Published in final edited form as:

Brain Res. 2016 June 1; 1640(Pt B): 278–288. doi:10.1016/j.brainres.2015.11.042.

Neural circuits in Auditory and Audiovisual Memory

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Abstract

Working memory is the ability to employ recently seen or heard stimuli and apply them to changing cognitive context. Although much is known about language processing and visual working memory, the neurobiological basis of auditory working memory is less clear. Historically, part of the problem has been the difficulty in obtaining a robust animal model to study auditory short-term memory. In recent years there has been neurophysiological and lesion studies indicating a cortical network involving both temporal and frontal cortices. Studies specifically targeting the role of the prefrontal cortex (PFC) in auditory working memory have suggested that dorsal and ventral prefrontal regions perform different roles during the processing of auditory mnemonic information, with the dorsolateral PFC performing similar functions for both auditory and visual working memory. In contrast, the ventrolateral PFC (VLPFC), which contains cells that respond robustly to auditory stimuli and that process both face and vocal stimuli may be an essential locus for both auditory and audiovisual working memory. These findings suggest a critical role for the VLPFC in the processing, integrating, and retaining of communication information.

Keywords

monkey; audiovisual; acoustic; frontal lobe; short-term memory

Introduction

We frequently rely on auditory working memory, for example, when we hear a phone number, and after a brief pause, successfully recall the number to place the call. We also depend on working memory when our train of thought is interrupted and we effortlessly return to it. Although there is much known about auditory pathways and processing, the underlying neural substrates of auditory working memory are poorly understood. Importantly, we do know that damage to sites within frontal, temporal, and parietal cortices can lead to auditory aphasia and memory deficits (Alain et al., 1998; Goerlich et al., 1995; Goll et al., 2010a; Goll et al., 2010b). Additionally, natural aging, strokes, traumatic brain injury and disease can damage the frontal cortex and impair auditory short-term memory

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capabilities, which can affect daily life. For example, patients with damage to the ventral frontal cortex suffer from language impairments, problems with auditory comprehension, and difficulties with understanding sentences with complex syntax. These are all functions that rely on auditory working memory (Kummerer et al., 2013; Szczepanski and Knight 2014). Thus, it is imperative to delineate the neural networks and processes that contribute to auditory working memory.

Working memory is defined in multiple ways. One classic definition describes working memory as a method to control attention through the ‘central executive’, composed of the visuospatial sketchpad, phonological loop, and ‘episodic buffer’ (Baddeley and Hitch 1974; Baddeley 2000). These are broad aspects of cognition and assist with decision making, language processing, and reasoning (Duncan 2010; Friederici and Gierhan 2013; Miller 2013). However, for this review we will use another common definition of working memory which is “to hold an item of information ‘in-mind’ for a short period of time and to update information from moment to moment” (Goldman-Rakic 1996).

It has been suggested that nonhuman primates (NHPs) do not have auditory working memory (Scott et al., 2012; Scott et al., 2013), but possess a much more limited short-term mnemonic ability termed ‘passive short-term memory’. Previous research argues against this point of view. Although NHP’s auditory memory abilities may be less than their capacities for remembering visual information they have demonstrated the ability to discriminate and remember auditory sounds over several seconds (Plakke et al., 2013), which is, by definition, auditory working memory. Evidence for intermediate to long-term auditory memory comes from the established ability of primates to recognize vocalizations of kin (Rendall et al., 1996) and to respond to conspecific and other primate species alarm calls (Zuberbuhler 2000). In the natural environment, various primate species are able to utilize syntax-like rules when listening to a complex series of call types and alter their behavior accordingly (Arnold and Zuberbuhler 2008; Lemasson et al., 2010; Zuberbuhler 2002). For example, if a Campbell’s monkey makes an alarm call for an eagle, Diana monkeys will also produce alarm calls signaling eagles, however, if a boom vocalization occurs before the alarm call of the Campbell monkey the Diana monkeys ignores the warning (Zuberbuhler 2002). The boom vocalization changes the meaning of the subsequent alarm call, and the Diana monkeys recognize this context and do not send out their own alarm calls. Monkeys housed in a laboratory can also recognize the vocalizations of monkeys from their shared housing room (Adachi and Hampton 2011; Habbershon et al., 2013). The ability to recognize meaningful vocalizations and alter behavior indicates that primates have some form of auditory memory, perhaps even long-term auditory memory for specific callers, and this leaves the door open for the manipulation of auditory information during working memory as well. The various forms of auditory memory (working, short-term, long-term) and the precise neuronal circuits that each form of memory relies on, is still under investigation. For purposes of this review, the ability to recognize matching or nonmatching auditory stimuli, over a period of several seconds, will be considered auditory working memory.

