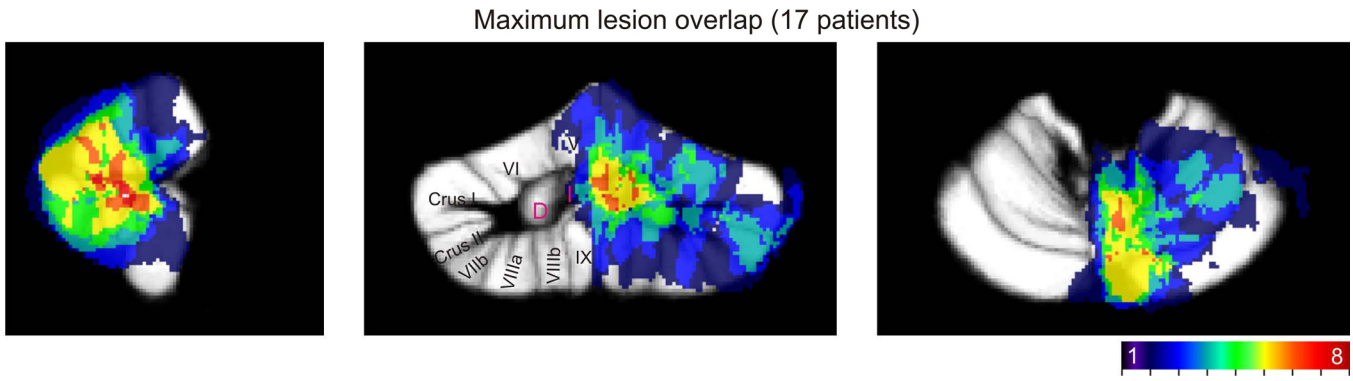

Fig. 1. Regions of brain injury for all patients with focal lesions overlapped on the maximum probability SUIT template of the cerebellum (see METHODS). For analysis, all lesions were flipped to the right. Maximum overlap (8 patients) was within vermal lobules VI and VIIIa.

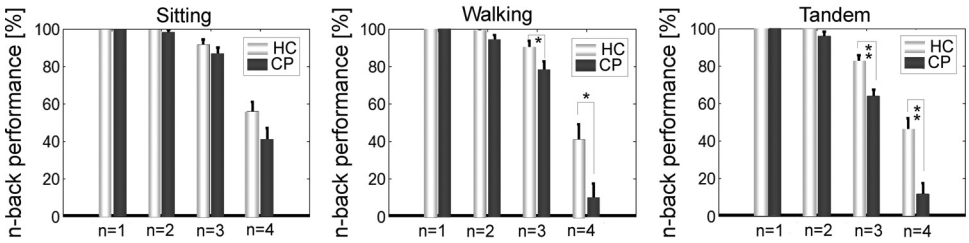

Fig. 2. Group *n*-back performance data for the different conditions: sitting (*A*), walking (*B*), and tandem walking (*C*). Shown are performances for healthy controls (HC) and cerebellar patients (CP) for $n = 1–4$. Significant group differences in the post hoc tests (Mann-Whitney *U*) are indicated (*$P < 0.05$; **$P < 0.05/12$).

mixed-model ANOVAs for each motor task (walking, tandem) and each gait parameter (step length, step width, step cycle, cadence, and variability of those measures). In cases where we found a significant main effect of Group or an interaction of Task Difficulty and Group, further paired comparisons were done using the nonparametric Mann-Whitney *U*-test. For the latter we report two significance levels: uncorrected ($P < 0.05$) and Bonferroni-corrected for multiple comparisons ($P < 0.05/n$).

Spearman's ρ was used to examine the correlation between clinical ataxia scores ICARS and *n*-back performance for the respective gait measures. All statistical analyses were performed using MATLAB and SPSS.

RESULTS

N-Back Task Performance in Different Motor Conditions

Figure 2 shows the *n*-back performance of patients and controls for the different conditions. As expected, the level of *n*-back difficulty had a strong impact on the performance of healthy controls and cerebellar patients. The performance decreased with increasing difficulty [$F(1.8, 57.62) = 361.40$, $P < 0.001$] as well as with increasing motor demands [$F(2,64) = 18.84$, $P < 0.001$]. Overall, cerebellar patients performed worse than healthy controls [Group: $F(1,32) = 25.77$, $P < 0.001$]. This group difference was most prominent in conditions with increased *n*-back task difficulty as reflected by the significant interaction Task Difficulty × Group [$F(1.8, 57.62) = 14.21$, $P < 0.001$].

Patients and controls differed significantly in the *n*-back task even in the sitting condition [ANOVA, main effect of Group: $F(1,32) = 4.486$, $P = 0.042$]. This group difference was more pronounced in the walking condition [$F(1,32) = 15.86$, $P < 0.001$] and strongest for the tandem walk [$F(1,32) = 24.177$, $P < 0.001$], which was the most demanding motor condition.

For the following post hoc analyses, we focused on the 3-back task, since *1*) both controls and patients revealed a performance with no significant difference from 100% (ceiling effect) for $n = 1$ and 2, and *2*) 4-back revealed to be a rather difficult task with a very high variability in both groups and no significant differences from 0% performance for patients (floor effect). For the 3-back task, significant group differences were exhibited for walking ($P = 0.03$) and tandem ($P = 0.001$), but not for the baseline condition during sitting. Intragroup analyses revealed that for healthy controls 3-back performance decreased significantly (compared with baseline) in the dual-task condition only for tandem gait ($P = 0.03$), not for walking ($P = 0.6$). In contrast, cerebellar patients showed a significant decrease in 3-back performance for comparisons of sitting and walking ($P = 0.01$), sitting and tandem walking ($P = 0.0002$), and also walking and tandem gait ($P = 0.007$).

Individual subject analysis on 3-back performance in sitting revealed that five patients were below a cutoff level of 10% quantile determined by the control group (Fig. 3*A*). Similarly, four patients were below the cutoff level for the walking condition (Fig. 3*B*), three of whom were also below the cutoff level for the sitting condition. In contrast, more than half of the patients (9) were below the cutoff level for the tandem condition. This result indicates an influence of motor task complexity on 3-back performance in the dual-task paradigm in particular for patients.

Within our patient population there was no correlation between *n*-back performance and the clinical ataxia score ICARS or its subscores including speech for any motor condition ($P > 0.35$), indicating that *n*-back performance is not correlated with general ataxia severity and motor symptoms.

