# Temporal dynamics of visual working memory

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## ARTICLE INFO

## ABSTRACT

The involvement of the human cerebellum in working memory has been well established in the last decade. However, the cerebro-cerebellar network for visual working memory is not as well defined. Our previous fMRI study showed superior and inferior cerebellar activations during a block design visual working memory task, but specific cerebellar contributions to cognitive processes in encoding, maintenance and retrieval have not yet been established. The current study examined cerebellar contributions to each of the components of visual working memory and presence of cerebellar hemispheric laterality was investigated. 40 young adults performed a Sternberg visual working memory task during fMRI scanning using a parametric paradigm. The contrast between high and low memory load during each phase was examined. We found that the most prominent activation was observed in vermal lobule VIIIb and bilateral lobule VI during encoding. Using a quantitative laterality index, we found that left-lateralized activation of lobule VIIIa was present in the encoding phase. In the maintenance phase, there was bilateral lobule VI and right-lateralized lobule VIIb activity. Changes in activation in right lobule VIIIa were present during the retrieval phase. The current results provide evidence that superior and inferior cerebellum contributes to visual working memory, with a tendency for left-lateralized activations in the inferior cerebellum during encoding and right-lateralized lobule VIIb activations during maintenance. The results of the study are in agreement with Baddeley's multi-component working memory model, but also suggest that stored visual representations are additionally supported by maintenance mechanisms that may employ verbal coding.

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## 1. Introduction

In the last decade, scientific investigations have confirmed that cerebro-cerebellar networks contribute to verbal and visual working memory (Chen and Desmond, 2005; E et al., 2014; Marvel and Desmond, 2010; Stoodley and Schmahmann, 2009; Stoodley et al., 2012). Previous studies have identified two cerebro-cerebellar networks for verbal working memory — the first is between inferior parietal regions and right inferior cerebellum, associated with the phonological store, and the second is between inferior frontal regions and right superior cerebellum, which was found to be linked with articulatory rehearsal processes (Desmond et al., 1997; Chen and Desmond, 2005). Based on these findings, Chen and Desmond (2005) proposed a cross-lateralized cerebro-cerebellar model of verbal working memory, with the right cerebellum being involved in language-related processing. The proposed model has been further verified by transcranial magnetic stimulation (Desmond et al., 2005;

Chen et al., 2014; Tomlinson et al., 2014) and functional neuroimaging studies (Macher et al., 2014; Ng et al., 2013). While this pattern of cerebellar activations has been consistently found in a number of studies (E et al., 2014), cerebellar contributions to visual working memory are much less consistently reported. In addition, our meta-analysis of verbal working memory using N-back and Sternberg paradigms showed differential activity in the cerebellum (E et al., 2014), suggesting a possible differing profile for visual working memory as well. For example, Thürling et al. (2012) observed bilateral superior and right inferior cerebellar activations for a N-back visual abstract figures task, but only superior cerebellar activations (more prominent on the right side) were observed when using a Sternberg paradigm for the same visual stimuli. Moreover, in our recent study of visual working memory qualitative inspection of results showed that bilateral superior and left inferior cerebellar regions are activated during a visual Sternberg task using abstract figures (Ng et al., 2013). However, further quantitative examination of the results with laterality index AveLI (Matsuo et al., 2012) revealed that not only superior but also inferior cerebellum is activated bilaterally (unpublished data). Therefore, to further our understanding of cerebellar involvement in visual working memory, investigation into a more precise understanding of cerebellar contributions to each of the key phases of

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visual working memory (i.e. encoding, maintenance and retrieval) is necessary.

One of the most influential working memory models is a cognitive framework proposed by Baddeley and Hitch in 1974. Baddeley conceptualized the working memory model as a system consisting of the central executive that controls cognitive processes, the visuospatial sketchpad that stores and manipulates images and the phonological loop that stores (phonological store) and manipulates (articulatory control rehearsal system) verbal information (Baddeley, 1986). Logie (1995) proposed a further clarification on the nature of visuospatial sketchpad. He introduced a distinction between the visual cache (visual component) and the inner scribe (spatial component). The visual cache performs a function of a temporary store that holds visual images. It stores features of object's physical appearance such as color, shape, visual texture and size. The inner scribe retains spatial information and can be used to rehearse the contents of the visual cache. It has been shown that visuospatial sketchpad can interact with previously stored knowledge when successful identification of the object to be memorized requires association with semantic content about similar-looking objects (Della Sala and Logie, 2002; Repovš and Baddeley, 2006). This suggests that mechanisms involved in active maintenance of objects may rely not only on the visual features of objects, but also on semantic verbal information that are automatically associated with the perceived object (Postle et al., 2005).

In terms of activation lateralization, Baddeley (2000) suggested that visual working memory is represented in the right hemisphere (areas 6, 19, 40 and 47); however the evidence from functional neuroimaging studies is inconclusive. For example, Courtney et al (1997) found that right-lateralized cortical activity changes when memorizing faces whereas Smith et al (1995) reported left-lateralized activations for spatial arrays of abstract shapes. A meta-analysis by Rottschy et al. (2012) of neuroimaging studies that examined visuospatial working memory linked activations in the bilateral middle frontal/precentral cortex, right inferior frontal cortex, left ventral visual cortex and left cerebellum with the visual component (the visual cache) of visuospatial working memory, whereas more posterior regions including bilateral posterior and right inferior parietal regions were associated with the spatial component (the inner scribe) of visuospatial working memory.

In our previous (unpublished data) fMRI block design study, we specifically examined the laterality of cerebro-cerebellar networks contributing to visual working memory of abstract patterns. We found that bilateral cerebro-cerebellar networks support visual working memory, including bilateral inferior frontal and inferior temporal regions, and bilateral superior (lobule VI) and inferior (lobule VIIb) cerebellar areas. The results of this study linked visual working memory with bilateral rather than right-left lateralized cerebro-cerebellar networks. However, the design used (block design) did not allow us to determine the precise contribution of each network to the principal components of visual working memory (the inner scribe and the visual store). Consequently, in the current fMRI study we employed an event-related design together with a Sternberg's paradigm (1966) that consisted of abstract visual patterns that were difficult to verbalize. A Sternberg paradigm consists of encoding, maintenance and retrieval phases. Participants are required to perform a specific task in each of the phases and thus separation of the experiment into encoding, maintenance and retrieval can capture the brain changes corresponding to the functions that dominate in each phase. In a typical Sternberg verbal working memory task, the encoding phase is usually not longer than 2 s (e.g. Chen and Desmond, 2005; Marvel and Desmond, 2010; Thürling et al., 2012) as acquisition of verbal information occurs quickly; thus there is not enough time for rehearsal processes to occur in that phase. Instead, rehearsal of verbal information can be measured in the maintenance phase, which has long enough duration to allow the contents of the store to be refreshed. In contrast, pilot studies of our visual working memory task with complex abstract patterns showed that the encoding of visual information requires a longer duration whereas maintenance of the representations

(when the external stimuli guidance is removed) needs to have shorter duration in order to achieve sufficiently high accuracy rates of 80%. The cognitive demands involved in different memory modalities appear to lead to a different temporal distribution of rehearsal processes in the Sternberg paradigm. For this study, we propose that there is a higher probability that rehearsal will occur in the encoding phase because the 4 s duration allows and requires that the contents of the store be refreshed. However, it is also possible that the rehearsal will still be present in maintenance if visual representations are refreshed in mental imagery, but given that the maintenance phase duration is only 1 or 2 s, it is likely that storage processes will be emphasized more. Discrimination between the visual contents maintained in the cache and response formation will take place in the retrieval phase. Hence, the Sternberg paradigm is ideal to allow close examination of the temporal dynamics of the network activity across the three phases.

