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Recognition Memory for Braille or Spoken Words: An fMRI study in Early Blind

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Abstract

We examined cortical activity in early blind during word recognition memory. Nine participants were blind at birth and one by 1.5 yrs. In an event-related design, we studied blood oxygen level-dependent responses to studied (“old”) compared to novel (“new”) words. Presentation mode was in Braille or spoken. Responses were larger for identified “new” words read with Braille in bilateral lower and higher tier visual areas and primary somatosensory cortex. Responses to spoken “new” words were larger in bilateral primary and accessory auditory cortex. Auditory cortex was unresponsive to Braille words and occipital cortex responded to spoken words but not differentially with “old”/“new” recognition. Left dorsolateral prefrontal cortex had larger responses to “old” words only with Braille. Larger occipital cortex responses to “new” Braille words suggested verbal memory based on the mechanism of recollection. A previous report in sighted noted larger responses for “new” words studied in association with pictures that created a distinctiveness heuristic source factor which enhanced recollection during remembering. Prior behavioral studies in early blind noted an exceptional ability to recall words. Utilization of this skill by participants in the current study possibly engendered recollection that augmented remembering “old” words. A larger response when identifying “new” words possibly resulted from exhaustive recollecting the sensory properties of “old” words in modality appropriate sensory cortices. The uniqueness of a memory role for occipital cortex is in its cross-modal responses to coding tactile properties of Braille. The latter possibly reflects a “sensory echo” that aids recollection.

Keywords

occipital cortex; magnetic resonance imaging; blindness; recollection

1. Introduction

Congenital or early blind people notably perform better than sighted on verbal memory tasks. Examples include significantly greater short-term memory for sequential digit-span on

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the verbal section of the Wechsler Intelligence Scale in blind children (Hull and Mason, 1995; Tillman and Bashaw, 1968) or adults (Rokem and Ahissar, 2009) and better recall of rehearsed word lists (Amedi et al., 2003; Azulay et al., 2009) and the serial order of studied word lists (Raz et al., 2007), and >60% word recognition of intensely studied words after a one year delay (Raz et al., 2005).

These verbal memory distinctions in early blind possibly reflect learning strategies with greater utilization of sensory information (Pring, 1988). A possible contributor to sensory processing in blind is cross-modal activation of occipital cortex. Additionally, a verbal memory role for occipital and occipitotemporal cortex in blind was suggested by activation during free recall of aurally presented lists of abstract words learned one week earlier (Amedi et al., 2003; Azulay et al., 2009), significantly greater responses for episodic retrieval when recognizing spoken words from well-practiced compared to barely-practiced lists encoded one year earlier (Raz et al., 2005), and working memory for words (Park et al., 2011). In these block design studies, it was not possible to evaluate whether enhanced activation resulted from retrieval success in recognizing familiar words or from larger responses to new words due to exhaustive recollection of remembered word lists. Consequently, in the absence of a single event design, it is difficult to know whether the proposed verbal memory function for occipital cortex involved the recognition mechanisms of familiarity or recollection of correctly identified studied words (Wheeler and Buckner, 2003). Additionally, episodic memory for Braille encoded word lists has not been studied despite the importance of Braille literacy in the blind (Millar, 1997), evidence of the functional importance of occipital cortex to reading Braille (Cohen et al., 1997; Hamilton et al., 2000; Hamilton and Pascual-Leone, 1998), and vigorous activation of occipital cortex when reading Braille (Burton et al., 2002a; Sadato et al., 1996). Thus, further investigation of verbal memory processes in occipital cortex is needed using a single event-related recognition memory paradigm for words learned through Braille or aurally.

A standard protocol to distinguish recognition and retrieval mechanisms is to note distinct cortical responses to encoded words (“old”) compared to “new” words (Donaldson et al., 2001a; Iidaka et al., 2000; Konishi et al., 2000; McDermott et al., 2003; Roskies et al., 2001; Wheeler and Buckner, 2003). The rationale for the current study in early blind participants was that retrieval monitoring of “old” words might yield different results in occipital compared to findings in modality specific effects in somatosensory and auditory cortex. Because participants were Braille literate, they learned and later identified Braille read words; they also learned and identified spoken words. By using two modes for word presentation in the same individuals, we were able to contrast activation during recognition testing in occipital, somatosensory, and auditory cortex. A finding of response differences for “old”/“new” words only in occipital cortex for both presentation modes might indicate a predominant role for this cortex in verbal memory processes. Additionally, assessment of responses in lower and higher tier visual areas from both hemispheres evaluated the hypothesis posed by Amedi and colleagues that left V1 particularly contributed to verbal recall processes (Amedi et al., 2003; Amedi et al., 2010; Raz et al., 2005).

The outcomes of word recognition testing can lead to differing interpretations of a verbal memory role for occipital cortex in blind individuals. Prior word recognition studies in sighted reported larger responses with successful retrieval of “old” words in several prefrontal and posterior parietal cortex regions, a finding interpreted as indicating retrieval success from greater familiarity with studied words (Buckner et al., 1996; Buckner and Wheeler, 2001; Donaldson et al., 2001b; Gold and Buckner, 2002; Henson et al., 1999; Konishi et al., 2000; McDermott et al., 2000; Wheeler et al., 2000; Wheeler and Buckner, 2003). Similar response differences for judging “old”/“new” words in occipital cortex of early blind might suggest a verbal memory role based on degree of familiarity. The

alternative outcome of larger responses for “new” compared to “old” words might indicate a role for recollection in remembering words (Gallo, 2004). Better recollections with more explicit remembering occurred in sighted when they studied words in association with pictures (Gallo et al., 2004; Gallo et al., 2006). Bigger responses to novel words suggested demanding rehearsal of remembered words before correctly rejecting a current word as “old.” Blind might utilize richer recollections of learned items as an alternative diagnostic monitoring process that results in larger responses to “new” words.