Lesion Mapping of 3-Back Performance

In the sitting condition, performance in the 3-back task was significantly reduced in patients with lesions of the ventral part of the dentate nucleus compared with patients with no lesions (orange and red color in Fig. 4*A*, baseline; maximum *Z*

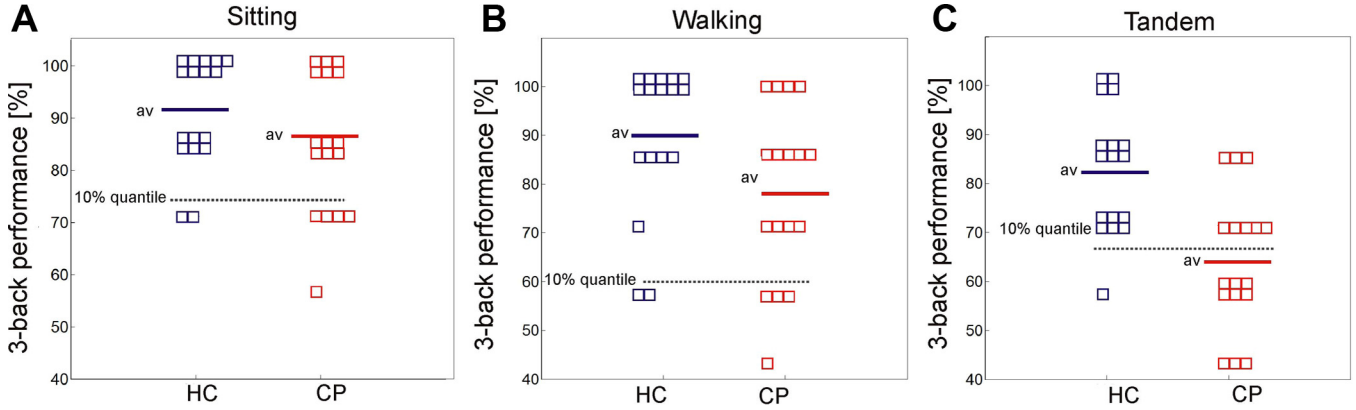

Fig. 3. Individual subject analysis of 3-back performance for healthy controls (blue) and cerebellar patients (red). Each quadrate denotes 1 subject. In addition, averages (av) for HC and CP as well as the 10% quantile for HC are given.

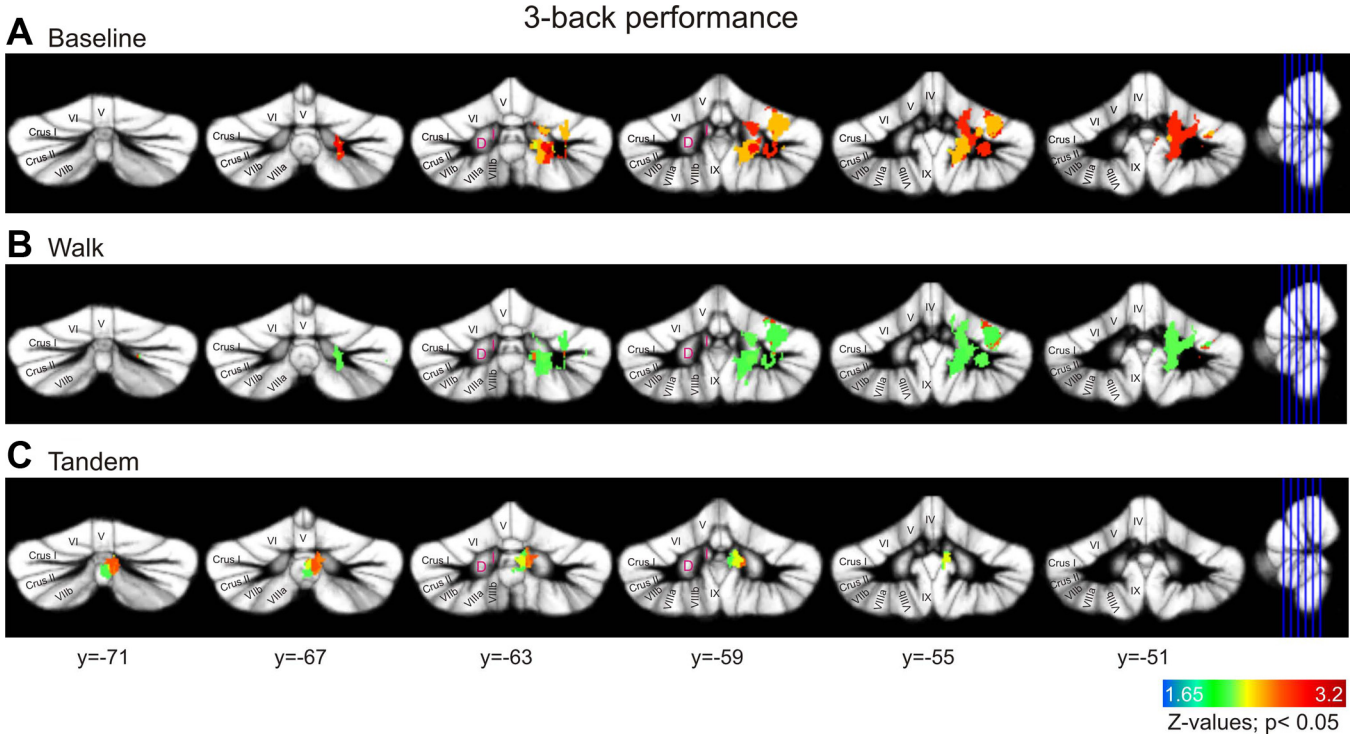

Fig. 4. Lesion-symptom mapping: comparison of regions that are associated with impaired 3-back performance for the 3 different conditions: baseline (*A*), walk (*B*), and tandem walking (*C*). For analysis, all lesions were flipped to the right. Shown are regions that are associated significantly with impaired 3-back task performance ($P < 0.05$). A Z value of 1.65 corresponds to a P value of 0.05.

value = 3.05, $x = 20$, $y = -62$, $z = -42$; see also APPENDIX B, Table A2). In addition, lesions within lobules V and VI with some extensions into the dorsal dentate nucleus (maximum $Z = 2.58$) and Crus I, and lesions within lobule VIII extending into lobule IX were significantly more likely in patients with reduced task performance.

In the walking condition, cerebellar areas related to impaired 3-back performance were very similar to those for the sitting (baseline) condition, but associations were less strong. Maxima were found in the ventral dentate nucleus (maximum $Z = 2.37$, green color), lobule VI with extension into dorsal dentate, lobule V and Crus I, and lobule VIII extending into IX (Fig. 4*B*, walking).

In contrast, for the more difficult tandem gait condition, lesion-symptom mapping of 3-back performance revealed a quite different pattern. In this condition, the strongest association to decreased 3-back performance was found with lesions in the dorsal dentate (maximum $Z = 2.41$, $x = 12$, $y = -63$, $z = -35$) in close neighborhood and extending into the interposed nucleus (maximum $Z = 1.96$, $x = 8$, $y = -62$, $z = -34$; orange and yellow in Fig. 4*C*, tandem), both known to be important for the control of precise goal-directed limb movement (see review in Thach and Bastian 2004 and DISCUSSION in this article). In addition, there were few associations with the cerebellar cortex, present primarily in vermal lobules VII–IX with some extension into Crus II (maximum $Z = 2.41$).

Remarkably, lesion areas related to the 3-back performance in the tandem condition showed no overlap with those lesion areas for the baseline and walking conditions. This indicates that in this dual-task condition, lesions found to be predictive for impairments in 3-back baseline condition no longer have a dominating influence on the behavioral outcome. However, it is important to note that the lack of association in the tandem walk condition does not mean that these areas do not contribute anymore to the cognitive task. Rather, it shows that lesions in a second, different area predominantly influence the task performance. In cases where two areas become important, the association for the less dominant cerebellar area might be weakened and fail to reach significance in lesion-symptom mapping.