Auditory Short-term memory in Non-human Primates and Humans

One reason the mechanisms of auditory memory have not been studied extensively is that it has been difficult to train non-human primates to perform auditory working memory tasks that are similar to those used in the study of visual memory. Nonetheless, there have been some auditory discrimination/memory paradigms used to study the performance of a wide array of species including dogs, dolphins, starlings and non-human primates (Colombo et al., 1990; D'Amato and Salmon 1984; Fritz et al., 2005; Herman and Gordon 1974; Kowalska et al., 2001; Wright 1999; Zokoll et al., 2008). It typically takes longer to train NHPs to learn an auditory discrimination or memory task than to learn a similar task using visual stimuli (D'Amato and Salmon 1984; Fritz et al., 2005; Hashiya and Kojima 2001). Wright was successful in training NHPs to learn and remember lists of auditory stimuli (Wright 1999) which led to great insights demonstrating that auditory memory differed from visual memory in capacity. He showed that monkeys could not remember as many auditory items as visual items. Comparisons of auditory and visual memory curves highlight the notion that auditory memory is more susceptible to interference and less robust compared to visual memory (Wright 2007). Another study by Fritz and colleagues demonstrated how much harder it was for NHPs to remember acoustic information over short intervals than visual information using the same paradigm (Fritz et al., 2005).

Interestingly, the limited capacity to store auditory stimuli over short temporal intervals is not limited to macaques (Bigelow and Poremba 2014). In fact, studies of typical human subjects have demonstrated steeper forgetting curves for auditory stimuli compared to visual stimuli (Bigelow and Poremba 2014; Cohen et al., 2009a; Cohen et al., 2011). This finding is similar to the forgetting curves in nonhuman primates (Figure 1), (Colombo and D'Amato 1986; Fritz et al., 2005; Hashiya and Kojima 2001); although, for an exception to the rule, see (Visscher et al., 2007). A study examining recognition found that human subjects were significantly worse at recognizing recently heard sounds compared to recently seen pictures (Cohen et al., 2009a). This was true even when participants were exposed to sounds paired with a picture, but tested on the sound alone (Cohen et al., 2009a). Interestingly, when participants were asked to identify the sound clip (e.g. Dog bark) they could do so, indicating that long-term storage to recognize sound type was intact, but the ability to recall the specific sound they had previously heard was still impaired. This suggests that there may be a different neural mechanism for retaining recently heard sounds than for long-term storage of auditory information across species. A follow up study found that musicians have better auditory memory compared to non-musicians, but that even with improved auditory memory performance their visual recognition abilities were still better (Cohen et al., 2011). In fact, when nonverbal auditory stimuli are used, human performance on auditory recall begins to decline around 30 seconds (Mercer and McKeown 2014) and this decline is exacerbated if similar distractor stimuli are played during the intervening inter-stimulus-interval (Deutsch 1975; Keller et al., 1995; Massaro 1970; Semal and Demany 1991). For example in one study, performance dropped to near chance levels for remembering tones when distracter tones were played during the inter-stimulus-interval (Pechmann and Mohr 1992). This suggests that during auditory memory, distraction occurring during the delay, may be more important than the length of the delay itself

(Berman et al., 2009; Lewandowsky et al., 2009; Reitman 1971; Wright and Roediger 2003; Wright 2007).

