Involvement of the cerebellar cortex and nuclei in verbal and visuospatial working memory: A 7 T fMRI study

M. Thürling a,b, H. Hautzel c,d, M. Küper a, M.R. Stefanescu a,b, S. Maderwald b, M.E. Ladd b,e, D. Timmann a,*

a Department of Neurology, University of Duisburg-Essen, Germany
b Department of Nuclear Medicine, Medical Faculty, Heinrich-Heine-University Düsseldorf, Germany
c Department of Nuclear Medicine (KME), Medical Faculty, Heinrich-Heine-University Düsseldorf, at Forschungszentrum Jülich, Germany
d Erwin L. Hahn Institute for Magnetic Resonance Imaging, University of Duisburg-Essen, Germany
e Department of Diagnostic and Interventional Radiology and Neuroradiology, University of Duisburg-Essen, Germany

A R T I C L E   I N F O
Article history:
Accepted 16 May 2012
Available online 24 May 2012

Keywords:
Cerebellum
Cognition
Inner speech
Phonological loop
Visuospatial sketch pad
Central executive

A B S T R A C T
The first aim of the present study was to extend previous findings of similar cerebellar cortical areas being involved in verbal and spatial n-back working memory to the level of the cerebellar nuclei. The second aim was to investigate whether different areas of the cerebellar cortex and nuclei contribute to different working memory tasks (n-back vs. Sternberg tasks). Young and healthy subjects participated in two functional magnetic resonance imaging (fMRI) studies using a 7 T MR scanner with its increased signal-to-noise ratio. One group of subjects (n = 21) performed an abstract and a verbal version of an n-back task contrasting a 2-back and 0-back condition. Another group of subjects (n = 23) performed an abstract and a verbal version of a Sternberg task contrasting a high load and a low load condition. A block design was used. For image processing of the dentate nuclei, a recently developed region of interest (ROI) driven normalization method of the dentate nuclei was applied (Diedrichsen et al., 2011). Whereas activated areas of the cerebellar cortex and dentate nuclei were not significantly different comparing the abstract and verbal versions of the n-back task, activation in the abstract and verbal Sternberg tasks was significantly different. In both n-back tasks activation was most prominent at the border of lobules VI and Crus I, within lobule VII, and within the more caudal parts of the dentate nucleus bilaterally. In Sternberg tasks the most prominent activations were found in lobule VI extending into Crus I on the right. In the verbal Sternberg task activation was significantly larger within right lobule VI compared to the abstract Sternberg task and compared to the verbal n-back task. Activations of rostral parts of the dentate were most prominent in the verbal Sternberg task, whereas activation of caudal parts predominated in the abstract Sternberg task. On the one hand, the lack of difference between abstract and verbal n-back tasks and the lack of significant lateralization suggest a more general contribution of the cerebellum to working memory regardless of the modality. On the other hand, the focus of activation in right lobule VI in the verbal Sternberg task suggests specific cerebellar contributions to verbal working memory. The verbal Sternberg task emphasizes maintenance of stimuli via phonological rehearsal, whereas central executive demands prevail in n-back tasks. Based on the model of working memory by Baddeley and Hitch (1974), the present results show that different regions of the cerebellum support different functions of the central executive system and one of the subsidiary systems, the phonological loop.

© 2012 Elsevier Inc. All rights reserved.

I n t r o d u c t i o n
The human cerebellum contributes to specific cognitive tasks (Beaton and Mariën, 2010; Stoodley and Schmahmann, 2009; Strick et al., 2009 for reviews). One of the best studied examples is working memory. Neuroanatomical, human cerebellar lesion and neuroimaging studies provide convincing evidence that the cerebellum plays a role in verbal working memory, which in turn may influence performance in a range of other cognitive domains (Bellebaum and Daum, 2007; Ben-Yehudah et al., 2007; Marvel and Desmond, 2010a, for reviews). The cerebellar contribution is most obvious in functional brain imaging studies. On the behavioural level, verbal working memory dysfunction is generally mild, and cerebellar patients, at least with chronic disease, frequently perform within the normal range (Ravizza et al., 2006; Timmann and Daum, 2010 for review).

The specific contributions of the cerebellum to working memory have not been conclusively resolved. Based on their extensive neuroimaging studies of verbal working memory, Desmond and colleagues (Chen and Desmond, 2005; Desmond et al., 1997; Kirschen et al.,...
suggest that different regions of the cerebellum are involved in different phases within the phonological loop: 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, 2010a for review). The phonological loop is one of the two “slave” systems of working memory according to the still popular model introduced by Baddeley and Hitch (1974); the visuospatial sketch pad is the other. Whereas the phonological loop is responsible for short-term storage of phonemes, visual and spatial information is stored in the visuospatial sketch pad. The superordinate component of working memory is the central executive system, which is thought to be the central coordinator and integrator of working memory regardless of the modality. Later, Baddeley added a third slave system to his model, the so-called “episodic buffer” (Baddeley, 2000).

A recent fMRI study by one of the authors suggests that the cerebellum contributes to the central executive system (Hautzel et al., 2009). Cerebellar cortical activations were compared in verbal and visuospatial working memory tasks. Lack of significant differences between tasks supported a more general role of the cerebellum in working memory that is an amodal contribution to the central executive system (Hautzel et al., 2009). No clear conclusions could be drawn on the cerebellar nuclei, most likely because of limitations in spatial resolution and signal-to-noise ratio using 1.5T MRI and in the normalization methods available at the time.

Findings of specific contributions of the cerebellum to the different phases of the phonological loop on the one hand and a more general contribution of the cerebellum to working memory independent of stimulus modality on the other are not mutually exclusive. Cerebellar contributions may differ depending on the demands of the working memory task. Desmond’s group examined the Sternberg task, whereas in the Hautzel et al. study n-back tasks were used. Demands on verbalization are notably higher in the Sternberg task, whereas central executive demands prevail in n-back tasks. In the Sternberg task subjects are required to maintain a list of verbal stimuli (most commonly letters) in short-term memory to be able to decide whether a test stimulus is part of the list or not. The experimental design of a Sternberg task emphasizes the sole stimulus maintenance via phonological rehearsal. Additionally, this effect is intensified by presenting considerably large numbers of stimuli at a time close to the capacity limits of working memory (Miller, 1956).

In contrast, in n-back tasks fewer verbal stimuli have to be stored in working memory concurrently. Verbal stimuli are presented one after the other, and subjects need to decide whether the present stimulus is the same as the n-to-last stimulus, for example the second-to-last in a 2-back task. Thus, stimuli change more quickly in n-back tasks and additionally need to be tagged, ordered and updated in terms of sequence.

The aims of the present study were twofold. First, we wanted to extend the previous findings of similar cerebellar areas being involved in verbal and spatial working memory to the level of the cerebellar nuclei. We took advantage of ultra-high-field MRI (7T MRI) and its increased signal-to-noise ratio, and of a recently developed ROI-driven normalization method of the dentate nucleus (Diedrichsen et al., 2011). Recent studies have shown that reliable activations of the dentate nucleus, in particular of its ventral part in more cognitive tasks, are feasible based on these advanced techniques (Küper et al., 2011a; Thürling et al., 2011). Histological data in monkey and recent structural and functional MRI connectivity studies suggest that the more ventral and caudal parts of the dentate nuclei contribute to more cognitive tasks, whereas motor function may be primarily located in the more dorsal and rostral dentate nucleus (Dum and Strick, 2003; Strick et al., 2009). We hypothesized that verbal and visuospatial n-back tasks would lead to activations within the ventral and caudal dentate bilaterally. Based on the previous findings in the cerebellar cortex, we hypothesized that these areas were similarly activated by both modalities.