Gait Analysis

Treadmill walking. Detailed gait analysis results for the treadmill walking condition are shown in APPENDIX D, Table A4. Patients showed an increased step length variability compared with the control group [ANOVA, $F(1,31) = 4.654$, $P = 0.039$; Fig. 5*A*]. This higher variability was independent of the task difficulty and had occurred already in the baseline walking condition without additional n-back task (Mann-Whitney U-test, $P = 0.021$). Similarly, step width variability was increased for patients ($P = 0.008$) independently of the task difficulty.

Treadmill tandem. For the more demanding tandem gait, we found a major difference between healthy controls and cerebellar patients in almost all analyzed parameters (see APPENDIX D, Table A5). An analysis of step length variability revealed a significantly higher variability in patients [ANOVA, effect of Group: $F(1,31) = 11.34$, $P = 0.002$; Fig. 5*B*]. Their step length variability was higher in all conditions as revealed by post hoc comparisons (Mann-Whitney U-Test: baseline, $P = 0.011$; 1-back, $P < 0.001$; 2-back, $P = 0.023$; 3-back, $P = 0.002$; 4-back, $P = 0.001$). In addition, patients' step length variability significantly increased for more demanding n-back tasks ($n = 3$ and 4) compared with the tandem baseline ($P < 0.03$), indicating an influence of the cognitive load on the motor task.

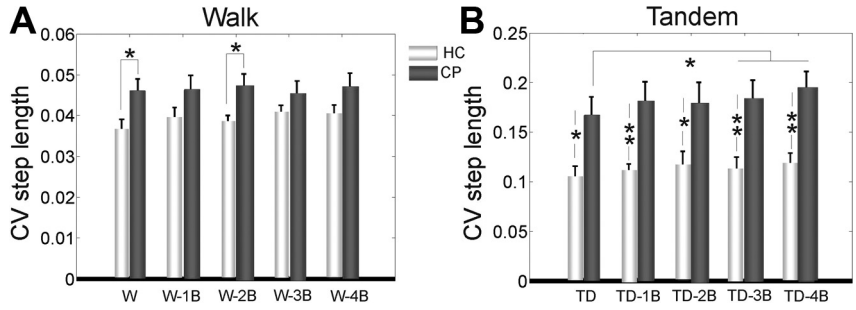

Fig. 5. Group data of patients and controls for the step length variability (coefficient of variation, CV) in treadmill walk (W; *A*) and treadmill tandem gait (TD; *B*). Shown are baseline conditions without *n*-back task as well as the different dual-task conditions for $n = 1–4$ (1B–4B). Significant differences are indicated (*$P < 0.05$;**$P < 0.05/10$). In the tandem dual-task condition there is a significant increase of gait variability for difficult *n*-back tasks ($n = 3$ and 4).

Similarly, step timing variability was significantly increased in patients for all conditions [ANOVA, $F(1,31) = 33.51$, $P < 0.001$]. For the intragroup analyses, step timing variability revealed a significant increase for all the dual-task conditions ($n = 1–4$) compared with baseline tandem gait ($P < 0.03$).

Lesion Mapping of Gait Parameters

In the baseline walking condition, variability of step length was significantly increased in patients with lesions of inferior parts of the vermis (lobule IX with some extension into VIIIa and VIIIb) compared with patients with no lesions (maximum $Z = 2.46$; dark orange and red color in Fig. 6*A*; see also APPENDIX B, Table A3). In addition, lesions within the dorsal dentate nucleus (maximum $Z = 2.06$, $x = 14$, $y = -63$, $z = -30$) extending into the interposed nucleus (maximum $Z = 2.10$, $x = 10$, $y = -58$, $z = -29$) and more intermediate parts of lobules V and VI, and lesions within the white matter of the posterolateral cerebellum with a small extension into the ventral dentate nucleus and Crus I were significantly more likely in patients with increased variability of step length.

During dual-task walking, step length variability was most strongly associated with lesions of the posterolateral