It is noted that previous studies listed in the meta-analysis of Rottschy et al. (2012) did not always consider the importance of the inferior cerebellum as it was not routinely included in data acquisition due to field-of-view limitations. Therefore, it is not possible to rule out the importance of this region to visual working memory on the basis of previous studies. Moreover, studies which focus on cerebellar function have provided evidence that both inferior and superior cerebellum contribute to visual working memory (e.g. Ng et al., 2013; Yeh et al., 2007; Salmi et al., 2010). Further support for cerebellar involvement in visual working memory is provided by neuropsychological and stimulation studies. Patients with cerebellar lesions have deficits in encoding relevant visuospatial information (Baier et al., 2014) and double-pulse TMS over left inferior and left superior cerebellum in healthy subjects diminishes task performance during a visual working memory task but not during a verbal working memory task (Chen et al., 2014). These findings suggest cerebellar lateralization for visual working memory even though results from functional neuroimaging studies usually reveal bilateral cerebellar activations (see E et al., 2014 for review). In the current study we propose that not only superior cerebellum but also the inferior cerebellum contributes to visual working memory.

Thus, the aim of the present study was to clarify the involvement of the cerebellum in visual working memory. We utilized an event-related design in our study to examine cerebro-cerebellar networks in encoding, maintenance and retrieval processes. Based on findings described above on cerebellar contributions to visual working memory and cross-lateralized cerebro-cerebellar networks for verbal working memory (Chen and Desmond, 2005), we hypothesized that during the encoding phase the left-lateralized superior cerebellum (crus I, lobule VI) and right-lateralized frontal regions will show increased activations, during the maintenance phase the left-lateralized inferior cerebellum (lobule VIIb) and right-lateralized parietal regions will be more active and in retrieval we will observe right-lateralized frontal and temporal activations together with superior cerebellar vermis activations.

## 2. Methods

### 2.1. Subjects

40 subjects (20 females and 20 males; mean age 23.2 ± 1.9 years) participated in the study. Participants were right-handed (Edinburgh Handedness Inventory score: mean = 88.4; SD = 12.6), had no history of neurological conditions, psychiatric conditions or noticeable brain abnormalities. Informed consent was obtained for all participants and the study was approved by the Institutional Review Board at the Nanyang Technological University and the National Health Group.

### 2.2. Task design

A modified Sternberg visual working memory task consisting of abstract patterns that were difficult to verbalize (Ng et al., 2013) was
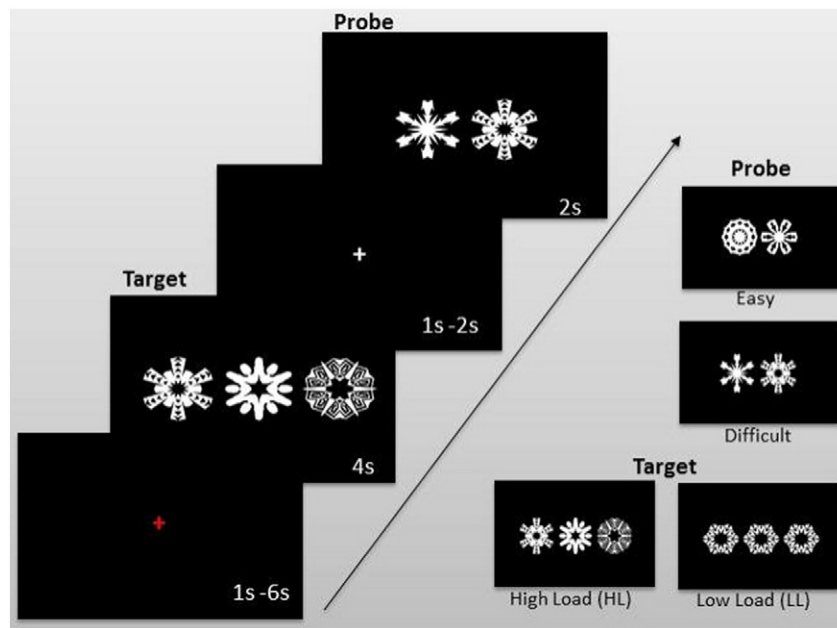
**Fig. 1.** Example trial structure for the visual working memory task used in the study. Left: trial presentation sequence. Right: sample probe images. Lower right: sample target images. Patterns presented in the probe were either similar (difficult retrieval trials) or different (easy retrieval trials).

employed. The task design consisted of three phases — encoding, maintenance and retrieval. Low and high load conditions were tested (see Fig. 1). During the high load condition, 3 different patterns were presented, whereas in the low load condition, 3 identical patterns were presented. The task was first piloted in order to establish the optimal phase durations that achieved sufficiently high accuracy rates of 80%. In the experimental task, the encoding phase lasted 4 s. The maintenance phase was the same for high and low load conditions and lasted 1 or 2 s. In the retrieval phase two patterns were presented for 2 s. In half of the trials presented in the retrieval phase, patterns were similar (high degree of difficulty) and in the other half the patterns were very different (low degree of difficulty). When selecting patterns for each trial, the patterns were distinguished primarily on the basis of the "roundness" versus "spikiness" of each stimuli. Round patterns had a greater quantity of white around their perimeter, prompting association with a circle as prototype, whereas spiky patterns tended towards a few prominent spokes, prompting association with a star as prototype (see Fig. 1). Trials were jittered with an inter-trial interval (ITI) that lasted 1–6 s. The task was presented in 4 runs. Each run had duration of 480 s. One run included 48 trials in total; there were 24 trials in each of the 2 conditions (high load and low load).

Participants performed a Sternberg visual working memory task in the scanner. The stimuli were presented using E-PRIME 2.0 software (http://www.pstnet.com/eprime.cfm). Before the scanning session, all subjects were trained on the task. Participants were required to have at least 80% accuracy before proceeding to the fMRI scan. The order of run presentation was counterbalanced across subjects. In the scanner, the stimuli were presented through a mirror mounted on the head coil. Participants were instructed to memorize them during the encoding phase. They were asked to refresh the images actively in their minds after images were removed from view (maintenance). Their task was to indicate which one of the two patterns was presented earlier with a button-press.

### 2.3. Scanning parameters

All data was acquired in a 3T Siemens Trio scanner with a standard 32-channel head coil (Trio, Siemens, Erlangen, Germany). Cushions were placed around the head to minimize the head motion. Functional data was collected using a T2* echo-planar imaging (EPI) pulse sequence (TR = 2000 ms, TE = 29 ms, flip = $90^0$, slice thickness = 3.5 mm, distance factor = 10%, 41 slices axial slices, FOV = 225 mm). A high resolution T1 image using the MPRAGE protocol (TR = 2300 ms; TE = 1.9 ms; voxel size $1 \times 1 \times 1$ mm; FOV = 256 mm) was acquired.

