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Recognition memory for vibrotactile rhythms: An fMRI study in blind and sighted individuals

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Abstract

Calcarine sulcal cortex possibly contributes to semantic recognition memory in early blind (EB). We assessed a recognition memory role using vibrotactile rhythms and a retrieval success paradigm involving learned “old” and “new” rhythms in EB and sighted. EB showed no activation differences in occipital cortex indicating retrieval success but replicated findings of somatosensory processing. Both groups showed retrieval success in primary somatosensory, precuneus, and orbitofrontal cortex. The S1 activity might indicate generic sensory memory processes.

Keywords

Human occipital cortex; magnetic resonance imaging; touch

Introduction

In blind but not sighted people, language tasks activate regions in occipital and temporal cortex that correspond to visually activated areas in sighted (Kujala et al. 1995a; Sadato et al. 1996; Büchel et al. 1998a, 1998b; Melzer et al. 2001; Burton et al. 2002a, 2002b, 2003, 2006; Röder et al. 2002; Amedi et al. 2003; Burton 2003; Burton and McLaren 2006). The functional reorganization of these regions in the blind possibly aids in semantic word generation and word memory retrieval (Amedi et al. 2003). However, tactile and auditory discrimination tasks and tactile short-term memory tasks lacking a language component also activate the same regions in occipital cortex in the blind (Kujala et al. 1995a; Arno et al. 2001; Burton et al. 2004, 2010; Gougoux et al. 2004). Pending then is determining the role of occipital cortex in retrieval memory tasks in blind people.

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Word recognition memory tasks involve learned words later distinguished from new words (McDermott et al. 2000; Donaldson et al. 2001a; Wheeler and Buckner 2003). A participant must decide whether a presented word is old or new. Trials with correct retrievals of old words are Hits, those with correct rejections of new words are CRs, failing to recognize old words are Misses, and categorizing new words as “old” are False Alarms (FAs). Recognition memory decisions associated with retrieval success involve functions of recollection and familiarity (Skinner and Fernandes 2007; Donaldson et al. 2010). A recollection process generally is effortful because it is contextual with regard to the conditions surrounding learning. Familiarity is more automatic engendered by assessment of trace strength. These two processes activate some cortical regions that overlap and others that are distinct (Skinner and Fernandes 2007). Old words learned without source-specific factors prompt a sense of familiarity, and areas of dorsolateral pre-frontal and posterior parietal cortex are more active when successfully judging an old word as known (e.g., familiar) compared to correctly rejecting (CR) new words (Iidaka et al. 2000; Konishi et al. 2000; Donaldson et al. 2001a, 2010; Roskies et al. 2001; McDermott et al. 2003; Wheeler and Buckner 2003). Recollection processes also evoke activity in parietal cortex and especially in orbitofrontal cortex when judging an old word as remembered (Skinner and Fernandes 2007; Donaldson et al. 2010). Prior reports that occipital cortex in the blind contribute to recollection of learned words did not differentiate retrieval success from correct rejections of new words. However, this deficiency is not definitive because not all task paradigms reveal retrieval success effects in frontal and parietal cortex. Gallo et al. (2007) found that frontal areas sometimes show little or no activation differences indicating retrieval success for distinctive stimuli such as pictures of objects. Cabeza and co-workers (Cabeza 2008; Cabeza et al. 2008) found activation differences related to retrieval success between dorsal and ventral parts of posterior parietal cortex that depended on task difficulty.

There have been no prior studies of retrieval success for tactile stimuli. In the present study, stimuli were vibrotactile sequences (rhythms) made up of interspersed and varied duration intervals of vibrations at one frequency and no vibration. Participants discriminated learned from new rhythms. Similar to findings with word recognition tasks, decisions in tactile rhythm recognition entail sensory processing, memory retrieval, formation of a decision, and planning and executing a motor response. Learning rhythms involved no contextual factors. Consequently and analogous to prior findings using word recognition tasks, we anticipated that retrieval success relied on a sense of familiarity and thus, activation of regions in parietal and dorsolateral prefrontal cortex. Additionally, we hypothesized three possible outcomes in occipital cortex of blind people. First, the distribution of activated regions could resemble that previously revealed with verbal tasks (Sadato et al. 1996, 1998; Büchel et al. 1998b; Amedi et al. 2003; Burton 2003; Burton et al. 2003, 2006; Noppeney et al. 2003). Such findings would fail to differentiate a role for occipital cortex other than to confirm activation only in the blind in a non-verbal tactile task. A second hypothetical outcome could be selectively enhanced occipital cortex activation that correlates with retrieval success for learned tactile rhythms, possibly in specific areas like calcarine sulcal (e.g., V1) cortex (Amedi et al. 2003; Raz et al. 2005). This result would suggest a prominent role for these regions in recognition memory of non-verbal tactile information. A third hypothesis is recruitment of occipital cortex to augment tactile sensory processing in the blind. Such

findings might reflect superior performance on some tactile tasks in the blind. A corollary question is whether the blind perform the tactile pattern task at higher accuracy or with shorter reaction times than sighted controls.

Materials and methods

Participants provided informed consent in compliance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) and guidelines approved by the Human Studies Committee of Washington University. Participants self-reported no neurological conditions or head trauma, and no contraindications to MRI. All brains showed normal structural anatomy. Eleven early blind (EB: 5 female; mean age = 39.8 years, min 22, max 59) and 11 normal sighted (NS: 5 female; mean age = 34.2 years, min 22, max 57) participants provided imaging and behavioral data. All EB had no sight from birth due to various peripheral pathologies (Table I). Four EB with retained awareness of light were unable to read print or see shapes. All EB were Braille readers (Table I). Inadequate task performance led to excluding data from one participant in each group.