Another factor affecting memory is proactive interference, or the fact that repeating stimuli are not only distractors but can induce problems for remembering a particular sound because of increasing load effects (too many items to store) or the features of the distractor items overwrite the original memory. These forms of interference can affect the ability of a subject to recognize a particular sound. Proactive interference can occur between or within trials and can also degrade auditory memory performance (Bigelow and Poremba 2013a; Bigelow and Poremba 2013b; Bigelow and Poremba 2015). It has been suggested that interference may play a greater role in decreased auditory memory performance than decay (Lewandowsky et al., 2008), but a recent study examining memory for timbre found that decay does play a role in memory performance when both interference and rehearsal are controlled for (McKeown and Mercer 2012). This suggests auditory memory can be affected by the passing of time itself, interference, as well as rehearsal, (for a review of these concepts see (Lewandowsky et al., 2009). Thus, even though humans have a superior capacity for short-term memory in general, decay rates for simple nonverbal stimuli indicate that it is an effortful process to remember temporally changing nonverbal auditory stimuli, (for a review of human auditory working memory see (Kaiser 2015). Thus, remembering pure acoustic information (i.e., non-language) is not only more difficult for non-human primates, but for humans as well.

A Cortical Network for Auditory Working Memory

Which cortical regions within the ventral stream are essential for non-spatial auditory working memory? The auditory cortex itself has been shown to undergo plasticity in a variety of auditory learning and memory paradigms across several species including humans (Fritz et al., 2007; Jancke et al., 2001; Menning et al., 2000; Ohl and Scheich 2005; Schreiner and Polley 2014; Weinberger 2015). Evidence from neurophysiological recordings in non-human primates suggests that the auditory cortex is involved in short-term auditory memory (Bigelow et al., 2014; Gottlieb et al., 1989). More conclusive evidence from lesion studies implicates auditory cortical regions in auditory discrimination. Colombo and colleagues examined the role of the superior temporal gyrus in auditory memory in New World monkeys with a simple same-different discrimination paradigm using a high and low pure tone. The delay between the cue and test stimulus varied between .5, 4 and 32 seconds. Large lesions of the superior temporal cortex impaired the monkey's performance (Colombo et al., 1990; Colombo et al., 1996). From the schematic in Figure 1 of their study, the lesioned area likely corresponds to the middle and anterior belt and the rostral parabelt. When lesioned, the animals performance was significantly impaired at all three time delays and remained that way even after extensive retraining, indicating the anterior belt and parabelt are critical for auditory memory processing (Colombo et al., 1990). A follow up study replicated these findings and illustrated that the impairment was not due to an inability to hear or discriminate individual sounds, although the ability to discriminate between ascending and descending tone patterns was impaired, confirming that the auditory cortex is required for auditory memory (Colombo et al., 1996).

Did the lesions interfere with auditory mnemonic processing because the essential cortical region was contained within the lesioned area? Or is it the case that lesions of the belt and parabelt prevent auditory information flow from proceeding to higher cortical regions which might serve an essential role in mnemonic processing of auditory stimuli. Since most lesions of the primate cortex have typically been made by aspiration, or electrolytic ablation, which damage fibers of passage in addition to cells, we must look to additional lesion studies of more anterior auditory cortical regions. Lesions of these anterior regions, including the rostral superior temporal gyrus (STG) have been shown to interfere with short-term auditory memory performance in macaques (Fritz et al., 2005). In this landmark study, performance was not impaired when the delay was less than 10 seconds. However, with delays at 10 seconds or longer, performance declined, confirming that the anterior temporal lobe is involved in auditory memory. In their pursuit of the auditory engram, Fritz and colleagues did not fully eliminate short-term auditory memory with medial temporal lobe lesions, suggesting other cortical regions are involved in auditory memory (Fritz et al., 2005). For a discussion of auditory long-term memory and possible contributions of medial temporal lobe structures like the hippocampus see (Munoz et al., 2009; Munoz-Lopez et al., 2015; Munoz-Lopez et al., 2010). In cats, lesions to portions of the auditory ventral stream also impair auditory discrimination. For example, Lomber & Malhotra (2008) dissociated the function of auditory cortical regions when they showed that inactivation of the anterior auditory field, AAF, in cats impaired auditory pattern discrimination, while lesions of area DP, a hypothesized dorsal stream region, impaired sound localization (Lomber and Malhotra 2008).