Several findings in the blind predicted that remembering through richer recollections might be more prevalent with Braille. Thus, there is evidence of better text comprehension with Braille in college educated students (García, 2004), greater short term retention of a series of Braille consonants despite concurrent articulatory interference (Cohen et al., 2010), and superior working memory performance for raised tactile letters (Bliss et al., 2004). Other data suggest blind might have richer recollections for spoken words. Thus, early blind were better at discriminating speech in noise (Hugdahl et al., 2004; Muchnik et al., 1991; Rokem and Ahissar, 2009), had exceptional recall of spoken words (Raz et al., 2005; Raz et al., 2007), and showed greater activation of a generic voice region in the superior temporal sulcus as opposed to medial occipital cortex (Gougoux et al., 2009). Consequently, better recollections of spoken words might similarly aid remembering “old” words and lead to larger responses for “new” words in auditory cortex and, through cross-modal activation, in occipital cortex.

2. Results

2.1 Behavioral data

Performance was close to ceiling for both presentation modes, because accuracy was greater than 94% correct recognition of “old” words with no forgetting (0 trials with Misses). Nevertheless, recognition accuracy was significantly superior with Braille (Braille Hits = $.98 \pm .01$ vs. listening Hits = $.94 \pm .02$, paired $t[39] = 2.5$, $p = .018$, two-tailed). Correct rejection of “new” words and rare false alarms (FAs) was nearly identical for both presentation modes (Braille CRs = $.99 \pm .01$ vs. listening CRs = $.96 \pm .01$, paired $t[39] = 0.33$, $p = .75$, two-tailed). These performance data indicated equivalent accuracy with both presentation modes despite the slightly higher accuracy in recognizing “old” words with Braille. The latter possibly reflected some interference by scanner noise in hearing all spoken words.

As expected from differences in stimulation durations for Braille and spoken words, reaction times were 4-5 times longer when reading words in Braille (Braille: CRs = $4382\text{ms} \pm 108$ and Hits = 3644 ± 92 ; spoken: CRs = $867\text{ms} \pm 46$ and Hits = 889 ± 53). RTs also were significantly slower for “new” words with Braille (paired $t[194] = 5.7$, $p < .0001$, two-tailed), but not for spoken words (paired $t[188] = 0.07$, $p = 0.95$, two-tailed).

2.2 ANOVA Maps

A whole brain ANOVA map for the time factor showed significant activation in occipital, parietal, superior temporal and frontal cortex (Figure 1). The distribution of affected medial and lateral occipital cortex was widespread, extended well-past calcarine/primary visual cortex, and was relatively similar between the hemispheres. The significant activation in the superior temporal gyrus bilaterally involved primary and surrounding auditory cortex (Figure 1). Similarly, significant activation involved somatosensory cortices bilaterally surrounding the mid-pericentral parietal and posterior intraparietal sulcal cortex. Dorsolateral prefrontal and medial superior frontal /cingulate cortex also contained patches of significant activity. The following sections present the statistical analysis of response time courses extracted from selected ROI in occipital, superior temporal, parietal, and

dorsolateral prefrontal cortex. The analysis assessed whether response differences to Hit and CR event-types (e.g., recognizing old vs. identifying new words) contributed to significant activation found in the ANOVA time factor map.

2.3 Time course analyses in sensory cortices

Both modes evoked BOLD responses that rose to a peak magnitude mostly centered at TR 4. The ANOVA and post hoc Tukey t-tests analyzed the contrast in response magnitudes to “old” vs. “new” Braille words from time points 4-6 because reaction times indicated slower word reading with the somatosensory presentation mode. The analysis assessed responses during time points 3-5 for the auditory mode because the reaction times suggested that lexical processing occurred earlier for spoken words.

Both presentation modes evoked positive BOLD responses in ROI that in sighted would be within lower and higher tier visuotopic areas, confirming prior reports of bilateral cross-modal sensitivity to tactile and auditory stimulation in occipital cortex of early blind. Occipital ROI showed larger magnitude responses during Braille reading of correctly identified “new” words compared to recognized “old” words. All but the responses from ROI in the superior occipital gyrus (V3+V3A) showed “old”/“new” response differences that were significant with a Bonferroni correction (Table 3). For spoken words, these same occipital ROI showed overlapping BOLD response amplitudes for “old”/“new” words. Figure 2 illustrates example BOLD responses from lower tier calcarine sulcal cortex (V1) and several upper tier regions located within the lateral occipital gyrus (LOC), superior occipital gyrus and transverse occipital sulcus (V3+V3A), and dorsal extensions of the posterior inferior temporal sulcus (hMT+).

Similar cross-modal sensitivity arose in anteriorly located ventral visual areas that in sighted have less distinctive or absent visuotopic representations. Larger responses occurred for “new” words for both presentation modes in these regions. Figure 2 shows example responses from ROIs in the right posterior fusiform gyrus within V8 and adjoining BA37 located ~1cm further anterior. The response differences for “old”/“new” words were significant for both presentation modes (Table 3).