Vibrotactile rhythm task

Tactile rhythms, applied to the right index finger using an MR-compatible vibrator (Burton et al. 2004), consisted of five segments of suprathreshold sinusoidal vibrations that differed in duration and four non-stimulus intervals (gaps). Vibration amplitude (40 μ m peak-to-peak) and frequency (50 Hz) were constant. Different rhythms were created using combinations of 100, 300, and 500 ms vibration and gap durations. An example rhythm (Figure 1A1) shows vibration durations (boxed areas) that successively cycle from short (100 ms) to long (500 ms) and then back to short (100 ms). Another example rhythm (Figure 1A2) shows successively shorter vibration durations (500–100 ms). Both example rhythms contain various gap intervals. Across 60 different rhythms, total rhythm durations ranged from 1300 to 2500 ms, most rhythm durations were from 1800 to 2500 ms, and the average duration was 2264 ms.

The onset of rhythm trials was synchronized to successive whole-brain acquisitions. However, for every trial, a rhythm ended 2500 ms after the beginning of the first echo-planar imaging frame of a multi-frame event by adding a delay prior to the beginning of shorter length rhythms. For example, a delay of 500 ms preceded a 2000 ms rhythm (Figure 1B). The incidence of presentation intervals between rhythm trials followed a negative exponential distribution of 6–11 repetition times (TRs) and were presented in pseudo-random order such that no consecutive interval repeated >2 times. Computations assumed an average event interval of 7 TRs (14 s) that spanned the overlap of jittered events (Miezin et al. 2000; Ollinger et al. 2001).

A functional imaging session consisted of four scan runs with uniquely different rhythms presented in each run (i.e., no rhythms repeated from one run to the next). An encoding task preceded each run. Imaging runs involved a recognition task.

During learning participants encoded a pair of rhythms. On each of 20 trials the two presented rhythms were identical or differed (match/no-match). A 1 s interval separated the

two rhythms in each trial. Rhythms matched 50% of the time and each rhythm was repeated 25% of the time in pseudo-random order. Instructions during encoding included an explanation of the match/no-match task and emphasized that the intended purpose was to learn the two rhythms for recognition in the immediately following imaging run. A delay of ~2 min separated the encoding task and the following recognition task scan. The just learned rhythms recurred together with new rhythms during recognition. Participants determined if the single rhythm presented in a trial was one of those learned during the previous encoding task and was therefore “old” or was a “new” rhythm. Each recognition run contained 32 trials. Old and new rhythms occurred on 50% of trials, in pseudo-random order.

Prior to imaging participants received training until they understood the task and performed at greater than 80% correct. Participants signaled “old–new” recognition by pressing one of two buttons with the left hand using a fiber optic response pad.

Image acquisition

We acquired images with a Siemens 3 Tesla TRIO scanner (Erlangen, Germany) and a 12-element RF head matrix coil. MRI headphones dampened scanner noise and a vacuum cushion stabilized the head. All participants had their eyes covered by a blindfold and kept their eyes closed in a darkened room during functional imaging. During all structural imaging and between functional scans room lights were on and sighted participants opened their eyes.

A gradient recalled echo-planar sequence (EPI, repetition time [TR] = 2000 ms, echo time [TE] = 27 ms, flip angle = 90° , $4 \times 4 \times 4 \text{ mm}^3$ voxels) captured images of blood oxygenation level-dependent (BOLD) contrast responses (Kwong et al. 1992; Ogawa et al. 1992). During each volume acquisition (TR frame), images covered the whole brain with 4 mm^2 in plane resolution across 33 contiguous, interleaved, 4 mm axial slices (i.e., 4 mm^3 isotropic voxels) aligned parallel to the anterior/posterior commissure plane. A 256-frame imaging run started with five frames without stimulation, followed by 242 frames with event trials, and ended with nine frames with no stimulation. Siemens software provided for magnetic equalization using default frames prior to image collection to which we added the first frame of image collection.

Additional structural images included a T1-weighted magnetization prepared rapid gradient echo (MP-RAGE) image acquired across 176 sagittal slices (TR = 2100 ms; TE = 3.93 ms; flip angle = 7° ; inversion time [TI] = 1000 ms; $1 \times 1 \times 1.25 \text{ mm}^3$ voxels). An additional T2-weighted structural image obtained across 33 axial slices was in register with the EPI (TR = 8430 ms, TE = 98 ms, $1.33 \times 1.33 \times 3 \text{ mm}^3$ voxels) and aided registration of the EPI to the sagittal MP-RAGE images (Ojemann et al. 1997).

Image processing

EPI image processing for each participant involved corrections to compensate for systematic slice-dependent image intensity differences due to interleaved odd–even slice acquisition and to realign image slices into atlas space. Processing started with aligning the time for each slice to the beginning of each volume acquisition using sinc interpolation. Next, corrections for intensity differences between slices used a whole-brain mean signal intensity

normalized to mode 1000 across EPI runs. These adjusted slices were realigned within and across runs using rigid body correction for inter-frame head motion. The across-run-realigned slices were resampled to 2 mm³, spatially smoothed using a 2-voxel Gaussian kernel (4 mm FWHM), and registered to an atlas template by computing 12 parameter affine transforms between an average from the first frames of each EPI run and an atlas template (Ojemann et al. 1997). The representative atlas template was created using MP-RAGE structural images combined from NS and EB participants (age and gender matched to the study sample); the template conformed to Talairach atlas space (Talairach and Tournoux 1988) based on spatial normalization methods (Lancaster et al. 1995).