Second, we asked the question whether different areas of the cerebellar cortex and nuclei contribute to different working memory tasks. In addition to verbal and visuospatial versions of the n-back tasks, a verbal and a newly developed visuospatial version of the Sternberg task were used. Regions related to both tasks were expected in the posterolateral cerebellar hemisphere and ventrocaudal dentate nucleus, that is in those regions thought to contribute to cognitive functions. The regions, however, may only partially overlap because the focus is more on the central executive in n-back tasks and on one of the subsidiary systems in Sternberg tasks. Whereas cerebellar regions related to n-back tasks were hypothesized to be largely the same in both the cerebellar cortex and nuclei, it was expected that regions in the Sternberg task may show different lateralization depending on the stimulus modality. Verbal Sternberg task-related activations were expected to be more prominent on the right, given that the right cerebellum (which is connected with the left cerebrum) has been shown to contribute to language (Fiez et al., 1992; Justus, 2004; Thürling et al., 2011). On the other hand, cerebellar cortical and dentate regions related to abstract (visuospatial) stimulus materials may be more prominent on the left (Stoodley and Schmahmann, 2009). The left cerebellum is connected with the right cerebrum, which is known to be more strongly involved in visuospatial function. Findings of lateralization of visuospatial tasks in the cerebellum, however, are less consistent than lateralization of language function to the right cerebellum (Frank et al., 2007 for review).

Materials and methods

Participants

N-back tasks: Initially, 25 healthy subjects (mean age 26.6±5.5 years, range 21–45 years, 14 males, 11 females) underwent the n-back tasks. Four participants were subsequently excluded due to technical problems (n = 2) or insufficient task performance below the statistically derived cut-off threshold of 66% correct responses (n = 2). The data from 21 subjects (mean age 25.5±3.9 years, 11 males, 10 females) were further analysed.

Sternberg tasks: 27 healthy subjects (mean age 27.4±4.8 years, range 20–43 years, 18 males, 9 females) participated in this study. Four participants had to be excluded due to insufficient task performance below the statistically derived cut-off threshold of 66% correct responses (n = 3) or intense head movements more than 2 mm or 2° (n = 1). Data from 23 participants (mean age 27.0±3.8 years, 15 males, 8 females) were subjected to the subsequent analyses.

All participants were right-handed as measured by the Edinburgh handedness scale (Oldfield, 1971). Informed consent was obtained from all participants. The study was approved by the local ethics committee.

Description and implementation of the paradigms

Verbal and abstract n-back, as well as verbal and abstract Sternberg tasks, were performed in separate fMRI runs. Generation and triggering of the visual stimuli as well as collection of behavioural data were done using E-PRIME software (http://www.pstnet.com/eprime.cfm). The visual stimuli were projected onto a screen and were viewed via a mirror mounted on a head coil inside the MR scanner.

N-back tasks

A total of 20 stimuli were visually presented one at a time over a total interval of 30 s. The stimulus presentation time was 1300 ms, with an inter-stimulus interval (ISI) of 200 ms in which a central...
fixation cross was presented. In the 2-back task the current stimulus had to be compared with the second-to-last stimulus. The subjects responded to correct or incorrect trials via button press (Lumitouch HHSC-1 × 4-CL/-CR, http://www.curdes.com/). In the 0-back task, two predefined stimuli indicated right or left presses. In the verbal working memory (WM) condition, six different letters (A, B, C, D for 2-back, X, Y for 0-back) served as stimuli, while six non-nameable shape stimuli (Attneave and Arnoult, 1956, compare Fig. 1) were used in the abstract WM version. All stimuli were projected in white on a black screen and had the same block-wise frequency; furthermore, in the 2-back sessions they were counterbalanced to achieve 50% correct trial combinations.

The verbal and abstract n-back runs were modelled in a block design fashion consisting of eleven 30 s rest blocks (white fixation cross on black screen), ten 6 s introductory blocks indicating the following 2- or 0-back condition, and ten 30 s WM blocks (5 × 2-back, 5 × 0-back). The total length of the n-back runs was 235 scans each. Fig. 2 illustrates the block design.

Before scanning, two blocks (one 2-back, one 0-back) were used to familiarize the subjects with the task at hand.

Sternberg tasks

The Sternberg tasks were composed of an encoding phase, a maintenance phase in which the subjects had to retain the encoded stimuli, and a retrieval phase. For both the verbal and the abstract WM conditions a high and a low load condition were tested (Fig. 3). Stimulus parameters were chosen in close accordance to Chen and Desmond (2005).

For verbal WM, 18 different consonants served as stimuli, avoiding Q, X and Y due to their low frequency in the German language. During the high load condition 6 letters (two rows with three stimuli) were presented for 1.5 s. The low load condition contained only one stimulus randomly displayed at one of the six locations with the others filled with hashmarks.

In the abstract Sternberg task, 16 non-nameable shape stimuli were used (Attneave and Arnoult, 1956). To adjust the performance rates of the verbal and the abstract Sternberg tasks, extensive pilot studies were performed. From those results a reduced stimulus number of four shape stimuli and a longer encoding time of 3 s were derived for the abstract high load version. In the abstract low load condition one shape was placed randomly at one of the four locations and the others were filled with hashmarks.

Maintenance and retrieval phases were the same in all Sternberg WM conditions: after a maintenance interval of 5 s, a target stimulus was presented for 1 s which matched one of the initial stimuli in 50% of the cases. Trials were separated by a 1.5 s inter-trial interval (ITI). The subjects responded to correct or incorrect trials by button press (see above). Due to the complexity especially of the high load conditions, the participants had the opportunity to correct their button press answer during the subsequent presentation of the fixation cross.

The Sternberg tasks were presented in a block design. The active blocks consisted of four trials each, resulting in a total time of 36 s for one block in the case of verbal Sternberg. The abstract Sternberg tasks required 42 s due to the longer encoding times. One total run was composed of six low load blocks and six high load blocks in counterbalanced order without introductory blocks. These trials were interspersed with thirteen 21 s rest blocks (white fixation cross on black screen) (Fig. 4). The total length of the verbal Sternberg run was 240 scans and that of the abstract Sternberg run 264 scans.

Before scanning, subjects were trained to familiarize them with the tasks. For the low load Sternberg condition one block, for the verbal high load task three blocks, and for the abstract high load condition four familiarization blocks were performed.
movements between scans were below 0.2 mm for translations and 1.1°. Movement parameters were used as regressors in the statistical images.

For each of the experimental tasks a significant change in the BOLD effect compared to the rest condition was tested by specifying the following contrasts: (i) 2-back verbal MINUS 0-back verbal to assess cerebellar activity related to verbal WM; (ii) 2-back abstract MINUS 0-back abstract to assess cerebellar activity related to abstract WM; (iii) Sternberg high load verbal MINUS low load verbal to assess cerebellar activity related to verbal WM; (iv) Sternberg high load abstract MINUS low load abstract to assess cerebellar activity related to abstract WM. Conjunction analyses were performed to show areas that were active in both the verbal and abstract task conditions. Finally, a 2x2 mixed full factorial design was performed for direct comparison between 2-back and Sternberg tasks. Tasks (2-back vs. Sternberg) were treated as between subject factor and conditions (verbal vs. abstract) as within subject factor.