Primary somatosensory cortex and intraparietal sulcal cortex showed robust positive BOLD responses during recognition trials for words input through Braille. Parietal cortex ROI showed larger magnitude responses during Braille reading of correctly identified “new” words compared to recognized “old” words. All but the “old”/“new” response differences in the left anterior postcentral gyrus (BA3) passed the Bonferroni corrected significance threshold (Table 3). Most participants read Braille with the left hand and pressed the choice button with right (Table 1). But some were the reverse, so Braille reading was mixed left-right stimulation/response, and hearing was bilateral stimulation with button press with the same hand as for Braille. For spoken words, responses overlapped for “old”/“new” words, generally were smaller than those evoked during Braille, and were not significantly different (Table 3). Figure 3 shows examples from bilateral anterior postcentral gyrus (BA3), posterior postcentral gyrus (BA2), and intraparietal sulcal cortex (BA7).

In auditory cortex, spoken “new” words evoked significantly larger amplitude BOLD responses than recognized “old” words (Figure 3). In contrast, there was little activation during Braille reading (Figure 3). Most auditory cortex ROI showed significant “old”/“new” response differences (Table 3). In the left primary auditory cortex located within Heschl's gyrus, the larger responses to “new” words were not sufficiently different to overcome the response variance to both word types.

2.4 Time course analyses in frontal cortex

Words presented with both modes evoked responses in the left dorsolateral prefrontal cortex. The response time course shown for Braille read words from the ROI in BA46 was significantly larger and sustained past TR6 for “old” compared to “new” words (Figure 3), leading to a significant difference (Table 3). Spoken words evoked slight positive responses that completely overlapped for “old”/“new” words (Figure 3).

3. Discussion

3.1 Occipital cortex

All studied occipital cortex ROI showed larger BOLD responses to identified novel words compared to recognizing studied words. Based on the anatomical locations shown in Figures 2 and 3 and referencing these to the registration of human visual areas in the PALS B12 atlas (Van Essen, 2005), the defined occipital ROI were within the borders of lower and higher tier visuotopic regions previously defined in sighted (Grill-Spector and Malach, 2004) and in visually responsive right ventral regions in the fusiform gyrus (Büchel et al., 1998). Widespread and bilateral parts of occipital cortex showed response differences for “old”/“new” Braille words. These findings did not confirm earlier reports that verbal memory processes for aurally studied and recalled words lead to greater activation of left occipital, and especially calcarine sulcal cortex (V1) (Amedi et al., 2003; Azulay et al., 2009; Raz et al., 2005). In the current study, occipital cortex showed response distinctions between “old” and “new” words only during Braille reading and not for spoken words. These differences were not due to performance because accuracy was comparable with both presentation modes. Positive BOLD responses for spoken words confirmed prior evidence of cross-model sensitivity of occipital cortex in various language (Amedi et al., 2003; Büchel et al., 1998; Burton et al., 2002b; Burton et al., 2003) and auditory stimulation tasks (Arno et al., 2001; Gougoux et al., 2004; Gougoux et al., 2005; Kujala et al., 1995; Leclerc et al., 2000; Röder et al., 1996; Röder et al., 2001; Weeks et al., 2000). Response distinctions in occipital cortex for judging “old”/“new” words only with Braille suggest, however, that this cortex might serve as a repository for the tactile features needed to remember studied words.

The absence of “old”/“new” response distinctions in occipital cortex for spoken words was unexpected for several reasons. First, several studies in early blind revealed distinguishable occipital cortex activation to auditory features that involved varied spectral (Gougoux et al., 2009), spatial (Weeks et al., 2000), learned spatial/spectral associations (Arno et al., 2001), and temporal (Kujala et al., 2005) parameters. Furthermore, learning Braille entangles spoken phonological and Braille orthographic word forms with supramodal lexical semantics (Millar, 1997). Consequently, we anticipated that activation of occipital cortex by spoken words would include phonological differences between “old” and “new” words. However, the balanced lexical characteristics of all word lists probably prevented any frank phonological differences between “old”/“new” words.

Prior studies hypothesized a verbal memory role for spoken words in occipital and occipitotemporal cortex in blind based on significant activation during free recall of aurally presented lists of abstract words intensely studied and memorized one week earlier (Amedi et al., 2003; Azulay et al., 2009) and by significantly greater responses across multiple subdivisions of occipital cortex when the same blind individuals recognized spoken abstract words learned one year ago with intense compared to barely-practiced list of nouns presented once incidental to generating a verb (Raz et al., 2005). In the study by Raz and colleagues (Raz et al., 2005), target “old” words contrasted with novel words in each task block. For the intensely studied abstract words, above chance recall accuracy suggested

vivid remembering and consequent easy rejection of novel words. For the barely studied nouns, separating studied from novel words was at chance levels, indicating a struggle to distinguish between old and new words. However, different factors possibly underlay the contrasting results from recognizing words from the two lists. In relationship to episodic memory, larger responses for intensely studied words might reflect greater retrieval success because these words were more familiar than the novel words during the task block. Alternatively, larger responses might have resulted when rejecting a new word as old because of exhaustive recollection of “old” words. Smaller responses for attempting to recognize words heard just once might indicate a low incidence of retrieval success or remembering as reflected by chance performance accuracy. There was no way to distinguish between these mechanisms of familiarity or recollection in contrasting the BOLD responses from the task blocks.