While lesions are beneficial in determining essential nodes in the auditory memory pathway along the auditory ventral stream, neurophysiological recordings can demonstrate mechanisms for mnemonic processing when neuronal activity is correlated with performance in auditory tasks. A neurophysiological study of the rostral superior temporal cortex (rSTC) (Scott et al., 2014) found that neurons in this region have clear sensory responses to acoustic stimuli within a delayed match-to-sample paradigm (Scott et al., 2014). Neural correlates of mnemonic function were also found within rSTC. For example, approximately 35% of neurons modulated their firing rate during the delay period, with half of these cells demonstrating delay suppression (Scott et al., 2014). Delay suppression, thought to represent a form of active maintenance, has also been observed in human auditory cortex when participants were remembering auditory stimuli (Linke et al., 2011). Other evidence of cognitive function including match suppression and match enhancement, which are common indices of memory or recognition, were also noted in rSTC (Scott et al., 2014). Additional studies have defined a voice recognition region in the anterior temporal lobe, which may prove to be involved in mnemonic processing (Gil-da-Costa et al., 2004; Perrodin et al., 2011; Perrodin et al., 2014; Petkov et al., 2008; Poremba et al., 2004). Further along the ventral auditory stream, recordings from the temporal pole (Ng et al., 2014) also show evidence of memory processes. Neurons within the dorsal temporal pole demonstrated match suppression at an early latency of 31-60 ms (Ng et al., 2014). This evidence suggests auditory memory information is processed within and along numerous regions of the temporal cortex, suggesting multiple streams of auditory information. Delineating the precise role that is played by each of these cortical regions in encoding,

maintenance, and retrieval of auditory stimuli is an ongoing endeavor. Clearly, techniques with better temporal resolution and spatial specificity are needed to determine the precise nature of information flow during auditory mnemonic processing.

Auditory Working Memory in the Prefrontal Cortex

The areas of the temporal lobe implicated in auditory memory processing project to the prefrontal cortex (Barbas 1992; Petrides and Pandya 1988; Plakke and Romanski 2014; Romanski et al., 1999a; Romanski and Averbeck 2009) and a large portion of the prefrontal cortex (PFC) is active during listening (Poremba et al., 2003). The projections target a number of areas which might play a role in auditory cognition. Combined anatomy and physiology have been used to study the precise route that acoustic information takes to the prefrontal cortex (Romanski et al., 1999b). When acoustically characterized regions of the auditory belt/parabelt region were injected with tracers, specific patterns of innervation have emerged. Anterior auditory belt and parts of ML show strong projections to the frontal pole, the ventrolateral prefrontal cortex areas 12 vl, 12 orbital and 45 (i.e. inferior convexity), and the rostral principle sulcus (Romanski et al., 1999b). In contrast, caudal auditory cortical regions, which respond to sound location, project to the caudal principal sulcus, frontal eye fields and dorsal premotor cortex. These studies indicate that the prefrontal cortex is poised to process auditory information, and use it during auditory working memory.