Cerebellar cortex

For the normalization of the cerebellar cortical data, the T1-weighted images were deformed to fit the spatially unbiased atlas template (SUIT) of the human cerebellum using the SUIT toolbox in SPM5 (Diedrichsen, 2006). The program initially isolates the cerebellum and creates a mask. These masks were manually corrected with the help of CARET software (http://brainvis.wustl.edu/wiki/index.php/Caret:About). Non-linear deformation was then applied to each contrast image from the individual participants. The normalized images were resampled at 1×1×1 mm³ resolution and then smoothed by a three-dimensional convolution with an isotropic Gaussian kernel of 4 mm Full Width at Half Maximum (FWHM).

The contrasts working memory minus control condition were calculated in single subjects before normalization. After normalization, one-sample t-tests of contrasts were calculated in second-level analyses. Small volume correction (SVC) was performed considering the entire cerebellar cortex. The probabilistic atlas of the cerebellar cortex introduced by Diedrichsen et al. (2009) was used to define the entirety of the cerebellar cortex. The cerebellar cortical activations are shown at a threshold of p<0.001, false discovery rate (FDR) corrected. This equates to paradigm-dependent thresholds of t=5.56/5.08/5.11/4.69 (n-back abstract / n-back verbal / Sternberg abstract / Sternberg verbal).

Dentate nuclei

The dentate nuclei were identified as hypointensities on the mean image and marked as regions of interest (ROIs) using MRICron software (http://www.sph.sc.edu/comd/roden/mricron/). For normalization, a newly developed modified version of the SUIT method described above was used. This normalization algorithm tries to deform the T1 image so that it fits to the SUIT template, while optimizing the overlap between the ROI and a dentate template (Diedrichsen et al., 2011). To avoid activation surrounding the dentate nucleus being smoothed into the ROI, the functional images were masked with the dentate ROI before normalization. The normalized functional data from the dentate nuclei were resampled at 1×1×1 mm³ resolution and then smoothed with a three-dimensional convolution with an isotropic Gaussian kernel of 4 mm FWHM.

Group analysis was performed with one-sample t-tests at a threshold of p=0.001 uncorrected. The option 'explicit masking' was used in SPM. SVC was performed using the dentate template as ROI. The random field (RF) cluster size correction was not considered suitable for this dataset because the search volume was very small. Bootstrap analysis was therefore used to correct the significance level for multiple tests (Hayasaka and Nichols, 2003). Sets of 21 or 23 random samples were drawn from all contrast images (with replacement) for the n-back and Sternberg tasks, respectively, and
multiplied with 1 or −1 to randomize the sign. For each of these fake data sets, a t-map was calculated and the maximal t-value and cluster size at the uncorrected threshold (t(21) = 3.55 for 2-back and t(23) = 3.50 for Sternberg, p = 0.001) was determined, searching both in the left and right dentate. Repeating this process 1000 times, the values that would only occur in 5% of the random data sets were determined. The corrected peak t-value was 3.9 for both data sets and the minimal cluster size 7 voxels (at t = 3.55) for n-back and 9 voxels (at t = 3.50) for Sternberg tasks. If one of these criteria was fulfilled, activation was regarded as significant.

To describe the localization of dentate activations, the dentate template was divided into four sections. The dentate was subdivided into a dorsorostral (DRDN), dorsocaudal (DCDN), ventroorostral (VRDN), and ventrocaudal (VCDN) section as described in Küper et al. (2011a).

Modality and laterality analysis

In a second step, activations were compared between abstract and verbal conditions, and between left and right side for each task in individual cerebellar lobules and dentate nuclei. The search volumes were defined as follows. To begin with, the same steps as used for group analysis were taken combining both abstract and verbal WM (2-back minus 0-back and high load minus low load Sternberg) to generate modality independent functional contrasts. FDR-thresholds were used based on individual analysis for each condition (n-back = 5.08, Sternberg = 4.69; see Image Analysis above).

Next, anatomical volumes of interests (VOIs) of individual cerebellar lobules were defined using the probability maps of the SUIT dataset (Diedrichsen, 2006). These initial VOIs were shrunk in size to avoid overlap between neighbouring VOIs (that is, lobules). Anatomical dentate VOIs were distinguished for the left and right side. Thereafter, mean values from normalized beta images were calculated for abstract and verbal datasets for those areas that showed activations in the combined abstract and verbal conditions of each task in every VOI (that is, the functionally defined VOIs). Only VOIs with cluster sizes > 50 were considered, which is similar to Hautzel et al. (2009). In that study the minimal cluster size was 20, but with greater voxel size (2 × 2 × 2 mm³).

Two-sided paired t-tests were used for comparisons of mean beta-values between side (right vs. left separately for the abstract and verbal tasks) and WM task (abstract vs. verbal tasks separately for the n-back and Sternberg tasks). P-values < 0.0133 were regarded as significant (Bonferroni corrected, p-values < 0.05/3 considering the three main comparisons in each WM task: right vs. left abstract, right vs. left verbal and abstract vs. verbal). In addition, to allow for direct comparison with data from a previous study of one of the authors (Hautzel et al., 2009), mean and maximum t-values were calculated for every functionally defined VOI.

Results

N-back tasks

Behavioural data

The number of correct responses and reaction times were calculated for each participant in the two conditions (2-back, 0-back) and for both tasks (abstract and verbal n-back tasks). As expected the mean number of correct responses was significantly lower in the 2-back compared to the 0-back condition (condition effect $F_{(1,20)} = 60.919$, p < 0.001; repeated measures ANOVA) (Fig. 5A). The mean number of correct responses was not different between the 0-back conditions of the abstract and verbal n-back tasks. However, subjects performed worse in the 2-back abstract task compared to the 2-back verbal task (task effect $F_{(1,20)} = 27.684$, p < 0.001; task by condition interaction $F_{(1,20)} = 29.037$, p < 0.001).

Reaction times were significantly faster in the 0-back compared to the 2-back condition (condition effect $F_{(1,20)} = 194.571$, p < 0.001; repeated measures ANOVA) (Fig. 5B). Again, there was no difference between reaction times in the 0-back conditions comparing tasks, but reaction times were significantly longer in the abstract 2-back task compared to the verbal 2-back task (task effect $F_{(1,20)} = 23.366$, p < 0.001; task by condition interaction $F_{(1,20)} = 29.236$, p < 0.001).

Cerebellar cortical activations

Activations of the cerebellar cortex are shown superimposed on the SUIT maximum probability map of the cerebellum (Diedrichsen et al., 2009) in Fig. 6. Local maxima are summarized in Table 1.

The pattern of activation was largely the same in the abstract and verbal 2-back tasks. Activation maxima were found within lobule VI extending into Crus I bilaterally. Additional activations were present in Crus II, VIIb, VIIIb, and IX. For both tasks activations were more pronounced on the right. Overall, activations appeared more prominent in the verbal 2-back task compared to the abstract 2-back task. Small additional activations were found in vermian lobules V, VI, and IX in the abstract 2-back task, and within vermian lobule VIIb and hemispheral lobule VIIIa in the verbal 2-back task.

The contrasts abstract 2-back MINUS verbal 2-back and vice versa showed no significant activations. Conjunction analysis showed that common areas were active on the right (maxima in lobules VI, Crus I, Crus II and VIIb) and to a lesser extent on the left (maxima in lobules VI and Crus I) (Fig. 6C, Table 1).