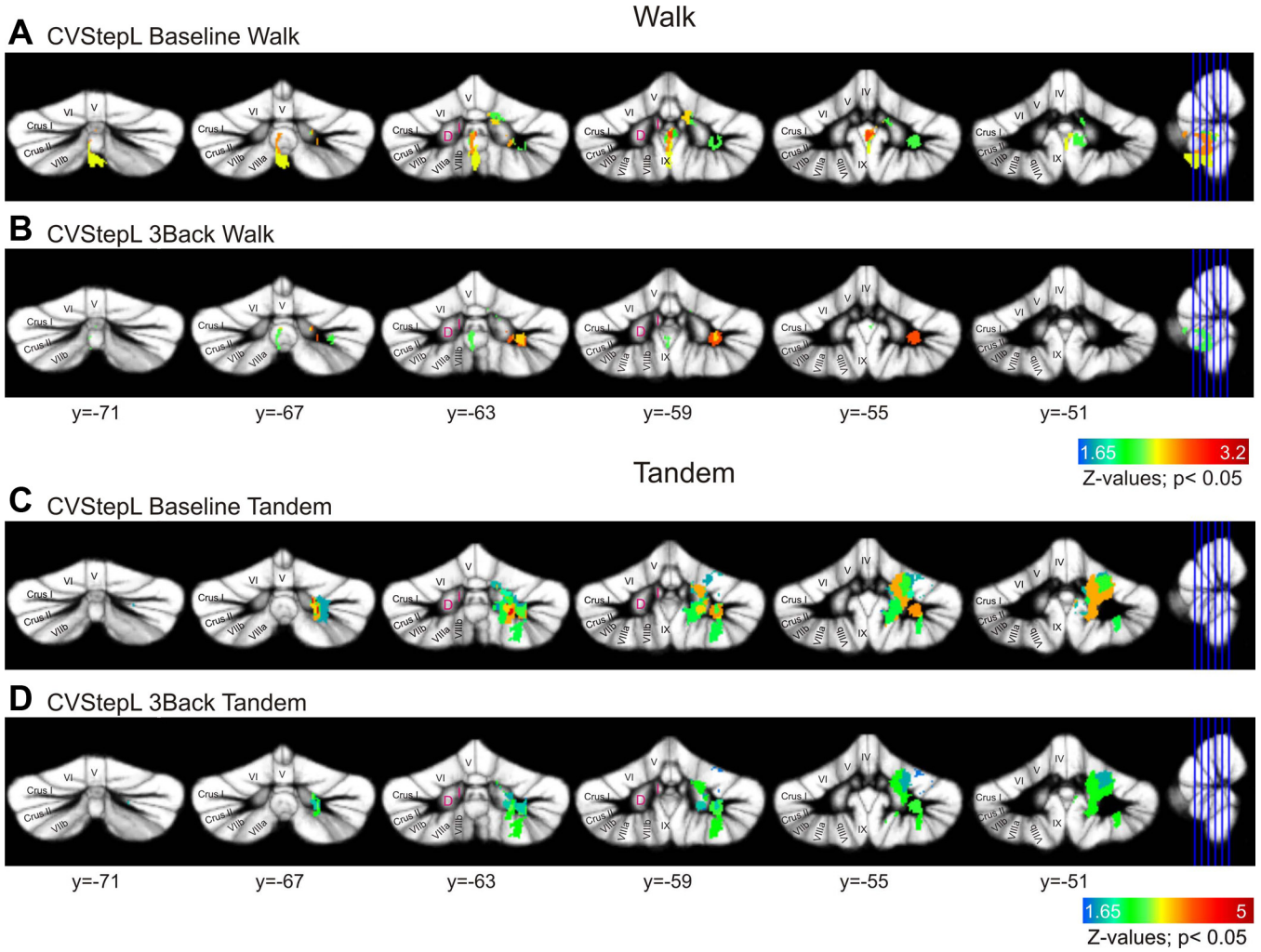

Fig. 6. Lesion-symptom mapping: comparison of regions that are significantly associated with increased gait variability (step length variability, CVStepL) in baseline walking (*A*), dual-task walking performing 3-back (*B*), baseline tandem (*C*), and dual-task tandem performing 3-back (*D*). For analysis, all lesions were flipped to the right. A *Z* value of 1.65 corresponds to a *P* value of 0.05.

white matter with extensions into Crus I and II (maximum $Z = 2.58$, yellow and orange color) and a small extension into the ventral dentate (maximum $Z = 2.43$, $x = 22$, $y = -60$, $z = -41$; Fig. 6*B*). There was also a relationship to the posterior vermis, but this was less strong compared with the same relationship for the single walking task (maximum $Z = 2.09$). Thus lesions in the more dorsal part of the dentate and adjacent interposed nucleus as well as most parts of the vermis were not significantly different in variability of step length compared with that in patients with no lesions in this area. Therefore, walking task performance was more strongly driven by the posterolateral cerebellum in the dual compared with the single task.

In the more difficult tandem gait, variability of step length was significantly increased in patients with lesions affecting both the ventral and dorsal parts of the dentate nucleus (ventral dentate maximum $Z = 4.52$, $x = 20$, $y = -62$, $z = -42$; dorsal dentate maximum $Z = 3.43$, $x = 17$, $y = -55$, $z = -32$; orange color in Fig. 6*C*). In addition, areas within lobule VI with extensions into lobule V and Crus I, and within lobule VIIIa with extensions into lobules VIIIb and IX were associated with increased variability of step length (maximum $Z = 3.43$, $x = 18$, $y = -65$, $z = -48$). In the tandem dual task, associations were weakened, but areas related to impaired task performance in tandem gait remained largely the same (see Z values in APPENDIX B, Tables A2 and A3). In the cerebellar cortex, maximum Z values were observed within lobules VI extending into V (maximum $Z = 2.63$) and VIII extending into IX (maximum $Z = 2.83$; Fig. 6*D*). Associations to the dorsal and ventral dentate were still present, but maximum Z values were reduced ($Z = 2.52$ and 2.83) compared with the single task.

Distinct and Overlapping Areas Associated With Baseline Motor vs. Baseline n-Back Tasks

To examine the specific or common involvement of cerebellar regions in working memory and in motor tasks, Fig. 7 shows overlaps of regions associated on the one hand with decreased performance in the 3-back baseline task and on the other hand with increased variability in walking baseline (*A*) and tandem baseline (*B*). First, there is little overlap of regions associated with decreased 3-back baseline performance and increased variability in the baseline walking (Fig. 7*A*). Second, Fig. 7*B* reveals for tandem gait an overlap of several regions associated with impairments in both tasks, including regions in the posterior cerebellum and the dentate nucleus (mostly ventral regions but also dorsal parts).

In contrast to the overlapping regions, specific impairments could be associated with regions within lobule VI. This lobule was involved in both tasks, but the localization within the lobules was different. Whereas in 3-back tasks the more posterior parts of the lobules were of importance (red color in Fig. 7), the more anterior parts contributed to tandem gait (blue color).

DISCUSSION

We examined dual-task effects in patients with focal cerebellar lesions by combining working memory and walking tasks. In dual-task conditions, we found an increasing influence of motor-related lesions on *n*-back performance. For the more difficult tandem gait, we identified strong dual-task interactions and an overlap of lateral cerebellar regions involved in both tasks.

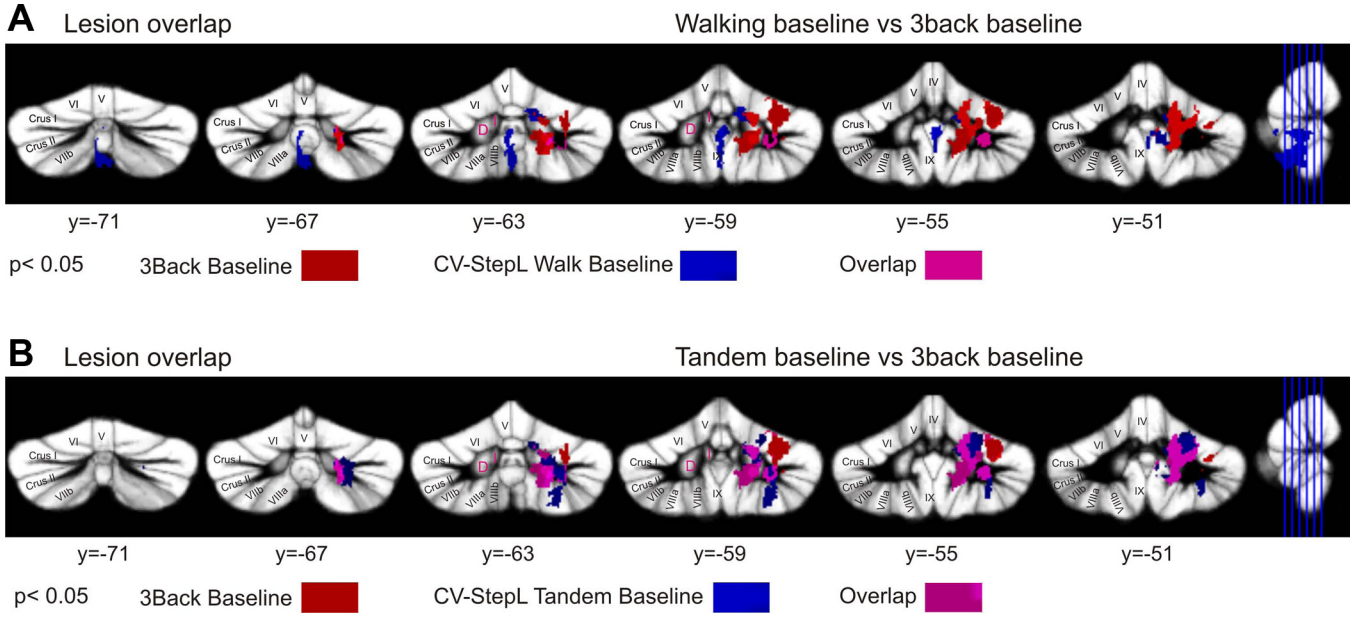

Fig. 7. Analyses of the overlap of lesions associated with impairments in the working memory task and lesions associated with impairments in the different gait tasks, treadmill walking (*A*) and treadmill tandem walking (*B*). For analysis, all lesions were flipped to the right. Regions correlated only with impaired 3-back baseline performance are indicated in red, and regions correlated only with increased gait variability in the corresponding gait baseline condition are indicated in blue. Overlap between regions correlated with both parameters is shown in purple. Almost no overlap can be seen for the comparison of associated lesion areas between 3-back baseline and walking baseline (*A*), whereas there is extensive overlap between associated lesion areas between 3-back baseline and tandem baseline (*B*). Data shown in the overlays were previously shown in Figs. 4 and 6.