### 2.4. Image analysis

#### 2.4.1. SPM

Standard image preprocessing was conducted using SPM8 (The Wellcome Trust Centre for Neuroimaging, UCL; http://www.fil.ion.ucl. ac.uk/spm/). Images were realigned to the middle functional image to correct for head motion. No subject's head moved by more than 3 mm or 1.5° during functional data acquisition. The functional images were co-registered to the structural image. The structural image was normalized using combined segmentation and normalization to the MNI-152 template. The parameters of this transformation were applied to the functional images, which were re-sampled to 3.5 mm isotropic voxels and smoothed using an isotropic Gaussian kernel (FWHM = 6 mm).

A general linear model (GLM) was used to calculate condition-specific effects. In order to make dynamics in cerebellar activity comparable, durations for all phases (encoding, maintenance and retrieval) were modeled in GLM as equal, each lasting 1 s (the longest common duration across memory phases). A duration of 1 s was inserted as every trial's duration across all conditions in GLM instead of simple modeling of events (duration = 0 s) to allow fuller characterization of memory functions that take time to arise.

Movement parameters were included to the design matrix and the following contrasts were specified in the 1st level analysis: (1) high vs low encoding load, (2) high vs low maintenance load, (3) high vs low retrieval load. In each of these phases, a simple subtraction was applied, for example, contrast for the encoding phase was created by subtracting low from high encoding load. The same procedure was repeated for all of the remaining phases. No significant cerebellar activations were found in the retrieval phase. As it is plausible that a higher number of correct difficult retrieval trials in the low load condition diminished the power of the high load condition, we conducted an additional analysis and created a new retrieval contrast accounting for retrieval difficulty and memory load. In this contrast, easy and difficult retrieval conditions were compared against the high and low load encoding

and maintenance conditions. A random effects group analysis was performed for each of those contrasts with a threshold of p < 0.001 (uncorrected) and minimal cluster size of 20 voxels and t-value > 5.

### 2.4.2. SUIT

Spatial Unbiased Infratentorial Template (SUIT) provides better than standard MNI template normalization for fMRI data for cerebellar regions (Diedrichsen, 2006). Additional image preprocessing was provided for SUIT analysis. From the T1 image of each participant that was co-registered with functional data, the cerebellum was isolated and warped to fit the SUIT cerebellum template using SUIT toolbox in SPM8. The non-linear deformation parameters were then applied to the contrast images obtained in native space for each participant. The normalized contrast images were re-sliced to 2 x 2 x 2 mm$^3$ resolution and smoothed using an isotropic Gaussian kernel (FWHM = 6 mm). Finally, the smoothed and normalized contrast images were submitted for second-level analysis, where one-sample t-test contrasts were calculated with a threshold of p < 0.001 (uncorrected) and minimal cluster size of 20 voxels and t-value > 4.

### 2.4.3. AveLI

The lateralization index (LI) was computed in AveLI (Matsuo et al., 2012) using the spmT images. The masks used in the lateralization analysis were created for the following ROIs (cortical: inferior frontal gyrus, inferior parietal lobule, precentral gyrus, supplementary motor area, superior parietal lobule; cerebellar: crus1, lobule VI, lobule VIIb, lobule VIIIa) using AAL template (Tzourio-Mazoyer et al., 2002) implemented in the WFU Pick Atlas toolbox (Lancaster et al., 1997; Maldjian et al., 2003) and cerebellum atlas implemented in SUIT (Diedrichsen, 2006). LI values between −0.2 and +0.2 were defined as 'not lateralized'. LI values higher/equal to +0.2 were considered as leftward asymmetries, whereas LI values lower/equal to −0.2, were considered as rightward asymmetries (Matsuo et al., 2012).

## 3. Results

### 3.1. Behavioral results

The median accuracy rate was 83% for high load (different patterns) condition and 97% for the low load (identical patterns) condition, whereas the median accuracy rate for difficult retrieval condition was 88% and for easy retrieval condition was 92% ($\chi2(3) = 113.95$, p < 0.0001). The median reaction time for correct responses was the fastest for the low load (635 ms) condition, slightly slower for the easy retrieval condition (775 ms) and difficult retrieval condition (833 ms), with the slowest median reaction time observed for the high load condition (955 ms) ($\chi2(3) = 102.99$, p < 0.0001).

### 3.2. Neuroimaging results

During the encoding phase, BOLD signal changes were observed in several brain regions (Tables 1 and 4, Figs. 2 and 3). The precentral and supplementary motor areas together with the caudate exhibited strong positive activations and were predominately confined to the encoding phase, showing only minimal activations in maintenance and retrieval. BOLD signal changes related to visual processing in the inferior and middle occipital cortex were present during the encoding and maintenance. Thalamus and brainstem activations were also observed in the encoding and maintenance, but their intensity was greater during encoding than during maintenance. The activations in the bilateral middle frontal and superior parietal cortex observed in encoding increased in intensity during maintenance. As hypothesized, activation of the inferior and superior parietal cortex was observed during maintenance together with the activations in the inferior cerebellum (lobule VIIb) (see Tables 2 and 4). The activations in parietal regions were present during the encoding and the retrieval phases, but the greatest intensity

**Table 1**
Local maxima of non-cerebellar activations for encoding, thresholded at p < 0.001, k > 20 and t > 5. Non-italicized entries represent local maxima within the main cluster.

| Hemisphere | MNI coordinates | | | | | | |
|---|---|---|---|---|---|---|---|
| | Cluster size | T-value | x | y | z | Brain region | BA |
| *Left* | *2817* | *13.27* | *−10* | *−81* | *5* | *Inferior occipital gyrus* | *BA17* |
| Left | | 12.59 | −24 | −74 | −9 | Inferior occipital gyrus | BA18 |
| Right | | 12.26 | 12 | −70 | 16 | Inferior occipital gyrus | BA17 |
| *Left* | *962* | *9.90* | *−38* | *−7* | *44* | *Precentral gyrus* | *BA6* |
| Right | | 9.68 | 40 | −4 | 51 | Precentral gyrus | BA6 |
| Right | | 8.03 | 8 | 14 | 51 | SMA | BA6 |
| *Left* | *57* | *7.04* | *−6* | *−28* | *58* | *Paracentral lobule* | *BA4* |
| Right | | 5.88 | 8 | −39 | 61 | Paracentral lobule | BA4 |
| Right | | 5.60 | 5 | −25 | 68 | Paracentral lobule | BA4 |
| *Left* | *64* | *6.74* | *−24* | *−60* | *51* | *Superior parietal gyrus* | *BA7* |
| *Left* | *24* | *5.77* | *−24* | *35* | *19* | *Middle frontal gyrus* | *BA9* |
| Left | | 5.34 | −34 | 46 | 16 | Middle frontal gyrus | BA46 |
| *Right* | *524* | *9.23* | *19* | *18* | *5* | *Caudate* | |
| Left | | 7.28 | −17 | 18 | 2 | Caudate | |
| Left | | 7.09 | −17 | 4 | 5 | Pallidum | |
| *Right* | *132* | *8.48* | *5* | *−32* | *−6* | *Brainstem* | |
| Left | | 7.38 | −6 | −21 | −6 | Brainstem | |
| Right | | 6.78 | 12 | −21 | 9 | Thalamus | |
| *Right* | *105* | *7.71* | *29* | *39* | *26* | *Middle frontal gyrus* | *BA46* |
| Right | | 6.51 | 29 | 49 | 16 | Superior frontal gyrus | BA46 |
| Right | | 5.72 | 26 | 25 | 30 | Middle frontal gyrus | BA48 |
| *Right* | *100* | *6.19* | *15* | *−60* | *58* | *Precuneus* | *BA5* |
| Right | | 6.09 | 26 | −49 | 51 | Superior parietal gyrus | BA5 |
| Right | | 5.64 | 22 | −70 | 44 | Superior parietal gyrus | BA7 |