The ambiguity in distinguishing the underlying mechanisms responsible for the BOLD response magnitudes to heard words in the two task blocks of these earlier studies, however, also raises the possibility of a non-memory basis for these results from Raz and colleagues (Raz et al., 2005). For example, the demands exerted when attending to the words in the different lists possibly varied; greater pop-out effects might have resulted in greater activation when recognizing well-known words and less when subjects realized there was no way to distinguish between novel and words only incidentally processed. Thus, activation might have arisen when early blind selectively attended during the recall task as they sorted through word lists. Several studies found that attention demanding tasks potently activated occipital cortex in the blind (Collignon et al., 2006; Garg et al., 2007; Hötting and Röder, 2004; Hötting and Röder, 2009; Liotti et al., 1998; Park et al., 2011; Stevens et al., 2007; Weaver and Stevens, 2007). Raz and colleagues argued attention was equivalent because reaction times for both word recognition tasks were comparable and slower than for a phonological task. But longer reaction times might only reflect the semantic demands during any word identifications for purposes of recognition whereas phonological detections were less demanding.

3.2 Factors of familiarity and recollection

The design of the current study avoided some of the concerns discussed above regarding evidence for a verbal memory role in occipital cortex. The following analysis is also sufficiently general that it includes findings in somatosensory and auditory cortex. Thus, somatosensory cortex showed larger BOLD amplitudes for judging Braille read words as “new,” but no cross-modal activation for spoken words. Auditory cortex showed significantly larger BOLD amplitudes only for judging spoken but not Braille words as “new.” Occipital cortex might then be viewed as exceptional in early blind solely from greater cross-modal sensitivity possibly arising from deafferentation induced plasticity (Bavelier and Neville, 2002).

We used a vetted recognition memory paradigm to assess the hypothesis that occipital cortex in the blind contributes to episodic trace memory for studied words. The current study involved direct contrasts, within a single event- protocol, between recognition of randomly intermixed studied and novel words (Donaldson et al., 2001a; Iidaka et al., 2000; Konishi et al., 2000; McDermott et al., 2003; Roskies et al., 2001; Wheeler and Buckner, 2003). Greater activation for judging a word as previously studied (“old”) would suggest memory processes based on a word familiarity factor (Buckner et al., 1996; Buckner and Wheeler, 2001; Donaldson et al., 2001b; Gold and Buckner, 2002; Henson et al., 1999; Konishi et al., 2000; McDermott et al., 2000; Wheeler et al., 2000; Wheeler and Buckner, 2003). Previously, sighted participants used source monitoring of recollected information to recognize whether a test word was present during encoding. In this “recall-to-reject” process, familiarity served to disqualify whether a test word had occurred, i.e., was “old”

(Gallo, 2004; Gallo et al., 2006). Larger amplitude BOLD responses for recognized studied words suggested that greater familiarity with “old” words precipitated larger responses. The results obtained in left dorsolateral prefrontal cortex of early blind were consistent with these earlier findings in suggesting a recognition mechanism based on word familiarity. These findings also confirmed the current task as one that examined episodic memory but only for studied Braille words. The responses for spoken words in DLPFC had greater variability, which possibly explains the absence of comparable significant effects for the auditory presentation mode.

Instead, ROI in all sensory cortexes had larger response amplitudes for novel words, indicating that a mechanism based on familiarity was not a feature. Alternatively, a mechanism based on recollection explains prior findings in sighted (Gallo, 2004; Gallo et al., 2004; Gallo et al., 2006; Gallo et al., 2010). Remembering in these studies improved when studied words occurred in association with a coincident corresponding picture, leading to diminished activation for judged “old” words (Gallo et al., 2006). In sighted, the associated information during learning served as a “distinctiveness heuristic” (Schacter et al., 1996), i.e., memory of a picture learned in association with the studied word. Picture memories served as sources in diagnostic monitoring of presented words and aided remembering during recognition trials (Gallo et al., 2006). The hypothesis was that recollection improved because during encoding, participants viewed words together with a picture of the named item (Gallo, 2004; Gallo et al., 2004; Gallo et al., 2010). Consequently, during testing for recognition of studied words, required resources for attention to memory declined compared to demands when deciding whether a novel word associated with some linking information (e.g., a picture).

In blind, recollection of studied words might be the source factor for a “distinctiveness heuristic” that enabled detailed remembering of learned words. Prior behavioral findings in blind are consistent with the hypothesis that blind might have used a heuristic based on better recollections. For example, early blind remarkably recall more learned words (Raz et al., 2005; Raz et al., 2007) even with articulatory interference during encoding (Cohen et al., 2010). Because blind lack visual guidance even for the most rudimentary tasks, they depend on a compensatory attention strategy (Hötting and Röder, 2004) that fosters recollections of nearly every aspect of their lives. Consequently, our blind participants similarly might have had exceptional recollection of studied words that possibly provided an associative heuristic. (Several blind participants recalled nearly all presented words after a scan, especially when they noted whether they had made an error in judging a particular word as “old”/“new”.) Less dependence on familiarity and greater reliance on remembering based on recollections possibly accounted for larger response amplitudes to novel words comparable to findings in sighted where better remembering occurred for words associated with pictures (Gallo et al., 2006).

Evaluation of a test word might then be against the features of a distinct, expected association (“i.e., trying to recall whether the item had been studied...” (Gallo et al., 2006)). Greater recollection of expected words leads to lower probabilities of false recognitions (Gallo, 2004) and possibly larger amplitude BOLD responses for judging a word as “new.” Falsely judging a “new” word as “old” was rare and the present study found no instances of missed “old” words, possibly resulting from monitoring recollections as opposed to familiarity. A correct rejection of a “new” word as “old” might then reflect a strategy “based on the absence of expected recollections” (p.489) (Gallo, 2004). In contrast, a correct rejection of a “new” word based on familiarity might then involve a recall-to-reject process.