Lesion-Symptom Mapping and Baseline 3-Back Performance

We found associations of impaired 3-back task performance with lesions in different cerebellar cortical areas, namely, with lesions within lobules VI (with some extensions into lobule V and Crus I), VIII (extending into lobule IX), and the corresponding parts of the dentate nucleus. These results reflected nicely the hypothesized specific functional roles of distinct cerebellar regions within the task of verbal working memory: the superior cerebellum and dorsal dentate nuclei in phonological encoding, and the inferior cerebellum and ventral dentate nuclei in retrieval and maintenance of the phonological store (Marvel and Desmond 2011, 2012).

In particular, our findings showed associations between reduced 3-back performance and lesions of the ventral and caudal part of the dentate, previously suggested by imaging studies (Kuper et al. 2011a; Thurling et al. 2012) to be involved in a "nonmotor" network with functional connectivity to prefrontal and parietal regions (Dum and Strick 2003; review in Strick et al. 2009). Furthermore, the most consistent association between lesions sites and baseline 3-back performance has been revealed for the dentate nucleus (Fig. 4). This finding is in line with the observation that functional compensation takes place to a much greater extent when lesions are restricted to the cerebellar cortex than in lesions involving the deep nuclei (Konczak et al. 2005; Schoch et al. 2006). Consistently, the involvement of the deep cerebellar nuclei were described as the key factors that determined cognitive deficits including working memory performance and executive function (Tedesco et al. 2011).

Lesion-Symptom Mapping and Baseline Gait Performance: Walking and Tandem

In accordance with the existing literature, our findings reflect specific functional roles for the different cerebellar regions in gait (reviews in Morton and Bastian 2004; Thach and Bastian 2004). Increased step length variability during normal walking was associated with lesions in the vermis (Fig. 6*A*). This reflects the important role of the medial cerebellum for balance in locomotion. Instead, during tandem gait increased step variability was predominantly associated with lesions in the lateral cerebellum (Fig. 6*C*), indicating the importance of this area for visually guided movements (Cerminara et al. 2005).

Likewise, the involvement of the interposed nucleus und the dorsal dentate nucleus in treadmill walking can be explained by known functions of the intermediate cerebellar regions related to the specific control of limb coordination and limb placement (e.g., Cooper et al. 2000), in particular when more gait precision is required. The most likely cause for the involvement of the ventral portion of the dentate is the strong influence of vision in tandem gait, since the ventral part of the dentate has been shown to be involved in visually guided limb movement (Prevosto et al. 2010).

This involvement of ventral parts seems to be in contradiction to the suggested compartmentalization of the dentate in a dorsal motor part and a ventral nonmotor part, responsible for higher cognitive functions (Dum and Strick 2003; Strick et al. 2009). Although there is various evidence of an essential involvement of the dorsal part in motor-related functions and involvement of the ventral part in nonmotor functions such as working memory, recent studies also deliver increasing evidence that the strict subdivision in motor and nonmotor part is an oversimplification and that complex motor function involves the function of the ventral dentate. In a 7T functional MRI (fMRI) study examining finger and foot movements (Kuper et al. 2011b), motor-related activation was not restricted to the dorsorostral dentate nucleus but also comprised caudal and ventral parts of the nucleus.

Thus these studies together with our results would speak against the hypothesis of a clear segmentation of the dentate in a motor and a nonmotor part. Instead, they would support a different view with motivation from neurophysiological animal studies, which have suggested motor representations to cover the entire dentate nucleus (Asanuma et al. 1983; Evrard and Craig 2008; Thach et al. 1993). The ventral part could be predominantly involved in more complex motor tasks (potentially when working memory plays an increasing role) and visually guided movements.

Distinct and Overlapping Areas Associated With Baseline Motor and n-Back Tasks

Lesion-symptom mapping revealed almost no overlaps for a comparison of baseline 3-back and baseline walking (Fig. 7*A*). In contrast, regions in the posterolateral cerebellum and dentate nucleus (mostly ventral regions) were associated with impairments in both baseline 3-back and tandem gait tasks (Fig. 7*B*). These areas likely contribute to both cognitive and motor functions.

Areas in lobule VI, however, did not overlap. Whereas in 3-back tasks the more posterior parts of the lobule were of importance (red color in Fig. 7), the more anterior parts contributed to tandem gait (blue color). This suggests that the more anterior parts of lobule VI are related to motor activities, whereas the more posterior parts are related to working memory tasks.

Indeed, this subdivision of lobule VI is further supported by recent connectivity studies showing connections from lobule VI to the ventral and to the dorsal part of the dentate nucleus (Bernard et al., in press) as well as to the cerebral somatomotor and the ventral attention networks (Buckner et al. 2011). The motor-related areas of lobule VI may particularly be involved in complex movement tasks (Schlerf et al. 2011).

Dual-Task Effects

In the dual-task walking condition, the *n*-back performance of cerebellar patients decreased moderately but significantly (in contrast to that of the control group), whereas gait variability showed no significant increase compared with that in the baseline conditions (Fig. 5). Consistently, lesions similar to those in the baseline condition were associated with decreased 3-back performance (Fig. 4). Additionally, there was practically no overlap between baseline *n*-back performance and baseline walking (Fig. 7). These results suggest that the moderate decrease in *n*-back during dual-task walking is caused by general effects of shifting attention due to prioritization of the walking task to avoid falls. This agrees with earlier results from Doyon et al. (1998) showing that cerebellar patients, as well as patients suffering from Parkinson's disease, have to rely more on cognitive resources for movement control.

We did not see an influence of cognitive load on gait pattern of the walking task, such as that seen by Lang and Bastian

(2002) on newly learned arm movements in the dual-task condition. This difference might be explained by our predominantly mildly impaired patient population (8 patients: ICARS gait and posture ≤2, showing no clinical signs in normal walking). In contrast, for the dual-task tandem condition, cerebellar patients revealed a more essential decrease in *n*-back performance as well as a significant increase of gait variability within the dual-task paradigm (Fig. 5).