was noted during the maintenance phase. However, contrary to our initial predictions, we additionally observed activations in the inferior frontal cortex and superior cerebellum (lobule VI) that were more
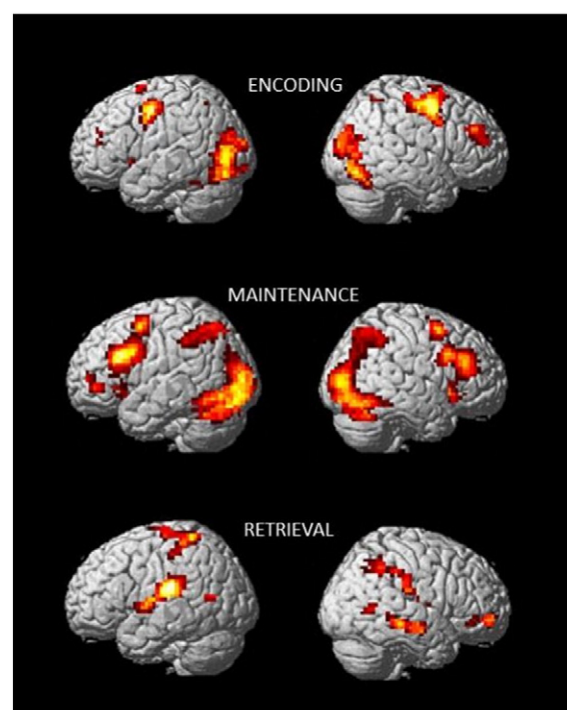


**Fig. 2.** Cortical activations observed during encoding, maintenance and retrieval in visual working memory task. Images are thresholded at p < 0.001 (uncorrected), t-value > 5.0. Activations depicted in the encoding and maintenance represent significantly greater activation for the high load relative to the low load condition, whereas activations shown for retrieval phase represent high and low load retrieval conditions greater than high and low load encoding and maintenance conditions.

**Fig. 3.** Brain activations observed in cerebellum for visual working memory task. Numbers appearing above the coronal slices represent normalized Y coordinate values of the space defined by the MNI152 brain template. Images are at a p < 0.001 threshold (uncorrected), t-value > 4.0. a) Cerebellar activations observed during encoding, maintenance and retrieval. Activations depicted in the encoding and maintenance represent significantly greater activation for the high load relative to the low load condition, whereas activations shown for retrieval phase represent high and low load retrieval conditions greater th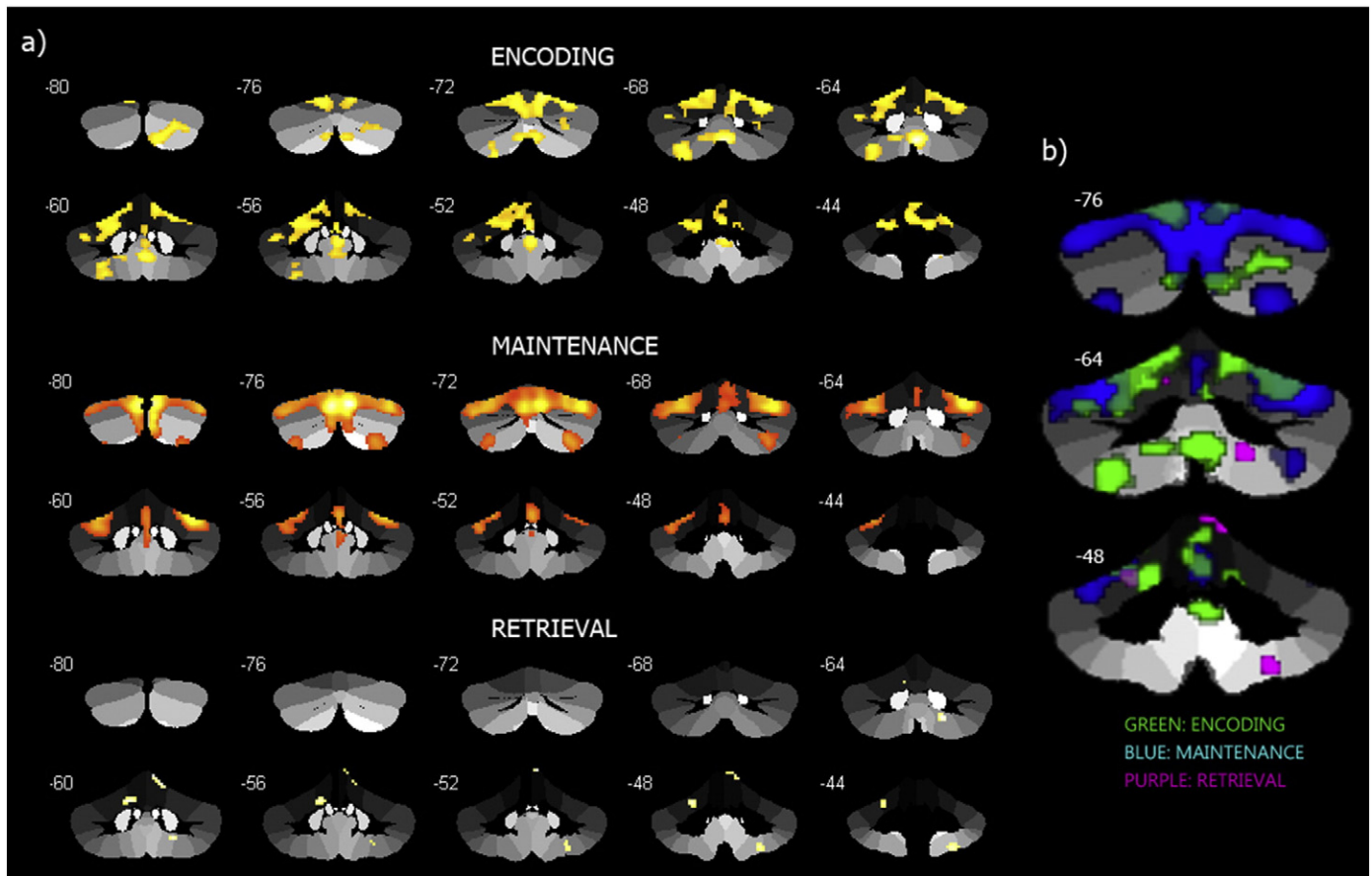an high and low load encoding and maintenance conditions. b) Summary of changes in cerebellar activations observed during all three phases: activations observed in encoding phase are shown in green, activations observed during maintenance are shown in blue and activations observed in retrieval are depicted in purple.

pronounced during maintenance than in encoding. Activations observed only in the retrieval phase included the superior and middle temporal cortex, parietal operculum and insula. The right inferior cerebellar activation was also present in the retrieval phase but it was much less pronounced than during maintenance (see Tables 3 and 4).