What role does the prefrontal cortex play in auditory working memory? Neuroimaging studies have found prefrontal activation in humans during verbal memory tasks (Barbey et al., 2013; Buchanan et al., 2000), as well as during speech and language processing (Caplan et al., 2000; Stromswold et al., 1996; Waters et al., 2003). In nonhuman primates, studies have explored the effect of prefrontal lesions on performance in auditory and in visual memory tasks. Most of these studies utilized lesions that were large and spread over several cytoarchitectonic regions. For example, a large lesion of dorsolateral prefrontal cortex led to performance deficits in auditory discrimination but not visual discrimination (Gross and Weiskrantz 1962; Gross 1963; Iversen and Mishkin 1973). In these studies, NHPs received lesions, which included the principle sulcus, or larger lesions which included both the principal sulcus and ventrolateral prefrontal cortex (inferior convexity) (Gross and Weiskrantz 1962). The animals were trained on a simple go-no-go auditory discrimination task where a white noise stimulus served as the go cue and a tone served as the no-go cue (Gross and Weiskrantz 1962). Animals with lesions that included damage to the ventrolateral prefrontal cortex were impaired on auditory discrimination but not on a visual discrimination task. While these were important findings, the lesions covered a very large area of both dorsal and ventral PFC, and the task did not explicitly examine working memory, since subjects learned a conditional association without a delay.

Neurophysiological recordings in the dorsolateral prefrontal cortex have revealed activity in spatial and non-spatial auditory tasks (Bodner et al., 1996; Ito 1982; Kikuchi-Yorioka and Sawaguchi 2000; Vaadia et al., 1989). These studies found evidence of delay related activity for auditory cues, indicating that the dorsolateral prefrontal cortex is involved in the mnemonic processing of auditory information. However, responses in DLPFC appear to be more “task-related” and less dependent on type of stimuli. In addition, these studies did not

employ a non-spatial auditory working memory task with a delay, similar to those used to assess auditory working memory as it was done in the superior temporal gyrus (Fritz et al., 2005).

More direct examination of lateral PFC in auditory working memory was demonstrated by Poremba and colleagues (Plakke et al., 2013). Animals were trained to detect matching sounds in a delayed match-to-sample task. Single-units demonstrated modulated responses to sounds when presented as the sample or as the matching/nonmatching stimulus. Neurons located in and around the principal sulcus demonstrated responses during the delay period, in addition to exhibiting match enhancement (Figure 2). The match enhancement effects observed in the PFC had an earlier latency during the matching sound presentation compared to the match enhancement seen in the dorsal temporal pole (Ng et al., 2014) or in the primary auditory cortex (Bigelow et al., 2014) suggesting top-down feedback is modulating the circuit during memory demand. Similar effects have been observed for visual working memory with more match enhancement in prefrontal regions (Miller et al., 1996) and match suppression occurring in temporal lobe regions (Miller et al., 1993). These neural correlates of cognition during auditory memory support the hypothesis that the lateral prefrontal cortex is engaged in the mnemonic processing of auditory stimuli in a parallel manner as it is for visual stimuli (Plakke et al., 2013). This may differ from VLPFC where individual neurons are strongly driven by acoustic stimuli, independent of a cognitive demand (Romanski et al., 2005). Identical studies of auditory working memory have yet to be conducted in VLPFC, although, it has been shown that VLPFC neurons respond to both stimulus and task variables in an audiovisual working memory task (Hwang and Romanski 2015).

VLPFC is Essential for Auditory Working Memory and Audiovisual Working Memory

In comparison to responses of neurons in DLPFC, single neurons in VLPFC respond robustly to complex sounds, including species-specific vocalizations but not to simple stimuli (Romanski and Goldman-Rakic 2002). FMRI studies in humans (Fecteau et al., 2005) and monkeys (Ortiz-Rios et al., 2015) have confirmed these vocalization responsive regions. Furthermore, VLPFC neurons show selectivity based on the acoustic characteristics of complex sounds when presented during fixation (Romanski et al., 2005). Surprisingly, most of the auditory responsive cells are clustered in this region while weakly responsive auditory neurons are spread across lateral prefrontal regions, most likely influenced by task and context. In 1997 O'Scalaidhe, noted that there were “face cells” in VLPFC areas 12 and 45. Noting that these “face cells” were located within the same regions as vocalization responsive auditory cells, Romanski and colleagues demonstrated that a large proportion of VLPFC neurons are multisensory and respond to faces and vocalizations (Diehl and Romanski 2014; Romanski and Hwang 2012; Sugihara et al., 2006).