Dentate nucleus activations

Dentate nucleus activations are shown superimposed on a template of the dentate nuclei (Diedrichsen et al., 2011) in Fig. 7. Local maxima are summarized in Table 2.

Although activation appeared to be more prominent in the verbal n-back task, the general pattern of dentate nuclei activation was similar for both tasks. Activations were most pronounced in the caudal dentate bilaterally. On the right, activations were located within the ventrocaudal parts of the dentate nuclei (Fig. 7A, B) in both tasks, with some extension to the dorsocaudal dentate in the verbal 2-back task. On the left, activations were most prominent in the dorsocaudal parts for both tasks, with some extension to the ventrocaudal part in the verbal 2-back task (Fig. 7C, D). For the verbal 2-back task, activation was more prominent on the right.

The contrasts abstract 2-back MINUS verbal 2-back and vice versa showed no significant activations. Conjunction analysis showed that a common area was active in the right ventrocaudal dentate nucleus (Fig. 7E, Table 2).
**Modality and laterality analysis**

Results are shown in Table 3. There were no significant differences in any of the lobules or the dentate nucleus comparing mean beta values between the abstract and the verbal n-back tasks. Note that p-values were corrected for multiple comparisons and only p values <0.0133 were considered significant. Regarding effects of lateralization none of the comparisons reached significance with the exception of lobule VIIIa in both the verbal and abstract tasks. Overall activations were small in lobule VIIIa. The significant side differences are explained by the fact that only voxels on the right but no voxels on the left survived the thresholds in the search volume (see Materials and Methods). No significant side differences were found for the dentate nucleus.

**Sternberg tasks**

**Behavioural data**

The number of correct responses and reaction times were calculated for each participant for the two conditions (high load, low load) and the two tasks (abstract and verbal Sternberg tasks). In the Sternberg tasks the mean number of correct responses was significantly lower in the high load compared to the low load condition (condition effect $F_{(1,22)} = 126.480, p<0.001$; repeated measures ANOVA) (Fig. 8A). The mean number of correct responses was not different between low load conditions in the abstract and verbal Sternberg tasks. However, subjects performed worse in the abstract Sternberg task compared to the verbal Sternberg task (task effect $F_{(1,22)} = 126.480, p<0.001$; task by condition interaction $F_{(1,22)} = 25.047, p<0.001$).

Reaction times were significantly faster in the low load compared to the high load condition (condition effect $F_{(1,19)} = 268.405, p<0.001$; repeated measures ANOVA) (Fig. 8B). There was no difference between reaction times in the low load and high load conditions comparing tasks (task effect $F_{(1,22)} = 3.824, p=0.063$; task by condition interaction $F_{(1,22)} = 0.818, p=0.376$).

**Cerebellar cortical activations**

Activations of the cerebellar cortex are shown superimposed on the SUIT maximum probability map of the cerebellum (Diedrichsen et al., 2009) in Fig. 9. Local maxima are summarized in Table 4.

Overall, activations appeared more prominent for the verbal than the abstract Sternberg task (Fig. 9A, B). Similar to the n-back tasks, however, the general pattern of activations was comparable between both modalities. Activations were more prominent on the right. The most prominent activations were found in lobule VI extending into Crus I. Activation of lobule VI extended into the vermis in the abstract Sternberg task. In both tasks, additional smaller activations were present in lobules I-IV, V, Crus II, and vermal lobules VIIIa, b and IX. Crus II activation extended into VIIb in the verbal Sternberg task. Activation on the left was observed predominantly in the verbal Sternberg task with a maximum in lobules VI and Crus I.

The contrast verbal Sternberg task MINUS abstract Sternberg task showed significant activation in the more anterior parts of lobule VI on the right. The contrast abstract Sternberg task MINUS verbal Sternberg task showed no significant activations.

Conjunction analysis showed that common areas were active predominantly on the right (maximum in the more posterior parts of lobule VI with extension into Crus I) and one small region on the left (maximum in Crus I) (Fig. 9D, Table 4).

**Dentate nucleus activations**

Dentate nucleus activations are shown superimposed on a template of the dentate nuclei (Diedrichsen et al., 2011) in Fig. 10. Local maxima are summarized in Table 5.

Both the abstract and verbal Sternberg task led to activations of the more dorsocaudal parts of the dentate nucleus on the right. Right-sided dentate activation extended into its ventrocaudal parts in the abstract and into its ventroorostral parts in the verbal Sternberg task. On the left, significant activation was observed only in the verbal task and was located in the ventroorostral nucleus.
The contrast abstract Sternberg task MINUS verbal Sternberg task and vice versa showed no significant activations. Conjunction analysis showed no common areas in the dentate nucleus.

**Modality and laterality analysis**

To further test for differences between activations in the abstract and verbal Sternberg tasks and to test for possible effects of laterality, activations were compared on the level of individual lobules and the dentate nucleus. Results are shown in Table 6.

In the verbal Sternberg task, activations were significantly higher compared to the abstract Sternberg task in lobule VI on the right side (t(22): 3.80, p<0.001). In addition, activations in lobules V (t(22): 2.82, p = 0.01) and VIIb (t(22): 4.26, p<0.001) were significantly higher on the right side in the verbal Sternberg task. No significant differences were found in the dentate between the two tasks. Regarding effects of lateralization, none of the comparisons were significant. No significant side differences were found for the dentate nucleus.

**Direct comparison of n-back and Sternberg tasks**

**Cerebellar cortical activations**

At a threshold of p<0.001 FDR corrected no significant main effects of task (2-back vs. Sternberg) and condition (verbal vs. abstract), and no significant interaction were found. Lowering the threshold to p<0.05 FDR significant main effects of task were observed primarily in the more posterior parts of lobule VI and Crus I bilaterally and in more anterior parts of the right lobule VI (Fig. 11A; Table 7). Main effect of condition and task by condition interaction did not become significant.

Posthoc comparisons of verbal 2-back and verbal Sternberg tasks were performed at the same threshold of p<0.05 FDR corrected. The verbal Sternberg task showed significantly more activation in anterior parts of right lobule VI than the verbal 2-back task (Fig. 11B), whereas the verbal 2-back task showed more activation in the more posterior lobule VI with extension into Crus I bilaterally (Fig. 11C). Comparing abstract 2-back and Sternberg tasks no significant differences were observed. Findings further confirm the bilateral cerebellar activations.
seen in the 2-back tasks (Fig. 6) and the right-sided predominance in lobule VI observed in the verbal Sternberg task (Fig. 8).

Dentate nucleus activations

Both at a threshold of $p < 0.001$ Bootstrap-corrected and $p < 0.001$ uncorrected no significant main effects of task (2-back vs. Sternberg) and condition (verbal vs. abstract) and no significant interaction were found.

Discussion

Our results show that similar regions in the cerebellar cortex and dentate nuclei are involved in abstract and verbal n-back working memory tasks. Lack of differences between abstract and verbal stimulus modality and lack of significant lateralization in both tasks provide further support that the cerebellum contributes to more general functions of working memory. In contrast, comparing an abstract and a verbal version of a Sternberg working memory task, we found that cerebellar cortical activation was significantly stronger in the verbal task, particularly within right lobule VI. These findings are in line with a contribution of the cerebellum to the phonological loop. Different areas of the cerebellum appear to contribute to central executive functions and the phonological loop depending on the requirements of the working memory task. No evidence was found for a contribution to the second slave system, the visuospatial sketch pad.