### 3.3. Laterality results

The results for the hemispheric laterality in the cortical and cerebellar regions that were examined using AveLI (Matsuo et al., 2012) are listed in Table 5. The left-hemispheric lateralization for the inferior

**Table 2**
Local maxima of non-cerebellar activations for maintenance, thresholded at p < 0.001, k > 20 and t > 5. Non-italicized entries represent local maxima within the main cluster.

| Hemisphere | MNI coordinates | | | | | Brain region | BA |
|---|---|---|---|---|---|---|---|
| | Cluster size | T-value | x | y | z | | |
| *Left* | *3391* | *13.46* | *−27* | *−63* | *37* | *Inferior parietal gyrus /Intraparietal sulcus* | *BA7* |
| Right | | 11.42 | 29 | −67 | 30 | Superior parietal gyrus | BA7 |
| *Left* | *695* | *12.31* | *−45* | *21* | *26* | *Inferior frontal gyrus* | *BA48* |
| Left | | 10.90 | −31 | 25 | −6 | Inferior frontal gyrus | BA47 |
| Left | | 9.48 | −48 | 11 | 33 | Inferior frontal gyrus | BA44 |
| *Right* | *501* | *13.75* | *29* | *25* | *−2* | *Inferior frontal gyrus* | *BA47* |
| Right | | 9.31 | 43 | 32 | 23 | Middle frontal gyrus | BA48 |
| Right | | 8.80 | 50 | 18 | 33 | Inferior frontal gyrus | BA44 |
| *Right* | *330* | *13.39* | *5* | *25* | *44* | *Superior frontal gyrus* | *BA8* |
| Left | | 12.86 | −6 | 21 | 47 | Superior frontal gyrus | BA32 |
| *Right* | *134* | *9.07* | *40* | *4* | *58* | *Middle frontal gyrus* | *BA6* |
| Right | | 8.24 | 29 | 7 | 51 | Middle frontal gyrus | BA6 |
| *Right* | *40* | *7.27* | *8* | *18* | *9* | *Caudate* | |
| Left | | 6.84 | −6 | 18 | 5 | Caudate | |
| *Right* | *21* | *6.54* | *29* | *−35* | *5* | *Hippocampus* | |
| Right | | 6.25 | 22 | −32 | 9 | Thalamus | |
| Right | | 5.52 | 26 | −32 | −2 | Hippocampus | |
| *Right* | *77* | *6.33* | *1* | *−4* | *5* | *Thalamus* | |
| Right | | 6.14 | 5 | −35 | −2 | Brainstem | |
| Right | | 5.92 | 5 | −14 | 12 | Thalamus | |

cerebellum together with the left-sided lateralization for the inferior and posterior parietal regions was found in the encoding. The right-sided lateralization for the inferior cerebellum was observed in the maintenance, together with the left-lateralized parietal regions and precentral/SMA. In the retrieval phase, left-hemispheric lateralization was observed in the parietal regions and precentral gyrus, but right-hemispheric lateralization was found in the inferior frontal gyrus.

## 3.4. Conjunction analysis

Having observed that there are overlaps in activated brain regions between the encoding and maintenance phase, a conjunction analysis (Friston et al., 2005) was conducted in order to formally characterize brain activations common to the encoding and maintenance phases. The conjunction analysis for high encoding and high maintenance against their respective baselines — low encoding and low maintenance — was used to identify cortical and cerebellar activations common to both task phases. The statistical threshold was set at p < 0.005 (uncorrected) with a cluster extent greater than 20 voxels. Then the conjunction contrast was used as a binary mask (exclusive) for encoding and maintenance contrasts in order to identify cortical regions unique to each of those phases. The statistical threshold was set to p < 0.001 (uncorrected, k > 20 voxels, t > 5). The same procedure was repeated to identify unique cerebellar results for encoding and maintenance with statistical threshold set to p < 0.001 (uncorrected, k > 20, t > 4).

The common brain activations for encoding and maintenance (Fig. 4, Table 6 and Table S1) included the left precentral gyrus, the bilateral middle and inferior frontal regions together with the bilateral cerebellar lobule VI. Activations related to visual processing such as occipital regions and cerebellar lobule I-IV were also present across the two phases.

**Table 3**
Local maxima of non-cerebellar activations for retrieval thresholded at p < 0.001, k > 20 and t > 5. Non-italicized entries represent local maxima within the main cluster.

| Hemisphere | MNI coordinates | | | | | | |
|---|---|---|---|---|---|---|---|
| | Cluster size | T-value | x | y | z | Brain region | BA |
| *Left* | *324* | *10.04* | *−59* | *−25* | *19* | *Parietal operculum* | *BA42* |
| Left | | 7.19 | −41 | −11 | 9 | Insula | |
| Left | | 7.01 | −55 | −4 | 2 | Superior temporal gyrus | BA48 |
| *Left* | *38* | *7.22* | *−31* | *−42* | *−9* | *Fusiform gyrus* | *BA37* |
| Left | | 5.58 | −27 | −53 | −2 | Lingual gyrus | BA37 |
| *Left* | *167* | *7.16* | *−17* | *−49* | *68* | *Superior parietal lobe* | *BA5* |
| Left | | 7.03 | −27 | −42 | 68 | Postcentral gyrus | BA2 |
| Left | | 6.86 | −20 | −25 | 75 | Postcentral gyrus | BA6 |
| *Left* | *30* | *6.56* | *−3* | *−91* | *19* | *Middle occipital gyrus* | *BA18* |
| Right | | 5.91 | 8 | −88 | 23 | Superior occipital gyrus | BA18 |
| *Left* | *21* | *5.67* | *−52* | *−60* | *9* | *Middle temporal gyrus* | *BA37* |
| Left | | 5.28 | −41 | −60 | 12 | Fusiform gyrus | BA37 |
| *Right* | *155* | *8.38* | *61* | *−32* | *−13* | *Inferior temporal gyrus* | *BA20* |
| Right | | 7.13 | 57 | −14 | −13 | Middle temporal gyrus | BA21 |
| Right | | 6.04 | 43 | −11 | −16 | Insula | |
| *Right* | *124* | *8.24* | *68* | *−25* | *30* | *Inferior parietal gyrus* | *BA2* |
| Right | | 7.19 | 47 | −49 | 44 | Inferior parietal gyrus | BA40 |
| Right | | 6.03 | 57 | −35 | 40 | Inferior parietal gyrus | BA40 |
| *Right* | *53* | *7.16* | *40* | *49* | *−6* | *Middle orbital gyrus* | *BA47* |
| Right | | 5.87 | 47 | 39 | −6 | Inferior frontal gyrus | BA47 |
| *Right* | *29* | *6.35* | *36* | *−32* | *−20* | *Fusiform gyrus* | *BA20* |
| Right | | 6.30 | 29 | −42 | −9 | Fusiform gyrus | BA37 |
| *Right* | *29* | *6.11* | *40* | *−7* | *2* | *Insula* | |
| *Right* | *20* | *6.07* | *54* | *−56* | *5* | *Middle temporal gyrus* | *BA37* |
| *Right* | *21* | *5.91* | *1* | *0* | *40* | *Posterior cingulate* | *BA24* |
| Right | | 5.86 | 1 | −11 | 40 | Posterior cingulate | BA23 |