Statistical analyses

Analysis of BOLD responses for the recognition task in each participant utilized a general linear model (GLM) on a voxel-by-voxel basis that coded for several factors: single event time points, within-scan linear drift, mean baseline activity, and a high-pass filter (0.014 Hz). BOLD responses per voxel were estimates of percent MR signal change relative to baseline over the time course for an event. Each of 32 events per run included presentation of a single rhythm. Two event categories were for correct responses to new and old rhythms as, respectively, CRs and Hits; and two event categories were for incorrect responses of falsely tagging a new rhythm as old (FAs) and an old rhythm as new (Misses).

A fixed effect analysis initially determined whether BOLD responses in a participant occurred for each type of response. For this determination, a computed *F*-test per voxel (transformed to equally probable uncorrected *z*-scores) assessed BOLD response variance associated with an event against variance in baseline activity. The *F*-test involved no assumptions about a hemodynamic response function.

Group-level contrast analysis utilized several repeated-measures, mixed-effects ANOVAs to investigate hemodynamic patterns over time without assumptions of the shape of the BOLD response. The dependent variable was percent change in MR signal per voxel using estimates from the GLM obtained in each participant. The repeated measures were results from three recognition runs with highest participant performance accuracy. The random factor was BOLD response variance across participants. Time was a seven-level fixed factor for each ANOVA. In separate ANOVAs for the NS and EB groups, fixed factors were trial-types (CR and Hit), time, and trial-types-by-time. A third ANOVA had group (NS and EB), time, and time-by-group as fixed factors. A fourth ANOVA had trial-types (CR and Hit), time, group (NS and EB), and the interaction terms as fixed factors. *F*-ratios for each factor in the ANOVA models were converted to *z*-scores whose degrees of freedom were adjusted for covariance (sphericity correction) and thresholded at $p = 0.05$. The *z*-score maps based on the interaction of time by a particular factor indicated where temporal profiles of BOLD responses differed in the underlying levels (trial-types or groups). To explore response per trial-type or group-dependent differences further, an automated algorithm first located peaks (local extremes) exceeding $p < 0.006$ significance in each ANOVA *z*-score map. Loci separated by less than 15 mm were consolidated (by center of mass calculation) to limit subdivisions due to spatially extended responses. Spherical (4 mm radius) regions of interest (ROI), centered on the Talairach atlas coordinates (Talairach and Tournoux 1988) of

consolidated peaks, had z -scores > 2.5 ($p < 0.006$, one-tailed). Time courses, extracted from selected ROI, consisted of seven time points per event from each scan and participant.

Repeated-measures, mixed-effects ANOVAs (PROC GLM, Statistical Analysis System version 9.1, SAS Institute, Cary, NC, USA) assessed these time-course data per ROI. The repeat factor was imaging run per participant. The random factor for each ANOVA was participant nested within group. The analysis of BOLD response magnitude, the dependent variable, included time points (TP) 2–7 after subtracting the value of TP1 from each time point, which anchored responses relative to the beginning of events and set the variance of time point 1 to zero. In ANOVAs, the factors were trial-type-by-group, trial-type, group, time point, and subject. Significant results for the interaction term were crucial as these indicated whether response magnitudes differed for trial-types across groups or for groups across trial-types.

Results

Task performance

Response accuracy (%Correct) during recognition runs was $>85\%$ for both groups (%Correct EB 91%; NS 91%; $T=-0.02$, $p=0.99$; RT EB 1316 ms NS 1174 ms; $T=0.72$, $p=0.48$). A two-way ANOVA found no significant effect for group ($F=0$ df 1, 60, $p=0.99$) or BOLD run ($F=1.57$, df 2, 60, $p=0.22$). A linear regression analysis also found no change in accuracy across successive runs; and the regression slopes based on averages by run were not significantly different from zero in each group. These results indicate that participants learned the recognition task during practice and, as intended, reached a performance plateau before functional BOLD runs.

ANOVA maps

Figure 2A illustrates activation patterns based on significant changes in the amplitude of the BOLD response as a function of time across a trial (main effect of time) in the ANOVA model of trial-types. It shows that the task particularly activated bilateral occipital cortex in EB, including visual areas defined in NS as V1 in the calcarine sulcus (BA17), lingual and cuneus gyri (V2, BA18), superior occipital gyrus (V3a and V7, BA19), anterior lingual gyrus (VP and V4v), fusiform gyrus (V8), lateral occipital gyrus (LOC), and inferior temporal–lateral occipital cortex (MT). In NS, only V1 and V2 were active at spatial extents and levels similar to EB. VP and V8 were active in NS at levels lower than EB. Other visual areas did not show significant activation in NS. In ROI in parietal and precentral regions, there was a greater extent of activation in NS compared to EB especially in the right hemisphere.

An additional term in the ANOVA assessed these differences in the distribution of activated regions between groups. Figure 2B illustrates maps of these significant interaction effects of time-by-group corresponding to regions of activity differences between the EB and NS groups, and from this analysis ROI were identified for investigation of BOLD time courses. These were especially located throughout the visual areas bilaterally in occipital and temporal cortex. Additional isolated patches similarly reflecting group activity differences

were in dorsolateral prefrontal, orbitofrontal, cingulate, peri-central sulcal, and intraparietal sulcal cortex. These results indicated an array of cortical regions that responded differently in the two groups and most particularly, these were in occipital cortex.

Figure 2C shows another set of ANOVA maps based on activity differences between CR and Hit trial-types (i.e., significant interactions of time with trial-type) with results combined for the NS and EB groups. Occipital cortex contained only isolated patches with significant *F*-ratios for the trial-type-by-time factor. Some of these partially overlapped the distribution of occipital regions showing group differences in Figure 2B. There were also patches of response differences by trial-type in dorsolateral prefrontal, orbitofrontal, cingulate, peri-central sulcal, and intraparietal sulcal cortex.