Cerebellar cortex

Cerebellar cortical activation found in all working memory tasks was present predominantly in the posterolateral hemisphere with maxima in lobules VI/Crus I and a smaller focus in lobules VIIb/Villa. These findings are in very good accordance with the brain imaging and human cerebellar lesion literature (Chen and Desmond, 2005; Cooper et al., 2012; Desmond et al., 1997; Hautzel et al., 2009; Kirschen et al., 2005, 2010). The same areas were reported by Stoodley and Schmahmann (2009) to contribute to working memory tasks in their meta-analysis of cerebellar neuroimaging studies. Likewise, Cooper et al. (2012) found a correlation between gray matter density in bilateral superior cerebellum and inferior cerebellum and performance in working memory tasks in a recent voxel-based morphometry study in patients with cerebellar degeneration. We were able to confirm the results of the previous study by Hautzel et al. (2009) that both verbal and abstract n-back tasks lead to activations of similar areas within the cerebellar cortex bilaterally. No significant predominance of activation of the right cerebellum in the verbal n-back task or of the left cerebellar hemisphere in the abstract n-back task could be found. Overlap of areas and lack of significant laterality confirm findings that the cerebellum contributes to working memory in a more general way independent of modality. Based on the model of Baddeley and Hitch (1974), these findings suggest that the cerebellum contributes to functions of the central executive system.

A comparison of the abstract and verbal Sternberg task activations showed some overlap. Overlap was found in particular in the more

Table 2
Local activation maxima in dentate nucleus for n-back tasks (2-back MINUS 0-back). The thresholds were calculated by bootstrapping with 7 voxels as critical cluster threshold or $t = 3.9$ as corrected height threshold (at $p = 0.001$ uncorrected). Activations which met one of these thresholds were considered significant. Activation maxima are underlined. DRDN = dorsorostral dentate nucleus, VCDN = ventrocaudal dentate nucleus, DCDN = dorsocaudal dentate nucleus, VRDN = ventrorostral dentate nucleus.

<table>
<thead>
<tr>
<th>Condition / Contrast</th>
<th>Side</th>
<th>x, y, z</th>
<th>Location</th>
<th>Cluster voxel size</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-back task abstract</td>
<td>Left</td>
<td>−10, −60, −34</td>
<td>DCDN</td>
<td>13</td>
<td>4.40</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>19, −61, −36</td>
<td>VCDN</td>
<td>7</td>
<td>3.93</td>
</tr>
<tr>
<td>2-back task verbal</td>
<td>Left</td>
<td>−19, −59, −36</td>
<td>VCDN, DCDN</td>
<td>47</td>
<td>6.07</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>21, −60, −35</td>
<td>DCDN, VCDN, VRDN</td>
<td>46</td>
<td>4.17</td>
</tr>
<tr>
<td>Conjunction abstract and verbal</td>
<td>Right</td>
<td>13, −60, −36</td>
<td>VCDN, DCDN</td>
<td>11</td>
<td>3.94</td>
</tr>
</tbody>
</table>
posterior parts of lobule VI and lobule Crus I, that is in the same areas mainly related to the n-back tasks. In fact, cerebellar cortical areas contributing to the abstract Sternberg task were comparable to those seen for both the abstract and verbal n-back tasks. There was no significant difference comparing the abstract n-back and Sternberg tasks. Cerebellar cortical areas in the verbal Sternberg task, however, were more extensive on the right side. Only the verbal Sternberg task was accompanied by activation of most parts of lobule VI, whereas activation in the other tasks was localized at the border between lobules VI and Crus I. Right lobule VI showed significantly higher activations in the verbal compared to the abstract Sternberg task. Similar findings, but to a lesser extent, were observed for right lobules V and VIIb. Furthermore, activation in the more anterior parts of right lobule VI was stronger in the verbal Sternberg compared to the verbal n-back task. Given the difference between the tasks and lateralization to the right cerebellum with its known contributions to language, this provides good evidence that the cerebellum is involved in the phonological loop. These data are in good accordance with the findings of Desmond and colleagues who showed that lobules VI/Crus I and lobules VIIb/VIII contribute to working memory. In their functional brain imaging studies, the verbal Sternberg task was used.

Taking the findings of the n-back and Sternberg tasks together, our results suggest that the cerebellum contributes both to the central executive system and to one of the slave systems (phonological loop). In tasks which emphasize function of the central executive system, in our case the n-back tasks, cerebellar areas with more general contributions can be observed, in particular the border zone of lobules VI and Crus I bilaterally. In a task that puts more emphasis on the phonological loop, such as the Sternberg task, additional areas play a role, in particular in lobule VI on the right side. Cooper et al. (2012) reached a very similar conclusion in their VBM study based on Wechsler working memory tests in patients with cerebellar degeneration, with different cerebellar areas contributing to the central executive and phonological loop. Different to our findings they found that the right inferior cerebellum contributes to the phonological loop.

Note, that although verbal n-back tasks depend on central executive functions to a larger degree than verbal Sternberg tasks, verbalization is also part of n-back tasks. Complete lack of lateralization is unexpected. In fact, in n-back tasks activation tended to be more prominent on the right, although this did not reach significance.

Table 3
Comparison of modality and laterality in the n-back tasks. Maximum t-values (and the corresponding x y z coordinates in MNI space) and mean t-values are given in functionally defined VOIs of individual cerebellar lobules and the dentate nuclei separated by task and side. Mean t-values are given as t(p<0.001, FDR-corrected; minimal cluster size 50 voxels) considering the abstract and verbal tasks together.