Recollecting studied words when presented with a “new” word might engage more exacting conscious remembering (Donaldson et al., 2001a; Kahn et al., 2004) in reaching a decision

than rejecting a word as “old.” In this context, effortful recollection emphasized remembering and a consequent enhanced activation to “new” words because of an exhaustive source review before reaching a decision. Remembered words would be more accessible and consequently elicit smaller responses during recognition.

3.3 Sensory echo

Similar findings in three different sensory cortices resembled prior descriptions of specific re-activation of encoded information for stimulus sensory characteristics (Buckner and Wheeler, 2001; Wheeler et al., 2000). This sensory memory feature, labeled “sensory echo,” possibly provided the appropriate basis for recollecting studied words with the responses predictably echoed in the appropriate sensory cortex for words learned with a particular presentation mode. Remembered features of studied words might require less processing and hence the observed smaller responses to studied words. In comparison, larger responses arose for novel words because the features of new words required greater attention. Superior memory in blind might then reflect greater dependence on learned sensory features (Pring, 1988; Rokem and Ahissar, 2009). However, improved perceptual processing probably relies on a behavioral cognitive compensation strategy of previously reported enhanced selective attention to non-visual inputs in early blind (Hötting and Röder, 2004).

An unresolved issue is whether a memory model for occipital cortex based on recollected sensory features of studied words can include prior notions of a role in verbal memory (Amedi et al., 2003; Raz et al., 2005). The two models are at odds especially because we found no evidence of response differences to “old”/“new” spoken words; and the prior studies exclusively involved study and recognition of heard words. However, as noted above, contrasting the two models is not appropriate given the design differences (e.g., block vs. single event) that make it difficult to know the precise responses to studied compared to novel words in the block design experiments. However, the generic modality specific response commonalities noted across sensory areas in the current study suggest that a similar result would be noted in occipital and auditory cortex of the blind with intensely studied spoken words, especially if evaluated using a single event design to assess responses to “old” and novel words. In the latter context, the reorganization of occipital cortex imposed by blindness might be to broaden cross-modal responsiveness rather than in assuming higher level cognitive verbal processing, functions retained in early and late blind in the same frontal and parietal language areas found in sighted (Burton et al., 2002a; Burton et al., 2002b; Burton et al., 2003).

3.4 Summary and conclusion

We used recognition of studied compared to identifying novel words in early blind to assess a role for occipital cortex in episodic memory for learned words. Additionally, modality specific effects of Braille read and spoken words examined cross-modal activity in occipital cortex. Specifically considered were the factors of word familiarity and recollection in recognition memory for words judged as “old” vs. “new.” Identifying “new” words in Braille evoked larger BOLD response amplitudes in occipital and somatosensory cortex and for spoken words in auditory cortex. The role of occipital cortex was unique only due to cross-modal responses that only distinguished between “old” vs. “new” Braille words.

Prior studies in sighted reported larger responses for identified novel words when a distinctiveness heuristic for diagnostic source monitoring, such as associated pictures, enhanced remembering and shifted dependence to recollection (Gallo et al., 2010). A possible distinctiveness heuristic in blind might be a demonstrated exceptional ability to remember learned words. Consequently, larger BOLD responses when identifying “new” words possibly reflected exhaustive word recollection in contrast to smaller amplitudes for a

remembered word requiring less attention to perceptual processing. Similar affects in occipital, somatosensory, and auditory cortex suggested blind particularly attended the sensory features of non-visual inputs of Braille read or spoken words. The results suggested that all sensory cortices provided a repository of the perceptual features of learned words.

4. Experimental procedures

4.1 Participants

Ten early blind individuals (4 female; mean age = 41.6 years, SEM $\pm$ 4.5, range 21-60) provided informed consent in compliance with guidelines stipulated by the Human Studies Committee of Washington University and the Code of Ethics of the World Medical Association (Declaration of Helsinki). All participants self-reported no additional neurological conditions, head trauma, current use of psychoactive drugs, or contraindications for magnetic resonance imaging.

Total blindness at birth in 9 and by 1.5 yrs in one individual was due to binocular peripheral disease that arose from retinopathy of prematurity (8 individuals), Leber's congenital amaurosis, or retinoblastoma (Table 1). Six had absolutely no vision. The four with light sensitivity had no pattern perception. The individual functional activation patterns in occipital cortex were identical to those with no light sensitivity. We showed comparable functional activation of occipital cortex in prior studies involving some of the same individuals included in the current study. For example, EB11, who had some light sensitivity, showed the same occipital activity as EB1, who had no light sensitivity, when the Braille reading finger was stimulated with an embossed tactile surface (Burton et al., 2006). Similarly, EB6, who also had some light sensitivity, showed similar occipital activity as EB1 and EB2 when these individuals performed a verb generate task after reading nouns in Braille (Burton et al., 2002a). In the current study, all functional imaging runs occurred in total darkness and with blindfolds in place for all participants. All participants became Braille literate during childhood. Reading fluency was moderate to fast (Table 1) with a single word in Braille II read in 2-3 seconds.

4.2 Design and procedure

4.2.1 Word presentation—A scan session involved separate runs with encoding trials preceding a recognition testing run. A ~2 minute delay separated runs for encoding and recognition testing. The present report describes findings obtained during recognition testing. Participants read words in Braille or heard spoken words in separate pairs of runs for each presentation mode. Some participants completed all eight runs and both presentation modes in one session. Most participants needed a separate imaging session for each presentation mode.