Numbered circles on the brain images in Figure 2B, C indicate non-overlapping ROI centers identified by the peak search algorithm based, respectively, on the time-by-group and trial-type-by-time in each group. Matching numbered panels shown in Figures 3 and 4 present the time courses extracted from 8 mm diameter spheres centered on these ROI.

Time-course analysis

Assessment of activation differences between trial-types or between groups involved data from ROI identified as showing a significant trial-type-by-group factor with *F*-ratio probabilities of <0.0001 in an omnibus ANOVA of time-course results combined across groups and trial-types. A separate ANOVA of data from these ROI evaluated activation when judging a rhythm as old (Hits) compared to rhythms identified as new (CRs) within groups. Another ANOVA of the same ROI examined activity differences between groups for each trial-type.

In EB, all ROI in occipital cortex showed positive BOLD responses (Figure 3, panels 1–10). Nevertheless, response magnitudes in no ROI significantly differed for Hit and CR trials ($p = 0.002$ strict significance level by Bonferroni correcting for multiple comparisons). These findings do not suggest blindness-induced reorganization in occipital cortex that supports a role in tactile recognition memory.

Several ROI in occipital cortex of NS also showed positive BOLD responses. Figure 3 illustrates for NS activation in ventral calcarine (V1v), posterior and anterior lingual (V2v and VP), and parietal–occipital sulcal (non-visuotopic BA19) cortex (Figure 3, panels 1–3 and 9). Larger positive BOLD responses when correctly judging a rhythm as old (Hits) differed significantly from those when identifying a new rhythm (CRs) in these ROI for NS but not EB. Several other ROI in occipital cortex also showed significant response differences at strict criterion between trial-types in NS (Figure 3, panels 6 and 7). Although prior studies report negative signals in occipital cortex of NS (Burton et al. 2004, 2006, 2010; Azulay et al. 2009), the relevance of the latter activation patterns is dubious because activity for Hit trials was at or near 0 compared to $<0.1\%$ negative MR signal change for CR trials in these ROI, and differences were mostly seen late in the trial period.

BOLD response magnitudes based on averages of each time point from frames 2–7 when identifying new rhythms (CR) were comparable for both groups in ventral calcarine (V1v),

posterior lingual (V2v), and LH parietal–occipital sulcal cortex (non-visuotopic BA19), but were significantly larger in EB in all remaining ROI in occipital cortex (Table II, $p < 0.002$ strict significance level by Bonferroni correcting for multiple comparisons). Both groups also showed equivalent response magnitudes when judging a rhythm as old (Hits) in ventral calcarine (V1v) and anterior lingual gyrus (VP). Response magnitudes were significantly larger in EB compared to NS for Hit trials in occipital cortex V2v, V3A, V7, V8, MT, and BA19 non-visuotopic (ROI # 2, 4–6, 8–10) based on a strict criterion and LOC (# 7) using a more liberal criterion in Table II. These findings confirm preferential vibrotactile activation of occipital cortex in EB exclusive of the lowest tier visuotopic areas.

This study focused on activation of visual cortex in the blind, but comparison with word and non-verbal tactile memory tasks required analysis of regions outside visual cortex. These analyses follow.

Several ROI in parietal cortex showed positive BOLD responses for both trial-types. The trial-type effects varied for each group and especially with hemisphere for the ROI in parietal cortex. When judging a rhythm as old, positive magnitudes were significantly larger in NS for the primary somato-sensory (S1) left BA2 and in EB for right BA1 ROI (Figure 3, panels 11 and 12, Table II). Response magnitudes for Hit trials were also significantly larger in EB compared to NS in left BA2 (Table II).

In both groups, differences in S1 activation due to trial-type immediately followed the end of stimulation, which suggests a possible sensory memory role.

All other parietal ROI with positive BOLD responses had comparable response magnitudes in NS between trial-types (Figure 3, panels 13–16), but in left medial parietal (precuneus) (Figure 3, panel 15), EB showed significantly larger late positivity when judging a rhythm as old. All of these ROI in the left hemisphere had larger responses in NS compared to EB and the reverse group difference for the right pIPS ROI (Table II).

Both groups showed negative BOLD responses in left angular gyrus (inferior lateral parietal cortex) that encompassed BA39. Response magnitudes for both trial-types were similar for each group (Figure 3, panel 17) and similar between groups for each trial-type (Table II). On the right, activation in NS compared to deactivation in EB resulted in significant magnitude differences between the groups for both trial-types (Figure 3, panel 18, Table II). This was due to a significantly larger response for judging rhythms as old in EB (Figure 3, panel 18). Despite these differences, the activation patterns in parietal cortex ROI indicated generally comparable processing and no dramatic evidence of reorganization in EB.

Response patterns for ROI in frontal cortex varied considerably. Figure 4 illustrates contrasts between positive and negative BOLD responses in dorsolateral prefrontal cortex (DLPFC) for, respectively, NS and EB groups (Figure 4, panels 25 and 26). There were no significant trial-type differences in both of these ROI despite the larger response amplitudes when rhythms were correctly identified as old in NS. In contrast, responses in left orbitofrontal cortex subdivision 47r on the inferior frontal gyrus (Ongür et al. 2003) showed significantly larger responses when judging rhythms as old in NS mainly due to delayed positivity after time point 4 (Figure 4, panel 19). A similar effect was seen in EB that

approached strict significance. Responses in two other ROI in frontal cortex showed positive BOLD responses that in NS were significantly larger at a liberal criterion of $p = 0.003$ when identifying new rhythms (Figure 4, panels 21 and 23). Responses in these ROI were of equal amplitude in EB for both trial-types. In summary, only an orbitofrontal 47r ROI had preferential activation when judging rhythms as old in both groups.