<table>
<thead>
<tr>
<th>Cerebellar lobule</th>
<th>Abstract n-back</th>
<th>Verbal n-back</th>
<th>Search vol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>maximum activation</td>
<td>maximum activation</td>
<td>Cluster</td>
</tr>
<tr>
<td></td>
<td>x, y, z</td>
<td>max t-value</td>
<td>mean t-value</td>
</tr>
<tr>
<td>I-IV left</td>
<td>−1, −49, −20</td>
<td>6.10</td>
<td>5.03</td>
</tr>
<tr>
<td>I-IV right</td>
<td>1, −49, −20</td>
<td>5.71</td>
<td>4.99</td>
</tr>
<tr>
<td>V left</td>
<td>0, −61, −19</td>
<td>6.52</td>
<td>5.25</td>
</tr>
<tr>
<td>V right</td>
<td>2, −61, −19</td>
<td>8.49</td>
<td>7.32</td>
</tr>
<tr>
<td>VI ver.</td>
<td>7, −71, −25</td>
<td>7.54</td>
<td>6.35</td>
</tr>
<tr>
<td>VI left</td>
<td>−30, −61, −30</td>
<td>6.91</td>
<td>7.30</td>
</tr>
<tr>
<td>VI right</td>
<td>32, −58, −28</td>
<td>9.47</td>
<td>8.22</td>
</tr>
<tr>
<td>Crus I ver.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Crus I left</td>
<td>−37, −54, −31</td>
<td>7.50</td>
<td>8.71</td>
</tr>
<tr>
<td>Crus I right</td>
<td>34, −58, −32</td>
<td>7.89</td>
<td>7.65</td>
</tr>
<tr>
<td>Crus II ver.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Crus II left</td>
<td>−42, −55, −49</td>
<td>6.55</td>
<td>6.79</td>
</tr>
<tr>
<td>Crus II right</td>
<td>42, −59, −48</td>
<td>7.61</td>
<td>6.64</td>
</tr>
<tr>
<td>VIIa ver.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>VIIa left</td>
<td>−30, −71, −52</td>
<td>4.35</td>
<td>3.99</td>
</tr>
<tr>
<td>VIIa right</td>
<td>27, −71, −48</td>
<td>8.10</td>
<td>6.30</td>
</tr>
<tr>
<td>VIIb ver.</td>
<td>−1, −63, −36</td>
<td>4.51</td>
<td>4.14</td>
</tr>
<tr>
<td>VIIb left</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>VIIb right</td>
<td>32, −42, −43</td>
<td>4.45</td>
<td>3.98</td>
</tr>
<tr>
<td>VIIib ver.</td>
<td>5, −59, −35</td>
<td>6.20</td>
<td>4.26</td>
</tr>
<tr>
<td>VIIib left</td>
<td>−10, −59, −51</td>
<td>5.25</td>
<td>5.11</td>
</tr>
<tr>
<td>VIIib right</td>
<td>13, −60, −45</td>
<td>7.04</td>
<td>6.05</td>
</tr>
<tr>
<td>IX ver.</td>
<td>4, −58, −35</td>
<td>6.23</td>
<td>5.15</td>
</tr>
<tr>
<td>IX left</td>
<td>−8, −55, −50</td>
<td>6.19</td>
<td>6.01</td>
</tr>
<tr>
<td>IX right</td>
<td>14, −54, −45</td>
<td>7.72</td>
<td>6.49</td>
</tr>
<tr>
<td>X ver.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>X left</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>X right</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Dentate left</td>
<td>−10, −60, −34</td>
<td>4.40</td>
<td>3.11</td>
</tr>
<tr>
<td>Dentate right</td>
<td>19, −61, −36</td>
<td>3.93</td>
<td>3.39</td>
</tr>
</tbody>
</table>

Fig. 8. Behavioural data for the abstract and verbal Sternberg tasks. (A) Correct answers in %+/− SD and (B) mean reaction times +/− SD. Gray bars: high load; open bars: low load.
Laterality effect in the verbal n-back tasks may have been overridden by dominating central executive contributions of the cerebellum (Hautzel et al., 2009). Results imply that n-back tasks are not ideal for examining lateralized activation.

We did not observe additional left-sided activations in the abstract Sternberg task. There are at least two possible explanations. First, stimulus maintenance, which is a central part of Sternberg working memory tasks, of abstract information may depend to a large part on cortical areas within the fronto-parietal network known to be involved in working memory, with the cerebellum being not or less important. In the abstract domain, contributions to the central executive may prevail. Due to the complexity of the newly introduced abstract stimuli they might not be rehearsed via subordinate routines like the highly familiar verbal stimuli, namely letters in our study. Thus, the cerebellar contribution to the visuospatial rehearsal of the abstract stimuli used here might be less as compared to its phonological counterpart. Overall, findings in the literature supporting contributions of the cerebellum to visuospatial tasks are less convincing than contributions to language tasks (Cooper et al., 2012; Dimitrov et al., 1996; Frank et al., 2007 for review; Richter et al., 2005). Furthermore, findings are conflicting regarding lateralization (Hildebrandt et al., 2002; Silveri et al., 2001). Second, the present (and other visuospatial tasks used in the literature) abstract Sternberg task may have allowed the use of verbal strategies. Some participants reported after the experiment that they had tried to verbalize the abstract stimuli, therefore reducing the visuospatial demands of the task. Thus, contributions to the visuospatial sketch path may have been missed.

One may argue that differences in behavioural performance contributed to the observed difference between the abstract and verbal Sternberg tasks. However, as outlined above, behavioural performance was poorer in the abstract task. The abstract task was more challenging to the subjects and one would expect a higher load on brain function. Despite this, cerebellar activation was smaller and present mainly unilaterally in the abstract task, but bilaterally in the verbal task. In addition, in the n-back task performance was worse in the abstract compared to the verbal task as well, but cerebellar cortical activations were largely the same.

**Dentate nuclei**

Strick and coworkers have proposed a functional subdivision of the dentate nucleus into a motor and non-motor domain (Dum and Strick, 2003; Strick et al., 2009). Based on their anatomical findings in monkeys, the more dorsostral parts of the dentate are involved in motor functions whereas the more ventrocaudal parts contribute to non-motor functions. The overall findings of the present study agree with this proposal. None of the activation was focused in the dorsostral dentate nucleus. In previous fMRI studies of our group using 7T MRI, we found that simple finger and foot movements...
clearly activated primarily the dorsorostral dentate nucleus on the side ipsilateral to the movement (Küper et al., 2011a, 2011b). Dentate activation was found within ventrocaudal and dorsocaudal parts of the nucleus in the abstract and verbal n-back tasks bilaterally. Activations of caudal parts of the nucleus agree with two prior studies of our group examining dentate activation in cognitive tasks. In a first study using 1.5 T MRI, comparison of two cognitive tasks (a visuospatial and a working memory task).

Table 4
Local maxima of cerebellar activation for Sternberg tasks (high load MINUS low load). The thresholds were calculated by small volume correction (at p<0.001, FDR-corrected) with threshold t=5.11 for abstract, t=4.69 for verbal, t=6.20 for verbal MINUS abstract, and t=4.75 for conjunction analysis.