During encoding, participants learned a list of 20 words by determining whether a presented word embodied an abstract or concrete concept. The list contained 10 abstract and 10 concrete words. During recognition, participants judged whether a word had been studied ("old") or was identified as novel ("new"). The list for recognition testing contained 10 previously studied and 10 novel words. Although concreteness was not tested during recognition, the list contained an equal number of abstract and concrete words. A different pseudo-randomization applied to the lists for encoding and recognition testing. Additionally, no more than 2 consecutive words had the same degree of concreteness. During recognition testing no more than 2 consecutive words were "old" or "new." Pressing one of two response keys on an MRI compatible fiber optic response pad signaled judgments of "old"/"new" words during recognition testing.

Words were from 180 words subdivided into nine 20 word length lists. Words in 6 of the 9 lists were encoded. Words in the remaining three lists were the source of “new” words during recognition testing. Each presentation mode used different counterbalanced word lists. Words across a list had lexical factors controlled for significant differences along a concrete vs. abstract continuum (Table 2). There were no significant differences between words in any presented list based on the criteria of word length, Kucera-Francis word frequency, familiarity, or concreteness.

4.2.2 Spoken words—Spoken words were digital renditions of a female speaking each word. We eliminated extraneous noise, equalized sound intensities between words, matched word onsets, and modulated the sound waves where necessary to clarify pronunciations using SoundForge software (version 7.0, Sony Pictures Digital Inc). Word presentation was binaural. For button responses, participants used the same hand as for the Braille mode.

4.2.3 Braille words—A Juliet Pro 60 embosser and Duxberry Braille Translator software embossed words in Braille II across connected fan-folded standard Braille paper. The array was a continuous column of one word per line with equal vertical spaces between lines. A locally constructed device (Burton et al., 2002a) with manual scrolling placed successive words into a window accessible to the preferred reading hand during scans. Seven participants read Braille words with the left hand and three used the right hand. Participants made button responses with the other hand.

4.2.4 Word presentation timing—Word presentation timing differed between modes because spoken words generally unfold within less than 1s whereas reading a word in Braille takes ~2-3s. In an attempt to accommodate differences in stimulus duration and the psycholinguistics of word processing, word presentation was relative to two sequential TR intervals. Only the operator who advanced the Braille paper heard two sequential chimes that signaled when to move the paper so that Braille word presentation synchronized with scan times. The first of two chimes occurred at the beginning of an EPI frame and signaled to start scrolling. Moving a word into the reading window took less than 1s; a second chime occurred at the beginning of the next frame indicating when scrolling had to be completed. Participants began reading immediately when the paper stopped moving, which was during the second half of the first TR. Thus, Braille word reading started within the first frame and generally ended during the second frame, extending across 2-3 seconds. Timing for spoken words was delayed one frame and presentation occurred within the next frame. The strategy of synchronizing word presentation offsets within the second TR interval for both modes could not completely correct for differences between presentation modes with respect to timing of word recognition, subsequent lexical processing, and somatosensory or auditory stimulation. Consequently, all analyses assessed BOLD time course differences for recognition response types within a presentation mode.

4.3 fMRI

4.3.1 Image acquisition—We acquired images with a Siemens 3 Tesla TRIO scanner (Erlangen, Germany) and a twelve-element RF head matrix coil. MRI headphones dampened scanner noise and a vacuum cushion stabilized the head. All functional imaging was with the scanner room dimmed and with blind folds on all participants.

A gradient recalled echo-planar sequence (EPI, Repetition time [TR]=2200ms, echo time [TE]=27ms, flip angle=90°) captured blood oxygenation level-dependent (BOLD) contrast responses across 36 contiguous, 4 mm axial slices, with 4X4 in-plane resolution. Interleaved odd and even numbered slices paralleled the anterior-posterior commissure plane.

Structural images included a magnetization prepared rapid gradient echo (MP-RAGE) T1-weighted sequence acquired across 176 sagittal slices (TR=2100ms; TE=3.93ms; flip angle=7°; inversion time [TI]=1000ms; $1 \times 1 \times 1.25$ mm voxels.). An additional T2-weighted structural image obtained across 36 axial slices was in register with the EPI (TR=8430ms, TE=98ms, $1.33 \times 1.33 \times 3$ mm voxels). The T2 images aided registration of the EPI to the sagittal MP-RAGE images after computing 12 parameter affine transforms between an average from the first frames of each EPI run (Ojemann et al., 1997).

4.3.2 Image processing—Locally available UNIX software scripts provided standard preprocessing of the EPI images that corrected for differences in slice acquisition times by sinc interpolation so that all slices aligned to the start of the first volume after correcting for head movements within and across slices. The effect of global differences in signal intensity was removed by normalization of each scan relative to the global mode of all scans set to 1000. A single algorithmic step resampled slices into 2mm^3 volumes and registered them to a Talairach atlas template (Talairach and Tournoux, 1988). The representative atlas template was created using MP-RAGE structural images combined from early blind individuals whose age and gender matched those in the study sample; the template conformed to Talairach atlas space (Talairach and Tournoux, 1988) based on spatial normalization methods (Lancaster et al., 1995).

4.4 Statistical analyses

4.4.1 GLM—Data analysis software available from the NeuroImaging Laboratory of Washington University (<http://www.nil.wustl.edu/labs/fidl/index.html>) provided for the GLM and whole brain ANOVA analyses. THE WU software was comparable to that available through SPM or FSL.