Considering 3-back performance, motor areas (dorsal dentate, interposed) became predominantly important, suggesting that the motor impairment becomes the dominating factor. Patients have to focus predominantly on the motor task (prioritization), e.g., to prevent falls, and thus performed worse in the 3-back task. However, prioritization of the motor task does not fully explain why working memory performance decreased and at the same time gait variability increased (Fig. 5), indicating an impact of cognitive load on the motor task, as well. One possible reason is the overlap between areas related to both tandem and *n*-back tasks. As stated above, posterolateral areas are of higher importance in tandem gait compared with walking (Fig. 7). At the same time, posterolateral cerebellar areas support verbal working memory (lobule VI; Marvel and Desmond 2012). An involvement of these regions in both tasks would explain why both performances in the cognitive as well as in the motor task significantly decreased during dual-task conditions. Increased difficulty of working memory tasks has been shown to involve an increasing contribution of the cerebellum (Marvel and Desmond 2012). Therefore, it made sense that interaction effects were most obvious in the most difficult tasks: 3-back and 4-back.

It is important to keep in mind that the lesion-symptom mapping approach delivers regions with the dominating influence, but not necessarily all involved areas. For example, a recent fMRI study in healthy subjects showed that areas in the cerebellum may be related to dual-task effects that are in close neighborhood to single-task-related areas but that do not overlap (Wu et al. 2013). We are unable to answer the question of whether in dual-task conditions new areas in the cerebellum become important that are not active in both single-task conditions. In addition, the present findings do not allow us to decide whether neural substrates involved in both tasks are the same or are located in adjacent areas.

Conclusions

In summary, we found specific associations between cerebellar lesions and performance deficits in single-task conditions for *n*-back, walking, and tandem gait. In the difficult dual-task conditions (3-back, tandem gait), we found interaction effects on both modalities. These effects were most likely caused by a mixture of divided attention, prioritization of the motor tasks, and a common involvement of lateral cerebellar regions in working memory and visuomotor control. Because dual (and multi)-task situations are common in everyday life, it is highly recommended to include dual-task exercises in motor rehabilitation programs for cerebellar patients (Ilg et al. 2009; Miyai et al. 2012). This has been shown to be beneficial in other movement disorders such as Parkinson's disease to prevent falls (Yogev-Seligmann et al. 2012).

APPENDIX A: NEUROANATOMIC LOCATION AND VOLUME OF INDIVIDUAL LESIONS

Details of neuroanatomic location and volume of individual lesions can be found in Table A1.

APPENDIX B: DETAILED RESULTS OF LESION SYMPTOM MAPPING

Detailed results of lesion-symptom mapping considering performance in the 3-back task during sitting, walking, and tandem are shown in Tables A2 and A3.

APPENDIX C: DETAILS OF QUANTITATIVE MOVEMENT ANALYSIS

The 3-D movement trajectories of the patients were recorded at a sampling rate of 120 Hz using a VICON 612 motion capture system with 10 cameras and 41 reflecting markers. The marker trajectories were preprocessed using the commercial software provided by VICON. This software fits a clinically evaluated kinematic model to the marker trajectories and extracts velocities, joint angles, and the course of the center of mass (CoM).

Gait cycles were automatically determined from the trajectories by detection of heel-strike events, based on the vertical components of the heel marker positions. Results of the automatic detection were verified manually using a stick figure animation to correct for different types of foot placement.

Step width was measured by determining the lateral distance between the right and left heel markers at the time of heel strike. Step length was measured by determining the distance between toe marker positions at the time of toe off and heel strike. Step cycle timing was determined by the time interval between subsequent heel strike events of the same leg. Patients were walking with shoes on.

APPENDIX D: GAIT PARAMETERS FOR TREADMILL WALKING AND TREADMILL TANDEM

Tables A4 and Table A5 show results from detailed gait analyses to examine the influence of dual-task conditions on treadmill walking and treadmill tandem walking, respectively.

APPENDIX E: RELATIONSHIP BETWEEN GAIT PERFORMANCE AND ICARS SCORE

Additional analyses of the gait variability were performed to examine gait performance in relation to the general level of ataxia symptoms measured by the ICARS score (see Fig. A1). In the walking condition, there is highly significant correlation between CV step length and the ICARS score (as well as for both relevant subscores: gain and posture, kinetics) (baseline walk: $\rho = 0.66$, $P = 0.004$; *n*-back walks: $\rho > 0.71$, $P < 0.001$). In contrast, there is no correlation of step length variability and the ICARS score for tandem gait. The underlying reason is illustrated in Fig. A1, which shows the relationship between the ICARS score and the temporal gait variability for baseline gait conditions (red circles) and dual-task conditions (black diamonds). Unlike in treadmill walking (Fig. A1*A*), there are several patients with very mild or no clinical symptoms (ICARS ≤ 1) who had already revealed high gait variability for baseline tandem walking (Fig. A1*B*), even increasing in number for the tandem 3-back condition.

ACKNOWLEDGMENTS

We thank Björn Müller and Beate Brol for help with the data analysis and Hans-Gerd Elles for technical support. In addition, we thank Julius Verrel from

Table A1. *Neuroanatomic location and volume of individual lesions*

Patient	Vermal	Paravermal	Lateral	WM	Nuclei	Volume, cm^3
CP1	VI, CRI, CRII, VIIb, VIIIa, VIIIb, IX, X	r: V, VI, CRI, CRII, VIIb, VIIIa, VIIIb, IX l: CRII, VIIb, VIIIa, VIIIb, IX	r: V, VI, CRI, CRII, VIIb, VIIIa, VIIIb, IX	V: 1, 2, 3 PV r: 1, 2, 3	ND r NI r NF r	15.06
CP2	VI, CRI, CRII, VIIb, VIIIa, VIIIb	l: VI, CRI, CRII, VIIb, VIIIa, VIIIB	l:VI, CRI, CRII	V: 2, 3 PV l: 2	ND l	10.99
CP3		r: (VIIb)	r: V, VI, CRI, CRII, VIIb	PV r: 2	(ND r)	8.19
CP4			l: CRI, CRII, VIIb, VIIIa	H l		13.48
CP5		l: CRI, CRII	l: CRI, CRII	PV l: 2, 3 H: l		2.31
CP6	VIIb, VIIIa, VIIIb, IX	l: VI,CRI, CRII, VIIb, VIIIa, VIIIb, IX	l: VIIIa, VIIIb	V: 3 PV l: 2,3	ND l	6.83
CP7			l: CRI, CRII			3.49
CP8		r: I-IV, V, VI, VIIIa,VIIIb, IX	r: I-IV, V, VI, CRI, CRII, VIIb, VIIIa, VIIIb, IX	V: 1, 2, 3 PV r:1, 2, 3 H r: 3	ND r NI r NF r	16.13
CP9	CRII, VIIb, VIIIa, VIIIb, IX	l: I-IV, V, VI, r: I-IV, V, VI		V: 1, 2, 3		10.78
CP10	VI, CRI, CRII, VIIb, VIIIa, VIIIb, IX	l: I-IV,V, VI, CRI, CRII, VIIb, VIIIa, IX r: I-VI, V, VI, VIIb, VIIIa, IX	l: VI, CRI	V: 1, 2, 3 PV l: 2, 3	ND bds NI bds NF bds	32.41
CP11	VI, CRII, VIIb, VIIIa, VIIIb, IX	r:I-IV, V, VI, CRII, VIIb, VIIIa, IX l:I-IV,V,VI,CRII, VIIb, IX		V: 1, 2, 3 PV r: 2	NF bds ND r NI r	9.16
CP12		r: CRI, CRII	r: CRI, CRII, VIIb			3.82
CP13		l: VI, CRI, CRII r: VI, CRI, CRII	l:VI, CRI, CRII			11.03
CP14	VI, CRI, CRII, VIIb, VIIIa	l: V, VI, CRI, CRII;VIIb r:V, VI		V: 1, 2, 3 PV r: 2 PV l: 2	ND bds	18.24
CP15	VI, VIIB, VIIIa, VIIIb, IX	l: I-IV, V, VI, CRI, VIIIa, VIIIb, IX r:I-IV, V, VI, IX	l: VI, CRI	V: 1, 2, 3 PV l: 1, 2, 3 PV r: 1, 2, 3	ND bds NI bds NF bds	13.05
CP16			l: VI, CRI, CRII, VIIb			4.84
CP17			l: VI, CRI, CRII			4.24