<table>
<thead>
<tr>
<th>Condition / Contrast</th>
<th>Side</th>
<th>x, y, z</th>
<th>Location</th>
<th>Cluster voxel size</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sternberg task abstract</td>
<td>Right</td>
<td>34, −60, −27</td>
<td>VI, Crus I</td>
<td>1729</td>
<td>10.45</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>6, −78, −19</td>
<td>Vermis VI, VI</td>
<td>1143</td>
<td>10.41</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>−6, −77, −29</td>
<td>I−IV</td>
<td>725</td>
<td>9.18</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>−9, −48, −17</td>
<td>I−IV</td>
<td>476</td>
<td>8.84</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>0, −60, −36</td>
<td>Vermis VIIIb, Vermis IX, Vermis VIIIa</td>
<td>423</td>
<td>7.66</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>13, −51, −18</td>
<td>V</td>
<td>23</td>
<td>5.99</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>1, −66, −4</td>
<td>Vermis VI</td>
<td>10</td>
<td>5.87</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>1, −65, −21</td>
<td>Vermis VI</td>
<td>9</td>
<td>5.49</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>7, −41, −18</td>
<td>Vermis VI</td>
<td>4</td>
<td>5.42</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>7, −73, −11</td>
<td>Vermis VI</td>
<td>4</td>
<td>5.33</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>7, −78, −36</td>
<td>Crus II</td>
<td>5</td>
<td>5.28</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>−8, −77, −36</td>
<td>Crus II</td>
<td>5</td>
<td>5.32</td>
</tr>
<tr>
<td>Sternberg task verbal</td>
<td>Right</td>
<td>28, −65, −23</td>
<td>VI, Crus I, V</td>
<td>8560</td>
<td>11.95</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>15, −74, −42</td>
<td>Vermis IX, Vermis VIIIa</td>
<td>842</td>
<td>9.40</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>2, −57, −37</td>
<td>Vermis IX, Vermis VIIIa</td>
<td>826</td>
<td>7.50</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>1, −69, −8</td>
<td>V</td>
<td>79</td>
<td>6.38</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>18, −44, −26</td>
<td>V</td>
<td>12</td>
<td>5.45</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>38, −63, −45</td>
<td>Vermis IX</td>
<td>3</td>
<td>4.89</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>1, −56, 1</td>
<td>Vermis IX</td>
<td>1</td>
<td>4.75</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>23, −35, −31</td>
<td>Vermis IX</td>
<td>3</td>
<td>4.85</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−36, −58, −27</td>
<td>Vermis I</td>
<td>511</td>
<td>6.90</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−32, −48, −23</td>
<td>Vermis I</td>
<td>88</td>
<td>6.13</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−5, −79, −16</td>
<td>Vermis I</td>
<td>199</td>
<td>5.75</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−16, −61, −14</td>
<td>Vermis I</td>
<td>48</td>
<td>5.68</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−51, −55, −35</td>
<td>Vermis I</td>
<td>15</td>
<td>5.45</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−7, −47, −9</td>
<td>I−IV</td>
<td>11</td>
<td>5.39</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−4, −81, −28</td>
<td>Vermis I</td>
<td>27</td>
<td>5.30</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−14, −68, −16</td>
<td>Vermis I</td>
<td>14</td>
<td>5.08</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−22, −49, −20</td>
<td>Vermis I</td>
<td>24</td>
<td>5.07</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−45, −64, −26</td>
<td>Crus I</td>
<td>7</td>
<td>4.87</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−12, −54, −18</td>
<td>Crus I</td>
<td>2</td>
<td>4.83</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−3, −78, −41</td>
<td>Crus I</td>
<td>1</td>
<td>4.71</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−8, −66, −52</td>
<td>Crus I</td>
<td>7</td>
<td>4.71</td>
</tr>
<tr>
<td>Sternberg task verbal MINUS abstract</td>
<td>Right</td>
<td>24, −69, −20</td>
<td>VII</td>
<td>310</td>
<td>9.70</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>39, −72, −22</td>
<td>Crus I</td>
<td>2</td>
<td>6.36</td>
</tr>
<tr>
<td>Conjunction abstract and verbal</td>
<td>Right</td>
<td>35, −60, −27</td>
<td>VI, Crus I</td>
<td>1062</td>
<td>8.18</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>7, −76, −19</td>
<td>Vermis VI, VI</td>
<td>394</td>
<td>6.66</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>2, −56, −35</td>
<td>Vermis IX, Vermis VIIIa</td>
<td>275</td>
<td>6.17</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>25, −53, −24</td>
<td>Vermis IX, Vermis VIIIa</td>
<td>93</td>
<td>6.14</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>1, −46, −17</td>
<td>VI</td>
<td>329</td>
<td>5.90</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−4, −79, −16</td>
<td>VI</td>
<td>66</td>
<td>5.67</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−2, −55, −9</td>
<td>VI</td>
<td>8</td>
<td>5.23</td>
</tr>
</tbody>
</table>

Fig. 10. Significant dentate nucleus activations on the right (A, B) and left (C, D) for the Sternberg tasks: abstract (A, C) and verbal (B, D) (high load MINUS low load). Activations are mapped onto axial slices of the dentate template (Diedrichsen et al., 2011) in MRicroN. Colour coding represents associated t-values (threshold t = 3.50).
with a motor control task (finger tapping) revealed activation in the same area as in the present study: caudal parts of the dentate nucleus extending from the ventral to the dorsal part (Küper et al., 2011). In our second study, we found that the right ventrocaudal dentate supported verb generation (Thürling et al., 2011). These findings agree with Strick's proposal that more caudal and ventral parts of the dentate contribute to non-motor functions. In the monkey these parts of the dentate nucleus have been shown to be connected with area 46d in the prefrontal cortex, which is known to be involved in executive function including working memory (Bellebaum and Daum, 2007; Strick et al., 2009 for reviews).

Similar to the findings in the cerebellar cortex, dentate areas related to abstract and verbal working memory in n-back tasks were comparable. There were no significant differences comparing tasks and comparing the right and left sides in either task. Again, lack of difference between the two stimulus modalities and lack of lateralization favour a more general contribution of the cerebellum to working memory. Thus, previous findings of the cerebellar cortex were confirmed and extended to the dentate nuclei.

In the abstract Sternberg task, activated areas in the dentate nucleus were in good correspondence with those observed in the n-back tasks. Activation was again present in the more caudal parts of the dentate. The activation pattern in the verbal Sternberg task, however, was different. Here activation was most prominent in the rostral and ventral parts of the dentate nuclei. This pattern of activation resembled findings related to inner speech effects seen in a previous study of our group (Thürling et al., 2011). In that study, the most prominent activation was also observed in the ventrostral dentate bilaterally. The verbal Sternberg task includes articulatory rehearsal, thus activation related to inner speech effects is not unexpected (Ackermann et al., 2004). In the verbal Sternberg task, activation of caudal parts was small and found only on the right. Activations of the caudal parts of the nuclei were more obvious in the abstract Sternberg and the n-back tasks, which rely less on verbalization as pointed out in the introduction.

### Table 5
Local maxima of dentate nucleus activation for Sternberg tasks (high load MINUS low load). The thresholds were calculated by bootstrapping with 9 voxels as critical cluster threshold or t = 3.9 as corrected height threshold (at p = 0.001 uncorrected). Activations which met one of these thresholds were considered significant. Activation maxima are underlined. DRDN = dorsoventral dentate nucleus, VCDN = ventrocaudal dentate nucleus, DCDN = dorsoventral dentate nucleus, VRDN = ventrostral dentate nucleus.

<table>
<thead>
<tr>
<th>Condition / Contrast</th>
<th>Side</th>
<th>x, y, z</th>
<th>Location</th>
<th>Cluster voxel size</th>
<th>t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sternberg task abstract</td>
<td>Right</td>
<td>17, 59, 36</td>
<td>DCDN, VCDN</td>
<td>65</td>
<td>4.72</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>–13, 54, 38</td>
<td>VRDN</td>
<td>96</td>
<td>5.53</td>
</tr>
<tr>
<td>Sternberg task verbal</td>
<td>Right</td>
<td>13, 53, 37</td>
<td>VRDN</td>
<td>41</td>
<td>5.11</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>12, 58, 33</td>
<td>DCDN, VCDN</td>
<td>16</td>
<td>3.92</td>
</tr>
</tbody>
</table>

### Table 6
Comparison of modality and laterality in the Sternberg tasks. Maximum t-values (and the corresponding x y z coordinates in SUIT space) and mean t-values are given in functionally defined VOIs of individual cerebellar lobules and the dentate nucleus separated by task and side. Mean t-values are given as (beta mean value / standard deviation of beta mean value) for n=23 subjects. T-tests are shown for comparisons of mean t-values. n.s.: no significant activated area. ver.: vermis; Search Vol = volume which fulfils the thresholds (p<0.001, FDR-corrected, minimum cluster size 50 voxels) considering the abstract and verbal tasks together.