Each run had 142 frames (TRs) including words in 126 frames for 20 trials with words. Trials with words occurred within events whose durations varied between 5 and 9 TRs with the incidence of different intervals adjusted to create a negative exponential frequency distribution (e.g., event durations of 5, 6, 7, 8, and 9 TRs repeated 15, 8, 4, 2, and 1 times, respectively). The sequence of different event durations was pseudo-random with no duration successively repeated >2 times. The overlap of event durations was entered into the design matrix with an assumed average duration of 7 TRs (15.4s) that spanned overlap of jittered intervals (Miezin et al., 2000; Ollinger et al., 2001). The first 6 and last 10 frames contained no words. Dummy frames built into the start of Siemens EPI sequence software and one excluded initial frame allowed for magnetic equalization. MR signals present during the next five and last 10 frames furnished images of baseline activity.

A Gaussian filter, with a full-width-at-half maximum of 4mm, smoothed the atlas realigned, 2mm^3 volumes (voxels) before the general linear model analysis (GLM). In every participant and for each run, the GLM estimated MR signal per voxel for each event. A separate GLM was computed per run and presentation mode. Each GLM included regressors for seven time points for four different event-types: Hits for correctly recognizing “old” words, correct rejections (CRs) for identifying “new” words, misses (MISS) for failing to recognize an “old” word, and false alarms (FAs) for falsely identifying a “new” word as “old.” Additional regressors modeled baseline, linear trend, and low frequency components (<.014Hz). Signal magnitude per voxel was an estimate at each time point over the time-course for an event.

4.4.2 Whole brain ANOVA—An initial analysis used a whole brain ANOVA in which the random effect was subject variance and the repeated measure was the two runs per presentation mode. The dependent variable was the time course of MR signal per voxel in

each participant. The ANOVA had within group fixed factors of time (7 time points) and event-type (CR and Hit)¹, between factor of presentation mode (Braille and Listening), and all interactions between factors. The software corrected the ANOVA for non-independence of time points by adjusting the degrees of freedom (e.g., sphericity correction). Additionally, a correction for multiple comparisons used a joint z-score/cluster size threshold of $z=3.5$ and cluster size of 24 face-contiguous voxels for a minimum $p=0.05$ in a Monte Carlo simulated distribution (Forman et al., 1995). The brain map for the time factor revealed significant BOLD signals for any activation irrespective of presentation mode or event-types.

4.4.3 Region of interest time course analysis—Two other whole brain ANOVAs examined for the effects of the event-types for data from each presentation mode. The fixed factor of time in this analysis showed brain areas with any significant activity differences between CR and Hit events. A z-score peak finding algorithm detected loci in the time factor results for each performance mode. These loci had a minimum cluster threshold of $z=3.5$ and were no closer than 10mm (Kerr et al., 2004). The coordinates of identified peak loci formed the centers of spherical regions-of-interest (ROIs) with 4 mm radii. Next, we extracted time courses, averaged over all voxels in a ROI, per participant, event-type, and presentation mode.

There were ~40 time courses available for “old”/“new” event-type effects across the two runs per presentation mode. Regional ANOVAs, in which the random effect was subject variance, assessed these time courses separately from each presentation mode because stimulation times did not match (PROC GLM, Statistical Analysis System version 9.1, SAS Institute, Carey, NC). The dependent variable was BOLD signal magnitudes per time points of the BOLD response after subtracting the value of TP1 from each time point, which anchored responses relative to the beginning of events. Cited significant response differences between the event-types met a Bonferroni corrected strict criterion for number of studied ROI.

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¹There were too few incorrect categorizations to include Misses and FAs in the analysis

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Research Highlights

An fMRI recognition memory study in early blind to Braille read or spoken words
Occipital and somatosensory cortex had larger responses to new vs. old Braille words
Auditory cortex had larger responses to new vs. old spoken words
Exceptional recollection in blind might explain larger responses to new words

Figure 1.

Statistical parameter maps of ANOVA results registered to the average fiducial surface of PALS-B12 CARET atlas and displayed on partially inflated cortical hemispheres. The whole brain ANOVA for the time factor revealed significant BOLD signals for any activation irrespective of presentation mode or event-types. The ANOVA included a random effect from subject variance and a repeated measure based on two runs per presentation mode. There was a correction for multiple comparisons using a joint z-score/cluster size threshold of $z=3.5$ and cluster size of 24 face-contiguous voxels for a minimum $p=0.05$ in a Monte Carlo simulated distribution. Additionally, there was a correction for non-independence of time points by adjusting the degrees of freedom (e.g., sphericity correction). The dependent variable was the time course of percent change in MR signal per voxel in each participant. The ANOVA had within group fixed factors of time (7 time points) and event-type (CR and Hit), between factor of presentation mode (Braille and Listening), and all interactions between factors.

Figure 2.

Response time courses by regions of interest (ROI) in occipital and inferior temporal cortex. Brain slices to the right of each plot show the ROI location and corresponding atlas coordinates. Table 3 lists the statistical analysis of the response contrasts for each presentation mode for these ROI (rows 1-9 and 20 in Table 3). Event-type labeled CR was for trials with correct rejection of a novel word as “old” (i.e., “new”); Hit was for trials with correct recognition of a studied word (“old”). Each time point is the mean and standard error of the mean (N=10) for an event-type with a presentation mode of Braille or spoken words.