In recent years, efforts have focused on determining the role of VLPFC and the principal sulcus region in auditory and audiovisual memory processing. Studies by Cohen and colleagues were among the first to show that VLPFC was involved in non-spatial auditory

cognition (Cohen et al., 2009b). In their study, neurons in VLPFC showed more modulation when animals detected auditory features than when animals detected changes in spatial location of sounds. In further studies, Cohen and others have recorded in the lateral prefrontal cortex, including both ventral and dorsal regions. The importance of prefrontal cortex in auditory cognition is apparent by its activation in a number of cognitive processes. The activity of single lateral prefrontal neurons was correlated with the monkey's choice in an auditory same-different task (Russ et al., 2008) and during an auditory categorization task (Lee et al., 2009).

As mentioned previously, neurons in VLPFC are responsive when face or voice stimuli are presented (Diehl and Romanski 2014; Romanski and Hwang 2012; Sugihara et al., 2006) or when they are required to be remembered during working memory (Hwang and Romanski 2015). Not only are single-units activated by particular face-voice combinations but they are also active during the correct detection of mismatching face-voice pairs (Hwang and Romanski 2015). In fact, single cells track which particular component changed, whether the nonmatch was a change in the face or voice component, Figure 3 (Hwang and Romanski 2015). A large proportion of cells recorded from VLPFC were also responsive during the delay period between stimulus presentations. These task related cells highlight the involvement of VLPFC during audiovisual working memory, indicating that VLPFC is keeping track of both stimulus components simultaneously (faces and voices) and evaluating information so that correct detection of the nonmatching stimulus can occur during the response period. Previous evidence supports the notion that VLPFC is active during the processing, integration, and maintenance audiovisual information online during working memory. However, is the VLPFC necessary for audiovisual working memory?

In order to examine this question we trained non-human primates in the same audiovisual delayed nonmatch-to-sample paradigm as utilized by Hwang and Romanski (2015) and temporally inactivated the VLPFC (Plakke et al., 2015). We used cortical cooling to temporarily inactivate VLPFC because it can be repeated within subjects and does not harm the cortical tissue (Lomber and Malhotra 2008; Yang et al., 2006). Furthermore, it allows for the inactivation of a large region of cortex over a short time period. In these experiments, subjects began by performing their audiovisual (AV) working memory task with the cortex kept at normal temperature (WARM block). Then the cortex was inactivated by cooling (COLD block). Animals performed 100 trials in each block. In Experiment 1, animals were required to remember both the face and vocalization presented in the sample movie to correctly detect a mismatching face-vocalization pair, where either the face or vocalization component differed from the previously presented sample movie (see task diagram Figure 4). Inactivation of VLPFC, by cooling, resulted in a significant impairment on both auditory mismatch and visual mismatch trials, indicating that VLPFC is necessary for audiovisual working memory (Figure 5).

The audiovisual memory paradigm described is quite difficult for subjects since it requires the maintenance of both face and vocal information during the delay periods. What if the memory load was decreased and subjects were asked to remember only one of the components, a face or a vocalization? Based on previous visual working memory lesion experiments (Bussey et al., 2002; Rushworth et al., 1997) we hypothesized that if asked to