Group response magnitude differences for each trial-type followed from the dissimilar response shapes in frontal cortex ROI (Figure 4). For example, opposite polarity BOLD responses in bilateral DLPFC differed significantly in magnitude between EB and NS for each trial-type (Figure 4, panels 25, 26; Table II). Where positive BOLD responses occurred in both groups (Figure 4, panels 21–24), NS overall showed larger responses that differed significantly from those in EB when identifying new rhythms and judging rhythms as old in OrbitoFrontal.G and, with a liberal criterion in BA44 (Table II). Only responses in EB were significantly larger for both trial-types from the orbitofrontal ROI in right BA11, where EB showed larger responses compared to essentially no activation in NS (Table II).

Discussion

ROI in occipital cortex

Confirming our first hypothesis, the distribution of activated occipital cortex regions resembled those previously revealed with verbal tasks. However, no occipital cortex ROI in EB showed significant response differences when judging a rhythm as old or identifying the rhythm as new. The dominant activation pattern in occipital–temporal cortex in blind confirmed findings of positive BOLD responses in studies employing Braille or auditory language (Büchel et al. 1998a, 1998b; Melzer et al. 2001; Burton et al. 2002a, 2002b, 2003; Amedi et al. 2003) and tactile or auditory non-language tasks (Kujala et al. 1995a, 1995b, 1997, 2005; Sadato et al. 1996, 1998, 2002, 2004; Leclerc et al. 2000; Röder et al. 2000, 2002; Weeks et al. 2000; Gizewski et al. 2003; Burton et al. 2004, 2010; Gougoux et al. 2004, 2005; Hötting et al. 2004; Stevens and Weaver 2009). These findings, therefore, did not confirm prior reports of selectively enhanced activation, especially in calcarine sulcal cortex (e.g., V1), during recall of heard words (Amedi et al. 2003; Raz et al. 2005). Consequently, the results failed to confirm our second hypothesis of selectively enhanced occipital cortex activation that correlates with retrieval success when judging tactile rhythms as ones that had been learned.

Amedi and co-workers (Amedi et al. 2003; Raz et al. 2005) reported that peak voxel amplitude in V1 correlated with the number of words recalled by blind participants 6 months after they had used these words in a verb-generate task. We assessed whether activation in calcarine sulcal cortex predicted response accuracy in the present study. We measured peak amplitude (positive or negative) of the response time course bilaterally across the calcarine sulcus in the EB group for each BOLD run and computed linear regressions as a function of %Correct. The slopes of linear regression lines for left (0.001%, $T=0.00$, $p=0.9999$) and right (8.55%, $T=0.80$, $p=0.4418$) calcarine cortex were not significantly different from 0. Thus, there was no correlation between discrimination accuracy and peak response amplitude in V1.

Finding widespread activation of ROI in occipital cortex of blind by vibrotactile stimulation possibly augments the third hypothesis that these regions contribute to tactile sensory perception and, thereby, might be a factor in superior performance on tactile tasks. However, the blind show superiority over sighted only for tactile tasks involving discrimination of Braille-like dot patterns but not of grating roughness and the frequency or amplitude of vibrations (Stevens et al. 1996; Grant et al. 2000; Sathian 2000; Van Boven et al. 2000; Goldreich and Kanics 2003; Burton et al. 2010). EB and NS also had similar accuracy and reaction times when recognizing tactile rhythms. Consequently, these findings did not support a predicted corollary that enhanced occipital activity might affect performance in terms of higher accuracy and/or shorter reaction times in the blind compared to sighted when successfully retrieving learned tactile rhythms. Comparable performance in both groups does not indicate that the unique distribution of activated occipital cortex regions in blind was an advantageous factor in judging rhythms as old or identifying them as new. Prior reports of superior performance in blind on some tactile tasks might simply reflect learned strategies in everyday reliance on tactile information.

EB showed larger response magnitudes from all ROI in higher tier visuotopic areas occupying superior (V3A, V7) and lateral (LOC) occipital gyri, posterior fusiform gyrus (V8), and posterior inferior temporal sulcal cortex (MT), especially compared to negative responses in NS. There was no preferential activation in left or right hemisphere regions. Prior studies reported similar positive compared to negative BOLD responses, respectively, in EB and NS in these occipital-temporal regions (Burton et al. 2004, 2006, 2010; Azulay et al. 2009). The negative responses in NS suggestively support the notion that suppressing information from cortex that processes vision, a non-attended or remembered modality in the current study, aided processing of the attended tactile modality (Azulay et al. 2009). Enhanced occipital cortex activity in blind suggests inclusion of that region for somatosensory processing when attending and remembering tactile rhythms. It remains undetermined what aspect of somatosensory processing this region contributes in the blind.

In blindfolded sighted individuals asked to explore and rate raised-dot surfaces, Merabet et al. reported significant activation in V1 and deactivation of extrastriate regions V2, V3, V3A, and V4 (2007). This prior study did not manipulate recall parameters, but recognition memory certainly contributed to dot array identification. Possibly comparable to these earlier findings, NS in the present study showed enhanced responses when judging rhythms as old in lower tier V1, V2, and VP visual areas. Our NS also wore blindfolds although complete darkness was present only during functional imaging runs. However, exposure to light was restricted throughout the imaging session, possibly leading to sufficient visual deprivation to alter occipital cortex activity in NS. In sighted participants who viewed words in a recognition memory study, McDermott et al. (2000) found response amplitudes higher for identifying new words compared to judging words as old in right occipital cortex, but they identified no specific visual areas. In the present study, most activation of ROI in occipital cortex in EB did not differ between trial-types and, therefore, did not indicate retrieval success. This discrepant finding might have resulted from using vibrotactile non-verbal stimulation.