Locations of lesions: r, right side; l, left side; b, bilateral; WM, white matter; NF, fastigial nucleus; NI, interposed nucleus; ND, dentate nucleus; V, vermis; PV, paravermal; H, lateral hemisphere. Lesion volumes were calculated on basis of normalized individual lesions.

the Max Planck Institute for Human Development (Berlin, Germany) for providing the software for generation of the *n*-back stimuli.

GRANTS

This work was financially supported by the Centre for Integrative Neuroscience, European Commission TANGO Project FP7 249858-TP3, and German Federal Ministry of Education and Research (BMBF) Grant FKZ 01GQ1002A.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

W.I. and D.T. conception and design of research; W.I., A.C., O.M.M., and S.L.G. performed experiments; W.I., A.C., O.M.M., S.L.G., and D.T. analyzed data; W.I., A.C., M.A.G., and D.T. interpreted results of experiments; W.I. and D.T. prepared figures; W.I. and D.T. drafted manuscript; W.I., A.C., S.L.G., M.A.G., and D.T. edited and revised manuscript; W.I., A.C., O.M.M., S.L.G., M.A.G., and D.T. approved final version of manuscript.

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Table A2. *Lesion-symptom mapping considering performance in the 3-back task during sitting, walking, and tandem walking*

Area	No. of Voxels	Maximum *Z* Score	*x, y, z*
		3-Back baseline	
V	250	2.58	23, −49, −29
VI	2,050	3.05	38, −54, −29
Crus I	291	3.05	35, −54, −33
Crus II	63	2.15	20, −70, −38
VIIIa	94	2.58	19, −65, −48
VIIIb	202	2.58	18, −62, −47
IX	433	2.58	11, −56, −50
Dentate	1,214	3.052.58	20, −62, −42 (ventral) 17, −54, −30 (dorsal)
		3-Back walking	
V	331	1.81	23, −49, −29
VI	1,315	3.12	38, −54, −29
Crus I	201	3.12	35, −54, −33
VIIIa	94	1.81	19, −65, −48
VIIIb	202	1.81	16, −58, −55
IX	418	1.81	11, −59, −51
Dentate	1,157	2,37	14, −62, −41 (ventral)
		3-Back tandem walking	
Vermis Crus II	57	2.41	4, −74, −36
Crus II	81	2.41	7, −74, −39
Vermis VIIb	33	2.41	5, −71, −36
VIIb	160	2.41	6, −71, −40
Vermis VIIIa	484	2.41	6, −70, −39
VIIIa	31	2.41	9, −67, −37
Vermis VIIIb	75	2.29	6, −64, −40
Vermis IX	28	1.95	7, −57, −34
IX	75	2.41	12, −57, −36
Dentate	153	2.41	12, −63, −35 (dorsal)
Interposed	133	1.96	8, −62, −34

Data are results of lesion-symptom mapping considering performance in the 3-back task during sitting, walking, and tandem walking (*t*-test, $P < 0.05$). Number of significant voxels, maximum *Z* score, and SUIT *x*, *y*, and *z* coordinates are given for individual cerebellar lobules and nuclei. Left-sided lesions were flipped to the right.

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Table A3. *Lesion-symptom mapping considering variability of step length during walking, dual-task walking, tandem gait, and dual-task tandem gait*

Area	No. of Voxels	Maximum *Z* score	*x, y, z*
		CV step length walk baseline	
V	58	2,09	9, −62, −25
VI	123	2,09	8, −62, −26
Crus I	178	2,34	17, −79, −26
Vermis VIIIa	148	2,46	1, −65, −36
Vermis VIIIb	285	2,46	1, −62, −38
Vermis IX	391	2,46	1, −53, −39
IX	386	2,46	5, −53, −37
Dentate	133	2,23	20, −62, −42 (ventral)
		2,06	14, −63, −30 (dorsal)
Interposed	33	2,10	10, −58, −29
		CV step length walk 3-back	
Crus I	101	2,58	16, −83, −24
Crus II	81	2,58	15, −88, −39
Vermis VIIIa	102	2,09	0, −68, −35
Vermis VIIIb	152	1,77	−2, −65, −48
Vermis IX	70	1,77	−1, −61, −47
Dentate	34	2,43	22, −60, −41 (ventral)
		CV step length tandem baseline	
V	250	3,43	23, −49, −29
VI	221	3,43	18, −67, −33
VIIIa	66	3,43	19, −65, −48
IX	221	3,43	11, −56, −50
Dentate	751	4,52	20, −62, −42 (ventral)
		3,43	17, −55, −32 (dorsal)
		CV step length tandem 3-back	
V	419	2,52	23, −49, −29
VI	713	2,52	18, −67, −33
Crus I	29	2,17	20, −70, −37
Crus II	42	2,17	20, −70, −38
VIIb	36	2,52	19, −67, −46
VIIIa	816	2,83	31, −58, −46
IX	223	2,53	11, −56, −50
Dentate	838	2,83	20, −62, −42 (ventral)
		2,52	17, −55, −32 (dorsal)

Data are results of lesion-symptom mapping considering variability of step length during walking (baseline), dual-task walking, tandem gait (baseline), and dual-task tandem gait (*t*-test, $P < 0.05$). Number of significant voxels, maximum *Z* score, and SUIT *x*, *y*, and *z* coordinates are given for individual cerebellar lobules and nuclei. Note that left-sided lesions were flipped to the right. CV, coefficient of variation.