encode the face alone our subjects might not be impaired when VLPFC was cooled. In contrast, previous lesion studies examining auditory discrimination (Gross and Weiskrantz 1962; Iversen and Mishkin 1973) have shown performance deficits with damage to the prefrontal cortex, suggesting that inactivation of VLPFC would impair auditory working memory. In experiments 2 and 3, we re-trained our subjects in the same paradigm with the bimodal face-vocalization movie as the sample, but in Experiment 2, the nonmatching stimulus was always a mismatching face and in Experiment 3, it was always a mismatching vocalization. This version of the task presumably requires less memory demand since in each experiment subjects only needed to remember the face (Experiment 2) or the vocalization (Experiment 3) but not both as they did in Experiment 1. In Experiment 2, when subjects were required to remember only the face information alone, VLPFC inactivation did not affect performance in detecting the mismatching face component (Plakke et al., 2015), Figure 6. In contrast, in Experiment 3, when subjects were required to remember only the vocalization, VLPFC inactivation by cooling resulted in a significant decrease in performance accuracy (Plakke et al., 2015), Figure 6. This auditory working memory deficit occurred in both subjects at a relatively short (1.25 second) delay, indicating that the prefrontal cortex may be more important for maintaining auditory information in memory than visual. These three experiments demonstrate that VLPFC is essential for audiovisual and auditory working memory but not for visual working memory.

Our cooling experiments show that both auditory memory and audiovisual memory are more reliant on VLPFC than visual memory processing. This may be due to the difficulty of remembering auditory information compared to visual information as demonstrated by both human and nonhuman primates (Bigelow and Poremba 2014; Colombo and D'Amato 1986; Fritz et al., 2005; Hashiya and Kojima 2001). It is also possible that during audiovisual processing, when VLPFC is maintaining an acoustic stimulus, this burdens working memory so that adding an additional item to remember (a face) absolutely requires the remaining temporary storage in VLPFC. For this reason, when VLPFC is inactivated performance declines. Conversely, remembering only a face does not require VLPFC and so is not affected by VLPFC inactivation. The differential effects where cooling of the VLPFC, impaired audiovisual and auditory memory, but not visual working memory are further borne out by localization of vocalization and face responses across the prefrontal cortex. Within the prefrontal cortex, a small anterolateral area within VLPFC contains most of the robustly responsive auditory neurons, including those that are selectively responsive to species-specific vocalizations (Romanski and Goldman-Rakic 2002; Romanski et al., 2005). As mentioned this area also contains some face responsive cells (O'Scalaidhe et al., 1997; O'Scalaidhe et al., 1999; Romanski and Diehl 2011) and so it is not surprising that this is a hot-spot for multisensory responsive cells (Diehl and Romanski 2014; Sugihara et al., 2006). Therefore, VLPFC can maintain both auditory and visual information for comparison during working memory. On the other hand, there are unimodal visual responsive neurons, found across a wide region of both dorsal and ventral prefrontal cortex; these cells are not confined to VLPFC as auditory responsive cells are. Consequently, inactivation of VLPFC affected a large proportion of auditory and multisensory cells while sparing visual neurons. The concentration of auditory-responsive cells within the VLPFC (Romanski and Goldman-Rakic 2002) may explain the deficits seen during auditory and audiovisual working memory.

Overall, the fact that there was impairment during both audiovisual and auditory working memory provides functional validation that VLPFC is critical for auditory mnemonic processing. Previous single-unit (Hage and Nieder 2015; Hwang and Romanski 2015; Romanski et al., 2005; Sugihara et al., 2006) and neuroimaging results (Grady et al., 2008; Rama et al., 2004; Rama and Courtney 2005; Strand et al., 2008; Zatorre et al., 1994) have suggested that ventral PFC is important for auditory processing and auditory working memory. The inactivation experiments in Plakke et al., (2015) provides direct evidence that VLPFC is an essential region for auditory working memory and suggests VLPFC is a major end point of the auditory ventral stream, necessary for auditory cognition.

Acknowledgements

This work was supported by grants from the National Institutes of Health grant (DC: 04845), the Training and Hearing Balance and Spatial Orientation grant (DC: 009974), the Schmitt Program on Integrative Brain Research and the Center for Visual Science.

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Highlights

Auditory working memory (WM) is inferior to visual WM in humans and animals.

The prefrontal cortex interacts with temporal lobe regions in auditory cognition.

Ventral prefrontal cortex is essential for auditory and audiovisual working memory.