**Table 4**
Local maxima of cerebellar activations for encoding, maintenance and retrieval, thresholded at p < 0.001, k > 20 and t > 4. Non-italicized entries represent local maxima within the main cluster.

| Hemisphere | MNI coordinates | | | | | |
|---|---|---|---|---|---|---|
| | Cluster size | T-value | x | y | z | Brain region |
| *ENCODING* | | | | | | |
| *Vermis* | *2986* | *7.20* | *2* | *−66* | *−47* | *Lobule VIIIb* |
| Right | | 6.05 | 28 | −70 | −19 | Lobule VI |
| Right | | 6.00 | 12 | −72 | −15 | Lobule VI |
| *Right* | *38* | *5.16* | *22* | *−38* | *−45* | *Lobule X* |
| *Left* | *268* | *5.74* | *−30* | *−66* | *−53* | *Lobule VIIb* |
| Left | | 5.50 | −24 | −70 | −59 | Lobule VIIb |
| Left | | 4.85 | −26 | −58 | −59 | Lobule VIIIa |
| | | | | | | |
| *MAINTENANCE* | | | | | | |
| *Right* | *3940* | *12.27* | *8* | *−76* | *−25* | *Lobule VI* |
| Vermis | | 11.40 | −4 | −76 | −25 | Lobule VI |
| Right | | 10.14 | 34 | −62 | −23 | Lobule VI |
| *Right* | *291* | *6.45* | *28* | *−74* | *−51* | *Lobule VIIb* |
| *Left* | *97* | *5.53* | *−30* | *−74* | *−51* | *Crus II* |
| | | | | | | |
| *RETRIEVAL* | | | | | | |
| *Right* | *33* | *5.07* | *20* | *−62* | *−47* | *Lobule VIIIa* |
| *Right* | *42* | *5.00* | *6* | *−60* | *−3* | *Lobule V* |
| Right | | 4.91 | 4 | −52 | 1 | Lobule I–IV |
| Right | | 4.83 | 12 | −60 | −9 | Lobule V |
| *Right* | *63* | *4.70* | *26* | *−46* | *−55* | *Lobule VIIIb* |
| *Left* | *40* | *4.94* | *−14* | *−58* | *−21* | *Lobule V* |
| *Left* | *28* | *4.82* | *−24* | *−46* | *−23* | *Lobule V* |

The inferior/middle frontal-superior cerebellum network was activated in both encoding and maintenance, but also (after excluding the common activations found in the conjunction analysis) a more posterior portion of the bilateral middle frontal gyrus together with the superior cerebellum was activated in the encoding phase only. On the other hand, a more anterior triangular part of the inferior frontal gyrus together with the lobule VI extending to crus I/crus II, was activated in the maintenance phase only. Additional cerebral areas that were uniquely activated in the maintenance phase included bilateral parietal regions and left temporal gyrus (Fig. 4, Table S2, S3, S4).

After excluding the common cerebellar activations found in the conjunction analysis, the strongest cerebellar activation in the encoding phase was in the vermal part of lobule VIIIb, but cerebellar activations were also observed in the left inferior cerebellum (lobule VIIb/VIIIa); this activation became bilateral in the maintenance phase.

**Table 5**
Lateralization Index for selected cerebellar and cortical brain regions. Mean values ≥0.20 or ≤−0.20 indicate left-lateralized (positive) and right-lateralized (negative) activations respectively.

| Brain region | Encoding | | Maintenance | | Retrieval | |
|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD |
| *Cerebellar laterality* | | | | | | |
| Crus1 | 0.10 | 0.38 | 0.09 | 0.36 | 0.11 | 0.48 |
| Lobule VI | 0.12 | 0.42 | −0.02 | 0.28 | 0.04 | 0.45 |
| Lobule VIIb | 0.19 | 0.47 | **−0.20** | 0.47 | −0.17 | 0.52 |
| Lobule VIIIa | **0.21** | 0.40 | 0.11 | 0.51 | −0.17 | 0.49 |
| *Cortical laterality* | | | | | | |
| Inferior frontal gyrus | 0.14 | 0.25 | 0.14 | 0.20 | **−0.36** | 0.27 |
| Inferior parietal lobule | **0.23** | 0.31 | **0.35** | 0.31 | **0.22** | 0.48 |
| Precentral gyrus | 0.01 | 0.29 | **0.47** | 0.31 | **0.52** | 0.37 |
| Supplementary motor area | 0.02 | 0.30 | **0.34** | 0.27 | 0.16 | 0.33 |
| Superior parietal lobe | **0.27** | 0.36 | **0.20** | 0.35 | **0.37** | 0.49 |
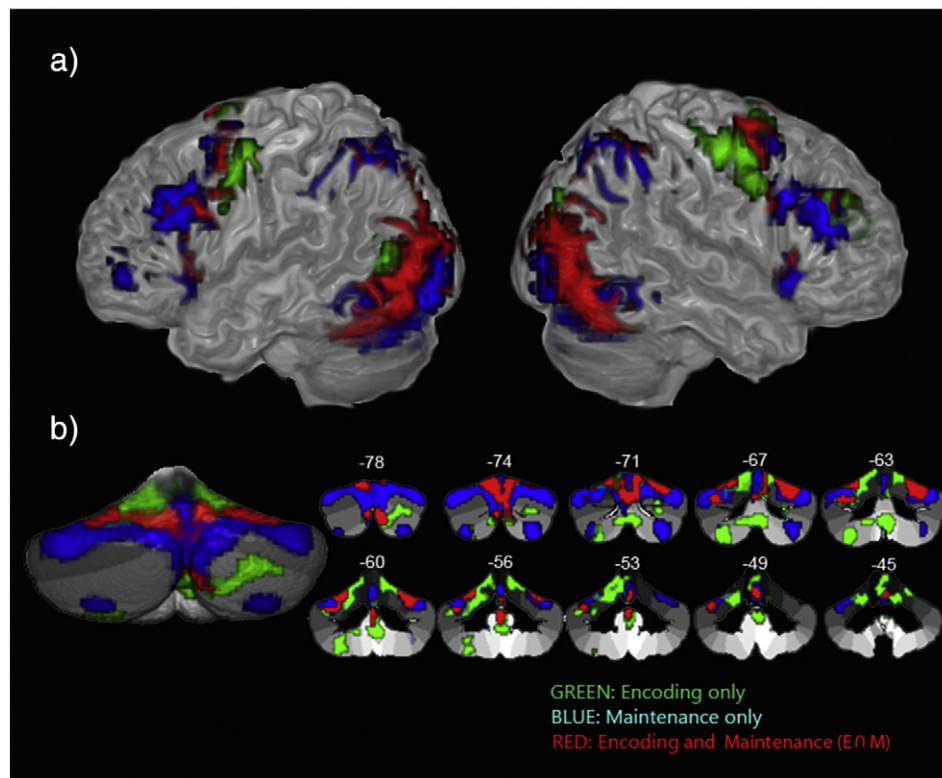
**Fig. 4.** Cerebral a) and cerebellar b) activations revealed in conjunction analysis. Common brain activations to both encoding and maintenance phase (E ∩ M) are shown in red (p < 0.005, uncorrected), activations observed during encoding only (E − (E ∩ M)) are depicted in green (p < 0.001, uncorrected), activations observed during maintenance only (M − (E ∩ M)) are shown in blue (p < 0.001, uncorrected). Numbers appearing above the coronal slices represent normalized Y coordinate values of the space defined by the MNI152 brain template.