Our hypotheses centered on possible activation differences in visual cortex between groups and from manipulations of trial-type. However, earlier studies of language and of non-verbal tactile stimuli reported changes in activity in parietal and frontal regions. Therefore, a valuable analysis is to examine activation patterns in these regions in the present study. This provides a basis for comparison of similarities and differences with these earlier studies particularly as it bears on response patterns in visual cortex and in possible strategies by which the tactile rhythm task was solved by the groups. These findings are discussed below.

ROI in parietal cortex

One view is that recapitulation of learned stimulation within an activated sensory cortex accompanies memory retrieval (Wheeler et al. 2000; Buckner and Wheeler 2001; Wheeler and Buckner 2004; Woodruff et al. 2005; Skinner and Fernandes 2007). Activation in fusiform areas normally responsive to pictures occurs particularly in source memory paradigms in which learned words associate with pictures during encoding and then retrieval of words, especially during Remember responses (Wheeler and Buckner 2004; Woodruff et al. 2005). Re-activation of content-specific sensory regions might contribute contextual details needed for recollection (Wheeler and Buckner 2004; Woodruff et al. 2005).

Activation in parts of somatosensory cortex in both groups that was greater when judging a rhythm as old possibly indicates recapitulation of the tactile parameters underlying a learned rhythm. Although the current study did not use a Remember/Know design, these enhanced somatosensory cortex responses especially in BA1 and BA2 possibly reflect that rhythm preservation or, in other parietal regions, retrieval of tactile information in sensory memory. Observing sensory cortex responses in both groups suggest they are generic recapitulations crucial for recollection processes and not instances of reorganization precipitated by acute (NS) or chronic (EB) visual deprivation.

We also observed positive BOLD responses in parietal operculum ROI (second somatosensory cortex, S2) that, however, showed no trial-type differences. This unexpected lack of response differences for trial-types in S2 failed to confirm prior meta-analyses that suggested representation of higher level somatosensory processing, particularly for tasks involving discrimination of surface roughness or shapes (Burton et al. 2008b). Another prior study reported response differences for S2 in vibrotactile attention tasks with selective compared to dividing attention (Burton et al. 2008a). The current lack of trial-type differences for activation in S2 possibly arose because attention did not need to shift from the stimulated fingertip throughout the trials.

Posterior to S2 in inferior supramarginal gyrus the ROI in BA40 responded to the vibrotactile rhythms. Prior studies also noted responses to tactile stimulation in inferior supramarginal gyrus (Burton et al. 2004, 2006, 2008a, 2010). Activation magnitudes in BA40 in both groups were greater when correctly identifying new rhythms, but these failed to differ significantly from responses when judging rhythms as old. These findings do not confirm prior evidence that retrieval success with learned words particularly activate inferior parts of parietal cortex irrespective of whether retrieval depended on familiarity or recollection (Wheeler and Buckner 2004; Skinner and Fernandes 2007; Donaldson et al. 2010). One possible explanation is that the BA40 ROI in the present study was in a different

location to the region activated by retrieval success for words. It was >10 mm anterior and in the left hemisphere, contra-lateral to the stimulated finger. Consequently, this sector of the inferior supramarginal gyrus might process tactile stimulation parameters.

ROI in intraparietal sulcal cortex showed no activation differences for trial-types in either group. Consequently, the vibrotactile recognition memory paradigm did not confirm reports of enhanced responses during working, long-term, and episodic memory processes involving visual or word recognition tasks (Buckner and Wheeler 2001; Wheeler and Buckner 2004; Skinner and Fernandes 2007; Cabeza 2008; Cabeza et al. 2008; Donaldson et al. 2010). Intraparietal sulcal cortex is part of the attention network devoted to voluntary focusing of attention (Corbetta and Shulman 2002; Corbetta et al. 2008). In association with DLPFC, the same intraparietal sulcal cortex facilitates attention to memory (Cabeza et al. 2008; Ciaramelli et al. 2008; Olson and Berryhill 2009; Uncapher and Wagner 2009). We previously noted enhanced activation in IPS cortex in EB and NS when participants had to redirect attention to different frequencies in a vibrotactile frequency working memory task (Burton et al. 2010). However, distinguishing “old” from “new” vibro-tactile rhythms required persistent as opposed to redirection of attention. Participants always focused on vibrotactile rhythms delivered to one fingertip. After initial sensory processing of a rhythm, participants had to retrieve learned patterns. Consequently, these reduced differences between trial-types for ROI in IPS possibly indicate that attention did not shift in the current study.

Posterior precuneus cortex (medial BA7) often shows activation for episodic retrieval (Skinner and Fernandes 2007; Vilberg and Rugg 2008; Donaldson et al. 2010). Functional connectivity with parahippocampal cortex (Vincent et al. 2006) suggests a role for medial BA7 in retrieval. A meta-analysis indicated greater association of responses for retrieval success based on a “familiarity-driven recognition” process (Vilberg and Rugg 2008). A subsequent study, however, found equal response magnitudes for remembered and known target words (e.g., recollection and familiarity functions) (Donaldson et al. 2010). Nevertheless, these reports of activation due to retrieval success are consistent with the current findings in EB of significant late enhanced activation when judging rhythms as old compared to negative responses for identifying new rhythms. However, because NS showed equivalent activation for both trial-types, and responses in EB showed early negativity for both trial-types followed by a very late positive upturn for “old” rhythms, it remains unclear the role this region may fulfill in retrieval success for tactile rhythms.