Figure 1.

Graphs depicting accuracy vs memory interval for four studies comparing auditory and visual short-term memory in different primate species. A) Human subjects demonstrating better retention for visual stimuli compared to auditory stimuli. This pattern is qualitatively similar to the results observed in a B) Chimpanzee, as well as C) Old world and D) New world monkeys. Adapted from Bigelow & Poremba, 2014.

Figure 2.

Normalized activity across the population of lateral PFC neurons for sample, match and nonmatch sounds during an auditory working memory task. The blue line is combined activity during the second sound presentation for correct Match trials; the green line is combined activity during the second sound presentation for correct Nonmatching trials. The orange line is combined activity during the first sample sound presentation (across correct Match and Nonmatch trials). During the second sound presentation on Match trials there was “match enhancement” effect, where there was significant difference between correct Match sound presentations compared to the first sample sound presentation ($p < 0.05$), signified by asterisk. Adapted from Plakke et al., 2013.

Figure 3.

Example neurons from the audiovisual working memory task in Hwang & Romanski, 2015. The left panel is Sample presentation; Right panel is Nonmatch or Match presentation. Each panel shows a spike-density plot with rasters above across 10-12 trials. Black= Sample or Match, Blue= Auditory Nonmatch, Red= Visual Nonmatch, Green= Audiovisual Nonmatch. Black and gray bars on abscissae indicate duration of the video and the audio track, respectively. The example neurons shown in A and B, demonstrate Nonmatch activity to the auditory Nonmatch (A) and to both auditory and visual Nonmatch trials (B). Cell A was most responsive when the auditory component changed during the Nonmatch. Cell B was responsive to a change in either the auditory or the visual component during the Nonmatch, but only when one of the components changed at a time. This cell was considered multisensory context-responsive. Adapted from Hwang & Romanski, 2015.

Figure 4.

Schematic of the audiovisual NMTS task used in the cooling study by Plakke et al., 2015. A vocalization movie (with an audio and video track) was presented as the sample stimulus and the subject was required to remember the auditory and visual components (vocalization and accompanying facial gesture) and to detect the change of either the face or vocalization component in subsequent stimulus presentations with a button press. On type 1 trials, half the trials, the Nonmatch occurred following the sample and delay period. On type 2 trials, a Matching stimulus intervened and the Nonmatch occurred as the third stimulus. In the example shown the vocalization in the 2nd stimulus of Type 1 trials and the 3rd stimulus of Type 2 trials, does not match the sample (Auditory Nonmatch). This occurred for 50% of the trials and for the other half of trials the video track was an incongruent face paired with the same sample audio track (Visual Nonmatch, not shown). Adapted from Plakke et al., 2015.

Figure 5.

Audiovisual Working Memory Performance. VLPFC inactivation by cooling significantly impairs overall performance accuracy on the audiovisual NMTS task (Experiment 1) $*=p<0.05$. The solid color bars denote performance during auditory component nonmatch trials and the striped bars denote performance during visual component nonmatches. For both subjects there was a significant decrease in performance during cooling (COLD trials – blue bars) compared to the control period (WARM trials- red bars) for both auditory and visual nonmatch trials. In addition, subject 1 demonstrated significantly worse performance on auditory trials compared to visual trials. Error bars are the SEM calculated. Adapted from Plakke et al., 2015.

Figure 6.

Inactivation of VLPFC does not significantly affect visual only working memory performance (A), but does significantly impair auditory only working memory performance (B). In experiment 2 during the visual-only condition (A, striped bars), there was no significant change in performance accuracy during cooling of the VLPFC (COLD trials – blue bars) compared to the pre-cooling trials (WARM – red bars) in either subject. In experiment 3 during the auditory-only condition (B, solid bars), there was a significant decrease in performance for both subjects during the COLD trials (blue bars) compared to pre-cooling performance (WARM – red bars). Error bars indicate SEM. $* = p < 0.05$. Adapted from Plakke et al., 2015.