## 4. Discussion

The present study examined cerebro-cerebellar contributions to the encoding, maintenance and retrieval phases in visual working memory. The results obtained allow us to conclude the following: Firstly, the posterior cerebellum was persistently activated during encoding, maintenance and retrieval phases during the visual working memory task, which provides strong evidence for cerebellar contributions to cognitive processes in all the phases of visual working memory. Secondly, different patterns of cerebro-cerebellar activations were observed depending on the type of cognitive processes utilized during the memory task. Thirdly, evidence for cross-lateralized cerebro-cerebellar networks supporting the processing of visuospatial sketchpad was not observed, but the results did reveal left-lateralized inferior cerebellar dominance for cognitive processes in the encoding phase.

### 4.1. Encoding phase

We hypothesized that the frontal-superior cerebellum network will be activated during the encoding phase. Indeed, we observed the

**Table 6**
Cerebellar activations common to encoding and maintenance phase (E ∩ M, high load > low load), thresholded at p < 0.001, k > 20 and t > 4. Non-italicized entries represent local maxima within the main cluster.

| Hemisphere | MNI coordinates | | | | | |
|------------|-----------------|---------|-----|-----|-----|-------------|
|            | Cluster size    | T-value | x   | y   | z   | Brain region |
| *Right*    | *1228*          | *4.67*  | *34*| *−64* | *−21* | *Lobule VI* |
| Left       |                 | 4.55    | −8  | −76 | −19 | Lobule VI   |
| Right      |                 | 3.79    | 10  | −80 | −43 | Crus II     |
| *Vermis*   | *81*            | *3.61*  | *2* | *−58* | *−33* | *Lobule IX* |
| *Right*    | *81*            | *3.29*  | *2* | *−48* | *−19* | *Lobule I–IV* |
| Right      |                 | 3.10    | 2   | −56 | −23 | Lobule I–IV |

bilateral precentral/supplementary motor and superior cerebellum activations in the encoding phase. These results are consistent with previous research that demonstrated that the dorsolateral prefrontal cortex (BA9, BA6, BA46) contributes to active processing in visual working memory (Bor et al., 2003; D'Esposito et al., 1999; Postle and D'Esposito, 1999; Postle et al., 2000). However, contrary to our initial predictions, the strongest cerebellar activation during the encoding phase was in the inferior part of cerebellar vermis (lobule VIIIb), instead of the superior cerebellum. Lobule VIIIb, which was previously found to be activated during visual working memory (Thürling et al., 2012), has been associated with motor- (Stoodley and Schmahmann, 2009) and spatial- (Stoodley et al., 2012) related activity and its vermal region is part of the cerebellar oculomotor vermis contributing to the control of eye movement (Grimaldi and Manto, 2012). The observed network of cerebro-cerebellar activations is likely to reflect the processing related to the rehearsal of the inner scribe. The processes implemented by the inner scribe have been previously associated with control of implicit oculomotor activity (Baddeley, 1986) and planning/execution of movement (Logie, 1995) that may represent the covert shifts of attention (Awh and Jonides, 2001). It is plausible that activation in the oculomotor vermis may contribute to these processes. However, an alternative explanation is that activation of the oculomotor vermis is related to co-occurrent eye-movement. It is possible that, during the encoding of three different patterns, participants were moving their eyes more frequently than during encoding of three identical patterns, despite the fact that the task was designed to minimize eye-movement.

### 4.2. Maintenance phase

In line with our initial predictions, the posterior parietal-inferior cerebellum network exhibited the greatest activations during the maintenance phase. Previous neuroimaging studies have linked visual working memory storage processes with the posterior parietal cortex

(Todd and Marois, 2004, 2005) and the inferior cerebellum with storage in verbal working memory (Chen and Desmond, 2005), therefore it is likely that the observed brain network activation in this phase supports the storage mechanism in the visual cache.

During the maintenance phase, we also observed activation of inferior frontal-superior cerebellum network that may reflect processing related to the phonological loop, especially given that the observed prefrontal and precentral activations were bilateral in the encoding phase but became left-lateralized during the maintenance phase. These shifts in activation occurred concurrently with the increase in activation of the superior cerebellum (lobule VI) and the right inferior cerebellum (lobule VIIb), both of which have been previously linked with the phonological loop (Chen and Desmond, 2005; Macher et al., 2014). The observed changes in brain activation suggest that during this phase participants were engaging processes specific not only to visual working memory but also those specific to verbal working memory. It is likely that while the visual patterns were presented on the screen their representations were maintained in a visual code. However, when the patterns disappeared and participants needed to rehearse them without visual cues, additional verbal codes were utilized unintentionally in order to retain the representations.

### 4.3. Retrieval phase

In the retrieval phase, when participants needed to discriminate between two patterns, the right inferior cerebellum was activated together with left-lateralized parietal, left-lateralized temporal and right-lateralized inferior frontal regions. The observed cortical activations in retrieval phase are consistent with past studies linking these brain areas with processing related to object recognition (Smith and Jonides, 1999). The right inferior cerebellum has been previously found to contribute to visual working memory (Thürling et al., 2012) and to verbal working memory (Chen and Desmond, 2005). It is possible that the observed inferior cerebellar activation supports item recognition in the retrieval phase. Alternatively, the inferior cerebellum activation may be linked to the phonological loop activity that has already begun in the maintenance phase.

### 4.4. Conjunction analysis

Additional conjunction analysis of encoding and maintenance allowed us to identify brain regions commonly activated in these phases, as well as brain regions activated exclusively in encoding and in maintenance, respectively. The common activations for the encoding and maintenance phases were identified in the inferior/middle frontal-superior cerebellum network. More posterior middle frontal activations were also present only in the encoding phase whereas more anterior inferior frontal activations were found uniquely in the maintenance phase. The anterior middle frontal activations present in both encoding and maintenance are likely to reflect processing associated with an internally guided rehearsal process that occurs across both phases, whereas more posterior activations of the middle frontal gyrus are likely to be linked with the rehearsal process that occurs under external guidance of stimuli during encoding. This explanation is supported by the findings from a verbal working memory study (Chen and Desmond, 2005), in which an analogous pattern of frontal activations for encoding and maintenance phases was observed with posterior frontal regions contributing to externally driven articulatory rehearsal, whereas anterior frontal activations were found to support more internally guided aspects of articulatory rehearsal.