ROI in frontal cortex

The enhanced responses in orbitofrontal cortex when judging a rhythm as old concur with findings from memory studies of language (Buckner and Koutstaal 1998; Henson et al. 1999; Rugg et al. 1999; McDermott et al. 2000, 2003; Donaldson et al. 2001b; Kahn et al. 2004). Activation patterns in bilateral orbitofrontal ROI (BA47 and 11) were illustrative. On the left, both groups showed late larger responses for Hits; on the right, only NS showed any activation and these positive responses occurred only during stimulation and were not differential for trial-type. In both groups, larger responses for Hits than CRs in orbitofrontal ROI suggest a differential signal associated with “retrieval success”: a suppression following

presentation of a “new” rhythm and less suppression followed by activation for an “old” rhythm. Orbitofrontal cortex shows activation peaks for recollective-based responses to remembered words with agreement across 59% of left hemisphere regions in studies that used Remembered/Know paradigms (Skinner and Fernandes 2007). Consequently, the current finding in both groups of a comparably activated retrieval success response in left orbitofrontal cortex possibly indicates engagement of recollection when judging old rhythms. Early suppression could serve to reduce noise prior to and during recollection of learned patterns.

Activation patterns in bilateral DLPFC differentiated NS and EB with, respectively, positive and negative polarity responses, indicating that the groups differed in utilization of DLPFC when retrieving tactile rhythms. There were no within-group trial-type response differences. The behavioral data indicated that both groups performed the task successfully, suggesting that whatever group differences exist for activation of DLPFC, they did not affect performance.

Some studies suggest that activation differences in dorsolateral prefrontal areas for retrieval success responses depend on the strategy used to solve the task or the difficulty of the task (Schacter et al. 1996; Henson et al. 1999; McDermott et al. 2000; Ranganath et al. 2000; Donaldson et al. 2001a; Roskies et al. 2001; Kahn et al. 2004; Gallo et al. 2006). Ranganath et al. (2000) used pictures of objects and found left anterior prefrontal activation increased with demands to recall specific perceptual information (source vs. old/new). McDermott et al. (2000) presented familiar lures that were conjunctions of words in a learned list. For example, if studied words included “nosebleed” and “skydive”, to identify the lure “nosedive”, participants might adopt a strategy of effortful recall of the studied words. DLPFC showed larger responses for familiar than unfamiliar lures. According to the distinctiveness heuristic of Schacter and co-workers, participants rely more on detailed recollections and less on familiarity when the stimulus contains details such as in a picture of an object coded by visual imagery and verbally (Schacter et al. 1996; Gallo et al. 2006). Remembering pictures may rely on detailed recollections and not recruit prefrontal regions activated by “familiarity”. Tactile rhythms most probably are less “familiar” and instead require a distinctiveness heuristic or effortful conscious process of recollection (Donaldson et al. 2001a; Kahn et al. 2004); these rhythms were not simply recognized as are more familiar words. Possibly more effortful recollection of vibrotactile rhythms might have tilted responses away from a “familiarity” metric and emphasized activation to new rhythms. This effect might explain the larger responses in some ROI when identifying new rhythms.

Conclusions

A main experimental question was the role of visual cortex in tactile memory in the blind. Higher tier visual regions were predominantly active in the blind and deactivated in the sighted. The present study for the first time allowed assessment of retrieval success using non-verbal tactile stimuli and showed that response patterns in visual cortex did not predict retrieval success, replicating the results of word recognition studies of similar design and extending those findings to tactile temporal patterns. Enhanced responses when judging rhythms as old in parts of primary somatosensory cortex in both groups suggested

recapitulation of the learned rhythms in sensory cortex as an aid to recognition memory. Similar enhanced responses in left orbitofrontal cortex in both groups suggested recollective processing in retrieval of learned rhythms.

In parietal and frontal regions, activations in the NS group were in general higher in amplitude than for EB, and in contrast, activations in visual areas were higher in EB. One possible interpretation is that this represents a shift away from reliance on memory resources in these regions and toward visual cortex by EB. However, the added activations did not correlate with better performance when EB recognized old or identified new rhythms. Consequently, we do not know what somatosensory activation of occipital cortex in EB contributes to tactile discriminations. The current study, which used a traditional paradigm that involved learned and new rhythms (e.g., old vs. new), did not support the notion that calcarine sulcal cortex contributes to retrieval success. One possible explanation is processing differences between verbal and non-verbal recognition memory tasks, with the rhythm task especially served by the possible recapitulation of sensory features observed in primary somatosensory cortex. Another explanation is that few tactile rhythms were learned but were complex, requiring processing demands similar to contextual recollection. In studies using word recognition, learned lists commonly contained >50 or more words but are distinctive enough that recognition may rely on familiarity. These different task contingencies may recruit diverse resources when judging whether a presented stimulus was new or old.

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Figure 1.

Example rhythms. Boxed areas represent intervals of stimulation with 50 Hz sinusoidal vibration at 40 mm amplitude, and spaces between the boxes indicate intervals with no stimulation (gaps). Periods of vibration and gaps varied in duration, creating unique vibrotactile rhythms. (A1) Rhythm with a cycle of longer followed by shorter duration vibrations. (A2) Rhythm with cycles of successively shorter vibration durations. (B) Rhythms always ended 2500 ms after the beginning of the first TR frame. Appropriate delays were added before starting any rhythm whose total time was less than 2500 ms to align all rhythms to end at 2500 ms.

Figure 2.