<table>
<thead>
<tr>
<th>Cerebellar lobule</th>
<th>Abstract Sternberg</th>
<th>Verbal Sternberg</th>
<th>Search vol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>maximum activation</td>
<td>maximum activation</td>
<td>T-tests</td>
</tr>
<tr>
<td></td>
<td>x, y, z</td>
<td>Max t-value</td>
<td>mean t-value</td>
</tr>
<tr>
<td>I-IV left</td>
<td>–50, 22</td>
<td>7.16</td>
<td>6.71</td>
</tr>
<tr>
<td>I-IV right</td>
<td>–49, 21</td>
<td>9.18</td>
<td>6.91</td>
</tr>
<tr>
<td>V left</td>
<td>–57, 9</td>
<td>5.78</td>
<td>4.34</td>
</tr>
<tr>
<td>V right</td>
<td>–53, 18</td>
<td>5.99</td>
<td>6.55</td>
</tr>
<tr>
<td>VI left</td>
<td>–5, 7, 18</td>
<td>10.02</td>
<td>6.71</td>
</tr>
<tr>
<td>VI right</td>
<td>34, 60, 27</td>
<td>10.45</td>
<td>7.28</td>
</tr>
<tr>
<td>Crus I left</td>
<td>–53, 35, 36</td>
<td>7.01</td>
<td>6.18</td>
</tr>
<tr>
<td>Crus I right</td>
<td>–57, 29</td>
<td>7.46</td>
<td>5.90</td>
</tr>
<tr>
<td>Crus II left</td>
<td>–57, 27</td>
<td>7.10</td>
<td>6.02</td>
</tr>
<tr>
<td>Crus II right</td>
<td>–50, 30</td>
<td>5.91</td>
<td>5.72</td>
</tr>
<tr>
<td>Crus III left</td>
<td>7, 8, 36</td>
<td>5.28</td>
<td>6.32</td>
</tr>
<tr>
<td>Crus III right</td>
<td>2, 36, 31</td>
<td>5.11</td>
<td>4.61</td>
</tr>
<tr>
<td>VIb left</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>VIb right</td>
<td>26, 72, 49</td>
<td>4.62</td>
<td>4.27</td>
</tr>
<tr>
<td>Villa ver.</td>
<td>–2, 62, 36</td>
<td>6.35</td>
<td>5.24</td>
</tr>
<tr>
<td>Villa left</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Villa right</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>VIb left</td>
<td>0, 60, 36</td>
<td>7.66</td>
<td>6.52</td>
</tr>
<tr>
<td>VIb right</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>IX left</td>
<td>0, 59, 35</td>
<td>7.53</td>
<td>6.62</td>
</tr>
<tr>
<td>X left</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Dentate left</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td>Dentate right</td>
<td>17, 59, 35</td>
<td>4.52</td>
<td>4.71</td>
</tr>
</tbody>
</table>
There is only one previous study reporting dentate nuclei activity in a Sternberg working memory task using verbal stimuli. Marvel and Desmond (2010b) subdivided the dentate into two parts: a dorsal and a ventral part. No further subdivisions into rostral and caudal compartments as in our study was done. They used an event-related design and examined activation in the encoding, maintenance, and retrieval phases of the phonological loop. They found contributions of the dorsal dentate to encoding and of the ventral dentate to retrieval. In our study we used a block design, which did not allow to distinguish between these phases. Our findings of predominantly ventral activation are, therefore not in contradiction with their findings.

Table 7
Cerebellar cortical activations comparing 2-back and Sternberg tasks. A main effect of task in a 2×2 mixed full factorial design with task (2-back vs. Sternberg) as between subjects factor and condition (verbal vs. abstract); B Sternberg verbal MINUS 2-back verbal task; C 2-back verbal MINUS Sternberg verbal task. All p values < 0.05, FDR corrected, thresholds: Main effect task F = 13.01; Sternberg verbal MINUS 2-back verbal t = 4.17; 2-back verbal MINUS Sternberg verbal t = 4.04. Peak location is underlined.

<table>
<thead>
<tr>
<th>Condition / Contrast</th>
<th>Side</th>
<th>x, y, z</th>
<th>Location</th>
<th>Cluster voxel size</th>
<th>F-value / t-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main effect 2-back vs. Sternberg</td>
<td>Right</td>
<td>31, −60, −33</td>
<td>VI, Crus I</td>
<td>448</td>
<td>31.61</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>25, −62, −20</td>
<td>VI</td>
<td>144</td>
<td>23.13</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>41, −58, −46</td>
<td>Crus II, Crus I, VIIb</td>
<td>167</td>
<td>22.70</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>37, −43, −39</td>
<td>Crus I, Crus II, VIIb</td>
<td>77</td>
<td>18.94</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>29, −69, −49</td>
<td>VII</td>
<td>60</td>
<td>18.82</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>8, −77, −23</td>
<td>VI, Crus I, Vermis VI</td>
<td>43</td>
<td>18.02</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−9, −77, −29</td>
<td>Crus I, VI</td>
<td>68</td>
<td>17.18</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−7, −56, −49</td>
<td>Crus I, VIIb</td>
<td>426</td>
<td>32.11</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−26, −36, −36</td>
<td>VI</td>
<td>360</td>
<td>26.89</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−30, −63, −30</td>
<td>VI, Crus I</td>
<td>143</td>
<td>24.64</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−43, −71, −33</td>
<td>Crus I</td>
<td>79</td>
<td>20.46</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−40, −56, −49</td>
<td>Crus II</td>
<td>80</td>
<td>16.33</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−36, −71, −49</td>
<td>Crus II</td>
<td>15</td>
<td>15.59</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−39, −66, −37</td>
<td>Crus I</td>
<td>17</td>
<td>14.64</td>
</tr>
<tr>
<td></td>
<td>Left</td>
<td>−39, −66, −37</td>
<td>Crus I</td>
<td>122</td>
<td>4.84</td>
</tr>
</tbody>
</table>

Sternberg verbal MINUS 2-back verbal

|                      | Right  | 26, −63, −20 | VI               | 294                | 5.50              |
|                      | Right  | 32, −61, −32 | Crus I, VI      | 90                 | 4.69              |
|                      | Right  | 41, −42, −45 | VII              | 12                 | 4.30              |
|                      | Left   | −9, −77, −29 | Crus I          | 80                 | 5.36              |
|                      | Left   | −31, −64, −30 | Crus I, VI     | 73                 | 5.24              |
|                      | Left   | −27, −35, −36 | VI, VII         | 53                 | 5.17              |

Fig. 11. Cerebellar cortical activations comparing 2-back and Sternberg tasks. A main effect of task in a 2×2 mixed full factorial design with task (2-back vs. Sternberg) as between subjects factor and condition (verbal vs. abstract); B Sternberg verbal MINUS 2-back verbal task; C 2-back verbal MINUS Sternberg verbal task. All p values < 0.05, FDR corrected.
In conclusion, our findings further support that the posterolateral cerebellum contributes to working memory. Based on the model of working memory proposed by Baddeley and Hitch (1974), our results suggest that different regions of the cerebellum support functions of the central executive system and one of the slave systems, the phonological loop. We did not find, however, evidence that the cerebellum supports the second slave system, the visuospatial sketch pad.

Acknowledgments

The study was supported by the German Research Foundation (DFG Ti 239/9-1) and a grant by the European Union (Marie Curie Initial Training Network “Cerebellar-Cortical Control: Cells, Circuits, Computation and Clinic”).

References


Cooper, F.E., Grube, M., Von Kriegstein, K., Kumar, S., English, P., Kelly, T.P., Chinnery, P.F., Grif


Miller, G.A., 1956. The magical number seven plus or minus two: some limits on our capacity for processing information. Psychol. Rev. 63, 81–97.