Figure 3. Response time courses by regions of interest (ROI) in parietal and superior temporal cortex. Brain slices to the right of each plot show the ROI location and corresponding atlas coordinates. Table 3 lists the statistical analysis of the response contrasts for each presentation mode for these ROI (rows 10-19 in Table 3). Event-type labeled CR was for trials with correct rejection of a novel word as “old”; Hit was for trials with correct recognition of a studied word. Each time point is the mean and standard error of the mean (N=10) for an event-type with a presentation mode of Braille or spoken words.

Table 1

Demographics of early blind participants.

ID ^a	Age	Sex	%RH ^b	Hand	Speed ^c	Blindness Onset Age	Eye at Onset	Light Sense	Years Braille Reading	Cause ^d
EB1	60	F	100	R	fast (145)	0	both	none	57	ROP
EB2	59	M	80	L	fast (152)	0	both	none	53	ROP
EB 6	34	M	40	L	mod (76)	0	both	some	30	ROP
EB10	43	M	90	L	mod (71)	0	both	slight L	49	ROP
EB11	33	M	90	L	slow (59)	0	both	some	28	CA
EB16	54	F	90	R	fast (186)	0	R @0, L@17 (mo)	none	49	ROP
EB18	56	M	73	both	fast (?)	0	both	some	50	ROP
EB21	33	F	100	L	mod (104)	1.5	both	none	25	RB
EB23	23	M	100	R	slow (?)	0	both	none	18	ROP
EB24	21	F	100	L	fast (?)	0	both	none	18	ROP
Average										
N10	41.6	4F/6M	86.3							
SEM (+)	4.48		6.1							

^aEarly blind (EB) identification tags retained across previously published studies.

^b%RH indicates percent right hand usage based on the Eidenburgh handedness inventory.

^cSelf-reported reading speed plus words per minute or computed for timed reading of a 356 word length text.

^dretinopathy of prematurity. ROP; congenital amaurosis, CA; retinoblastoma, RB

Word characteristics

Table 2

	Concrete Words ^a				Abstract Words			
	Length ^b	K-F Freq ^c	Familiarity ^d	Concrete ^e	Length	K-F Freq	Familiarity	Concrete
Mean	5.49	49.42	529.7	557.79	5.89	53.24	530.57	272.26
SEM	.11	2.74	3.42	2.99	.13	2.86	3.57	2.54
t-test p=	.02	.34	.86	>.001				

^aWord characteristics available from the second version of the MRC Psycholinguistic Database (www.psych.rl.ac.uk/MRC_Psych_Db_files/psych.htm).

^bLength is the letter count per word.

^cKucera-Francis Frequency (K-F Frequency) is the written frequency of occurrence as given in: Kucera and Francis, W.N. (1967). Computational Analysis of Present-Day American English. Providence: Brown University Press.

^dFamiliarity stands for 'printed familiarity' with FAM values in the range of 100 to 700 (maximum of 657; a mean of 488 and a SD of 99).

^eConcrete indicates the concreteness of an item with a value range of 100 to 700 (minimum of 158; maximum of 670; mean of 438; s.d. of 120).

Table 3

Event type contrast results by presentation mode per ROI.

Cortex	ROI Name	Coordinates [@]	Spoken		Braille	
			CR vs. Hit		CR vs. Hit	
			F value	Pr > F [*]	F value	Pr > F [*]
Occipital	V1/V2d, Calc S	-3,-86,6	18.6	<.0001	1.3	NS
	V1d/V2, Cuneus	6,-81,10	14.6	.001	3.3	NS
	LOC, LOG	-32,-88,4	10.7	.002	0	NS
	LOC, LOG	38,-82,6	26.4	<.0001	0.8	NS
	V3A SOG	-22,-83,25	6.2	.002	0.2	NS
Ant Parietal	V3+V3A SOG	5,-89,25	9	.003	0.6	NS
	MT+, pITS	-40,-78,1	22.6	<.0001	1.3	NS
	MT+, pIT	46,-62,-4	18.8	<.0001	10.7	.001
	V8, pFG	31,-66,-15	11.4	.0001	3.9	NS
	BA3, aPCG	-42,-30,56	7.6	.007	3.5	NS
Pos Parietal	BA3, aPCG	37,-22,52	32.5	<.0001	0.6	NS
	BA2, pPCG	-40,-39,50	12.4	.0006	0.1	NS
	BA2, pPCG	44,-30,51	10.1	.0002	2.9	NS
	BA7, IPS	-34,-54,51	19.1	<.0001	0.8	NS
Temporal	BA7, IPS	30,-52,58	15	.0002	4.4	.04
	BA41, HG	-52,-40,15	1.6	NS	4	.05
	BA41, HG	49,-25,15	1.1	NS	18.3	<.0001
	BA22, STS	-55,-53,55	0.9	NS	10.7	.001
	BA22, STS	47,-33,-2	3.2	NS	14.1	.0003
Frontal	BA37, FG	14,-55,-14	14.8	.0002	4.6	.03
	BA46, DLPFC	-32,36,31	4.2	NS	23.9	<.0001

* Pr>F: probability of F-ratio greater than observed F value.

@ Coordinates are the X, Y, Z values for the Talairach atlas.

* aPCG: anterior postcentral g.; BA: Brodmann Area; Cal S: calcarine sulcus.; DLPFC, dorsolateral prefrontal cortex; FG: fusiform g.; HG: Heschl's g.; ITG: inferior temporal g.; IPS: intraparietal sulcal; LOG: lateral occipital g.; pITS: posterior inferior temporal sulcus; pPCG; posterior postcentral g.; SOG: superior occipital g.; STS superior temporal sulcus