Statistical parameter maps of ANOVA results that show the z-score probabilities of computed F -ratios for specified model factors. (A) The time factor ANOVA maps show regions of significant activation across the brain for NS (A1) and EB (A2) as a function of time during a trial. (B) The time-by-group ANOVA maps show regions where BOLD responses significantly differed between the EB and NS groups. Black dots and circles mark foci identified from the time-by-group ANOVA. Time-course data were extracted per participant from spherical regions (8 mm diameter) centered on these foci. (C) The trial-type-by-time ANOVA maps from combined EB and NS group data show regions where BOLD responses significantly differed between the CR and Hit trial-types. Green circles indicate foci for time-course extractions. Numbered foci correspond to panels in Figures 3 and 4 and list of ROI in Table II. ANOVA z-score results registered to the average fiducial surface of PALS-B12 CARET atlas and displayed on partially inflated cortical hemispheres.

Figure 3.

BOLD response magnitudes per time point (TR frame) in selected regions of interest (ROI). Each time-course point shows the mean and standard error of the mean for a group and trial-type. (1–10) ROI in Occipital cortex. (11–18) ROI in Parietal cortex. Inserted *p*-values in each panel are the ANOVA F-ratio probabilities for the contrast between trial-types within a group (early blind, EB and sighted, NS).

Figure 4.

BOLD response magnitudes per time point (TR frame) in selected regions of interest (ROI). Each time-course point shows the mean and standard error of the mean for a group and trial-type. (19–26) ROI in Frontal cortex. Inserted p -values in each panel are the ANOVA F -ratio probabilities for the contrast between trial-types within a group (early blind, EB and sighted, NS).

Table I

Participant demographics.

ID #	Age ^a	Sex	% R hand ^b	Reading hand	WPM ^c	Onset age	Light sense	Cause ^d
EB1	59	F	100	Both	145	0	None	ROP
EB2	57	M	100	Left	152	0	None	ROP
EB6	33	M	63	Both	76	0	Some	RF
EB11	32	M	95	Left	59	0	Some	LCA
EB16	53	F	90	Both	186	0	None	RF
EB18	55	M	72	Both	NA	0	Some	RF
EB20	27	F	100	Both	>120	<1	Some	ROP
EB21	32	F	100	Left	104	0	None	RB
EB22	34	F	100	Right	~75	0	None	LCA
EB23	22	M	100	Right	>120	0	None	ROP
EB24	20	F	100	Left	>120	0	None	ROP
Avg	38.6		92.7					
SEM(±)	4.4		3.9					
NS1	45	M	92					
NS2	27	M	92					
NS3	30	M	92					
NS4	37	M	92					
NS5	23	M	100					
NS6	30	F	83					
NS7	22	F	83					
NS8	57	F	100					
NS9	28	F	92					
NS10	27	F						
NS11	50	F	83					
Avg	34.2		90.8					
SEM(±)	3.5		2.0					

^a *t*-test of group age difference had a *p*-value of 0.45.^b Percent right-handedness based on a modified Edinburgh handedness inventory.^c Words per minute (WPM) reading a fixed length (~350 words) Braille text.^d Cause of blindness: retinopathy of prematurity, ROP; retrolental fibroplasias, RF; Leber's congenital amaurosis, LCA; retinoblastoma, RB.

Table II

Group differences per ROI for each of the trial-types.

Cortex	ROI		CR trials		Hit trials	
			<i>F</i> -value	Pr> <i>F</i>	<i>F</i> -value	Pr> <i>F</i>
Occipital	1 V1v	-7, -63, 3	3.72	NS	3.47	NS
	2 V2v	4, -71, 3	0.17	NS	13.48	0.0003
	3 VP	-21, -74, -12	16.22	<0.0001	1.23	NS
	4 V3A	17, -87, 35	51.29	<0.0001	38.55	<0.0001
	5 V7	-13, -85, 33	37.17	<0.0001	39.77	<0.0001
	6 V8	26, -61, -11	35.14	<0.0001	45.25	<0.0001
	7 LOC	-27, -90, 5	59.78	<0.0001	10.97	0.001
	8 MT	44, -68, 6	60.52	<0.0001	33.2	<0.0001
	9 BA19 (non-V)	-17, -74, 18	0.37	NS	22.9	<0.0001
	10 BA19 (non-V)	30, -78, 24	41.65	<0.0001	48.39	<0.0001
Parietal	11 BA2	-45, -33, 51	3.12	NS	29.17	<0.0001
	12 BA1	40, -27, 63	0.87	NS	6.31	NS
	13 BA7 (pIPS)	-40, -54, 42	16.28	<0.0001	23.84	<0.0001
	14 BA7 (aIPS)	39, -39, 41	7.66	0.006	13.04	0.0003
	15 BA7-med	-6, -69, 38	47.06	<0.0001	4.11	NS
	16 BA40	-58, -47, 25	15.02	0.0001	15.41	0.0001
	17 BA39	-50, -64, 33	0.38	NS	4.47	NS
	18 BA39	43, -68, 39	49.89	<0.0001	11.29	0.0009
Frontal	19 OrF-47r	-38, 48, 2	5.43	NS	0.64	NS
	20 BA11	35, 48, -5	36.54	<0.0001	14.43	0.0002
	21 OrF-G	-33, 13, 5	37.67	<0.0001	12.07	0.0006
	22 BA44	52, 7, 14	8.84	0.003	7.92	0.005
	23 FO	-33, 14, 11	22.2	<0.0001	2.67	NS
	24 FO	30, 13, 15	14.13	0.0002	1.34	NS
	25 BA9 (DLPFC)	-36, 20, 41	17.6	<0.0001	38.47	<0.0001
	26 BA8 (DLPFC)	17, 26, 47	18.93	<0.0001	24.06	<0.0001

Cutoff significance of $p = 0.002$ corrected for multiple comparisons.