In contrast to the results of the encoding and maintenance conjunction analysis, regions activated uniquely for the maintenance phase included parietal and inferior cerebellar (lobule VIIb) areas, providing further support for the assertion that this brain network is likely to support storage process of the visual cache. Furthermore, activation of the anterior triangular portions of the inferior frontal gyrus, together

with the activation of the bilateral lobule VI, was also observed in the maintenance phase. This is seen to be consistent with the activation pattern linked with articulatory rehearsal in verbal working memory. This further suggests that the processes utilized during this phase are likely to be those associated not only with visual working memory but also those associated with verbal working memory.

### 4.5. General discussion

The findings of the current study are generally in agreement with Baddeley's model of working memory, even though the results demonstrated that storing of mental representations of presented patterns is supported not only by the visuospatial sketchpad but is additionally supported by active maintenance mechanisms that use verbal coding. The past studies linked the visual cache with retention of low resolution visual representations that contain overall shapes and colors but not precise details (e.g., Logie, 1995; Borst et al., 2012). The retention of more precise, detailed information requires an active maintenance that involves repeated image generation of previously presented items (Darling et al., 2009) and semantic information may be automatically associated with the perceived patterns (Postle et al., 2005). In the current study, the stimuli used consisted of complex visual patterns that required remembering specific details of presented images in order to identify the presented pattern in the retrieval phase. Therefore, it seems likely that functional changes in brain activity observed during the maintenance phase reflect not only the visual storage mechanism but also active rehearsal processes of the phonological loop. It has been shown previously, that the utilization of the visuospatial sketchpad in maintenance of visuospatial information is not always required. For example, Garden et al (2002) asked subjects to learn a route through an unfamiliar city while performing spatial tapping or suppressed articulation. The performance was disrupted by spatial tapping for those participants who reported memorizing the route by using a mental map but not for those who used landmarks. The performance of the latter was disrupted by concurrent articulatory suppression. In the current study, during the post-scan briefing when participants were asked if they used any particular strategies for memorizing presented patterns, only a few participants reported that they had some automatic verbal associations with the presented patterns (although not done intentionally). Therefore, it seems that verbal processing contributing to the visual working memory may be more inherent to the stimulus material and automatic rather than result from a consciously undertaken coding strategy by participants. The extent of the current study does not provide enough evidence to fully support this interpretation; however the past behavioral studies provide indirect support to this conjecture. For example, Postle et al. (2005) demonstrated that introducing verbal distraction during the maintenance phase of visual abstract shapes led to decreased task performance. This led them to conclude that semantic code contributes to visual working memory and multiple representational codes can represent visual information concurrently. It is possible that an analogous mechanism underlies the observed brain changes in our study, but additional investigations will be needed to ascertain this. However, if the above interpretation is correct, this would raise the question as to whether the visual working memory is truly separate from verbal processing. Interestingly, it has been already demonstrated that in children with specific language impairment, poorer visuospatial working memory is associated with greater language impairment (Vugs et al., 2013).

An alternative explanation of the observed changes in brain function during the maintenance phase could point towards an additional domain-general attention resource (the central executive) used while retaining visual information that is no longer being displayed. This possibility cannot be excluded given that past studies exploring cerebellar contributions to visual working memory using N-back tasks (Hautzel

et al., 2009; Küper et al., 2015) suggested that increased demands of executive control may lead to the central executive dominance over the slave systems and overriding asymmetries in cerebellar function induced by the visuospatial sketchpad or phonological loop. However, in contrast to studies using N-back paradigm, the current experiment employed a Sternberg paradigm, which emphasizes stimulus maintenance rather than executive demands and therefore the changes observed should be associated with retaining the stimulus rather than the executive control involved in stimulus manipulation. Furthermore, if enhanced executive demands in the maintenance phase of the Sternberg paradigm were to override the cerebro-cerebellar asymmetry of the slave systems, this would also be observed in the verbal working memory. However, results from the previous study examining the temporal dynamics of verbal working memory did not provide support for this assertion (Chen and Desmond, 2005).

Given the crossing neural pathways connecting the cerebrum with the cerebellum (Palesi et al., 2014), we hypothesized right-lateralized cerebral and left-lateralized cerebellar activations in visual working memory. Our results provided evidence only for left-sided lateralization in the inferior cerebellum during encoding but not in maintenance and retrieval. The results did not reveal right-sided lateralization for cortical regions but instead showed left-lateralized frontal and parietal activations in maintenance, which were co-activated with right-lateralized inferior cerebellum. The fact that the observed cerebro-cerebellar activations lacked the hypothesized hemispheric asymmetries (right cortical-left cerebellar) may result from the possibility that not only visuospatial but also verbal rehearsal and storage strategies were utilized in the current study.

Some limitations of the study need to be addressed. Firstly, the possibility of eye-movements contributing to the observed activations in the encoding phase cannot be excluded. Even though the visual patterns were presented at the same spatial location, it is possible that encoding of the detail included in the three different patterns in the high load condition caused more eye movements than encoding of the three identical patterns in the low load condition. To complement our results, future studies should use objective measurements of eye movements such as using eye-tracker during the memory task. Nevertheless, the cerebellar contributions to visual working memory are not purely due to eye-movements as cerebellar TMS studies do obtained reduced accuracy in performance (Chen et al., 2014, 2015). Secondly, even though the visual stimuli used in the study were carefully designed to be relatively non-verbalizable, the obtained brain responses suggest that not only spatial but also verbal coding was utilized during maintenance of visual information in working memory, but to determine this, additional investigations will be needed. Lastly, it is important to acknowledge that based on results from the current study it cannot be determined whether the observed changes in the patterns of cerebro-cerebellar activations that reflect engagement of the inner scribe and the inner cache are dissociated from each other, even though the results obtained from the conjunction analysis suggest that more internally guided aspects of rehearsal are present in both encoding and maintenance phase, whereas an externally driven rehearsal process is employed only in the encoding phase.

In conclusion, our findings provide further evidence that the superior and inferior cerebellum contributes to visual working memory. The frontal-superior cerebellar loop is likely to support the inner scribe functions and the parietal-inferior cerebellar loop is likely to contribute to processing of the visual cache. The results revealed a tendency for left-lateralized inferior cerebellar dominance in encoding of visual information but we did not find, however, evidence for right-lateralized cerebral and left-lateralized cerebellar networks supporting the processing of visuospatial sketchpad as most of the observed activations were bilateral or left-lateralized. Hence, the investigation into the various phases of visual working memory allowed us to observe the temporal dynamics of specific cerebellar contributions in tandem with the cerebral cortical network activity.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.neuroimage.2015.09.038.

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