Table A4. *Gait measures for treadmill walking at baseline and for dual-task conditions with concurrent n-back tasks*

Measures	Group	Walk	W-1B	W-2B	W-3B	W-4B	Group Effect
Step length, cm	HC	54.47 ± 2.4	53.6 ± 2.0	53.7 ± 1.8	55.23 ± 1.7	55.3 ± 2.1	$F(1,31) = 0.301$
	CP	52.93 ± 1.0	53.08 ± 1.1	52.48 ± 1.0	53.90 ± 1.1	54.45 ± 1.1	$P = 0.587$
CV step length	HC	0.036 ± 0.00	0.039 ± 0.00	0.038 ± 0.00	0.0406 ± 0.0	0.0404 ± 0.0	$F(1,31) = 4.65$
	CP	0.046 ± 0.00	0.046 ± 0.00	0.047 ± 0.00	0.045 ± 0.00	0.047 ± 0.00	$P = 0.039$*
Step width, cm	HC	19.47 ± 1.0	19.47 ± 1.0	20.95 ± 1.0	20.83 ± 1.1	21.46 ± 1.1	$F(1,31) = 0.32$
	CP	19.40 ± 1.2	19.30 ± 1.3	19.11 ± 1.2	19.18 ± 1.2	19.03 ± 1.1	$P = 0.572$
CV step width	HC	0.21 ± 0.02	0.21 ± 0.04	0.18 ± 0.02	0.17 ± 0.01	0.18 ± 0.02	$F(1,31) = 8.17$
	CP	0.25 ± 0.02	0.25 ± 0.02	0.26 ± 0.02	0.26 ± 0.02	0.27 ± 0.02	$P = 0.008$*
Step cycle time, s	HC	1.05 ± 0.06	1.09 ± 0.08	1.00 ± 0.02	1.01 ± 0.02	1.02 ± 0.02	$F(1,31) = 3.95$
	CP	0.95 ± 0.02	0.96 ± 0.02	0.99 ± 0.04	0.97 ± 0.02	0.98 ± 0.02	$P = 0.056$
CV step cycle time	HC	0.05 ± 0.01	0.07 ± 0.02	0.06 ± 0.02	0.06 ± 0.02	0.06 ± 0.01	$F(1,31) = 2.62$
	CP	0.09 ± 0.02	0.09 ± 0.03	0.10 ± 0.02	0.10 ± 0.02	0.10 ± 0.02	$P = 0.116$
Cadence, steps/min	HC	114.9 ± 6.6	113.9 ± 5.8	120.4 ± 2.8	118.9 ± 2.8	118.1 ± 2.8	$F(1,31) = 3.01$
	CP	126.1 ± 2.4	125.8 ± 2.5	122.9 ± 3.6	123.9 ± 2.4	122.7 ± 2.4	$P = 0.093$

Data are gait measures for treadmill walking at 1 m/s at baseline (Walk) and in the dual-task conditions with concurrent *n*-back tasks for $n = 1$-4 (W-1B–W-4B). Group effect describes the probability of a difference between healthy controls (HC) and cerebellar patients (CP) for each kinematic parameter as revealed by a 2 (Group) × 4 (Task Difficulty) mixed-model ANOVA. Significant differences are indicated by stars.

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Table A5. *Gait measures for treadmill tandem walking at baseline and for dual-task conditions with concurrent n-back tasks*

Measures	Group	Tandem	TD-1B	TD-2B	TD-3B	TD-4B	Group effect
Step length, cm	HC	37.63 ± 2.43	37.06 ± 2.50	37.30 ± 2.74	35.39 ± 2.45	35.26 ± 2.68	$F(1,31) = 7.42$
	CP	41.78 ± 2.40	44.56 ± 1.65	43.07 ± 1.84	44.30 ± 1.40	42.04 ± 2.33	$P = 0.011$*
CV step length	HC	0.10 ± 0.02	0.12 ± 0.01	0.11 ± 0.02	0.12 ± 0.02	0.12 ± 0.01	$F(1,31) = 11.34$
	CP	0.17 ± 0.02	0.18 ± 0.02	0.18 ± 0.02	0.18 ± 0.02	0.19 ± 0.02	$P = 0.002$*
Step width, cm	HC	5.50 ± 1.08	5.02 ± 1.05	4.94 ± 1.00	4.99 ± 0.94	4.95 ± 0.92	$F(1,31) = 2.69$
	CP	4.17 ± 0.48	4.23 ± 0.44	4.06 ± 0.39	4.44 ± 0.36	4.33 ± 0.33	$P = 0.111$
CV step width	HC	0.31 ± 0.05	0.42 ± 0.08	0.37 ± 0.05	0.31 ± 0.04	0.33 ± 0.04	$F(1,31) = 8.19$
	CP	0.49 ± 0.04	0.49 ± 0.04	0.51 ± 0.04	0.43 ± 0.03	0.47 ± 0.03	$P = 0.007$*
Step cycle time, s	HC	2.05 ± 0.10	2.01 ± 0.09	2.01 ± 0.10	2.02 ± 0.10	2.02 ± 0.09	$F(1,31) = 11.37$
	CP	1.70 ± 0.12	1.57 ± 0.12	1.57 ± 0.10	1.60 ± 0.10	1.62 ± 0.10	$P = 0.002$*
CV step cycle time	HC	0.11 ± 0.03	0.12 ± 0.03	0.13 ± 0.03	0.11 ± 0.03	0.14 ± 0.03	$F(1,31) = 33.51$
	CP	1.05 ± 0.16	1.39 ± 0.22	1.48 ± 0.23	1.39 ± 0.21	1.41 ± 0.23	$P < 0.001$*
Cadence, steps/min	HC	59.21 ± 2.6	59.51 ± 2.3	58.73 ± 2.3	59.48 ± 2.5	59.73 ± 2.2	$F(1,31) = 17.10$
	CP	73.52 ± 4.1	81.41 ± 5.1	77.09 ± 4.4	77.29 ± 4.5	77.16 ± 4.4	$P < 0.001$*

Data are gait measures for treadmill tandem walking at 0.3 m/s at baseline (Tandem) and for the dual-task conditions with concurrent *n*-back tasks for $n = 1$-4 (TD-1B–TD-4B). Group effect describes the probability of a difference between HC and CP for each kinematic parameter as revealed by a 2 (Group) × 4 (Task Difficulty) mixed-model ANOVA. Significant differences are indicated by stars.

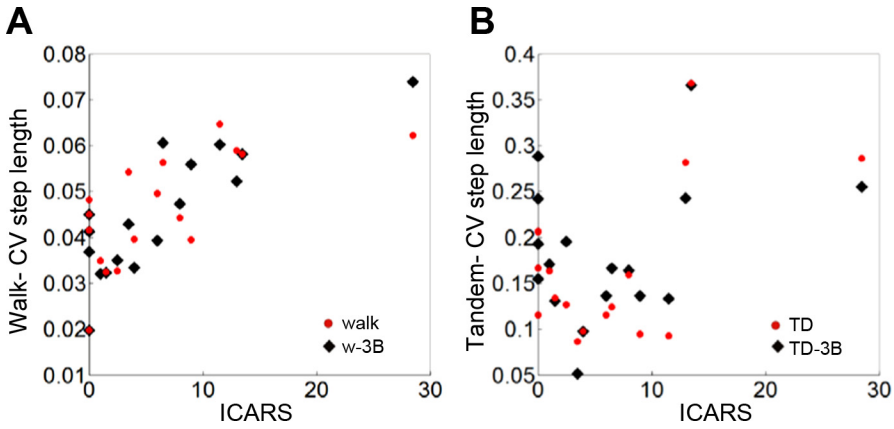

Fig. A1. Relationship between the ICARS score (*x*-axis) and the step length variability (*y*-axis) in treadmill walking (*A*) and treadmill tandem gait (*B*). Red circles denote the baseline conditions without *n*-back task, and black diamonds denote values of step length variability in the dual-task conditions while concurrently performing the 3-back task.

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