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Multisensory and unisensory neurons in ferret parietal cortex exhibit distinct functional properties

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Abstract

Despite the fact that unisensory and multisensory neurons are comingled in every neural structure in which they have been identified, no systematic comparison of their response features has been conducted. Towards that goal, the present study was designed to examine and compare measures of response magnitude, latency, duration and spontaneous activity in unisensory and bimodal neurons from the ferret parietal cortex. Using multichannel single-unit recording, bimodal neurons were observed to demonstrate significantly higher response levels and spontaneous discharge rates than did their unisensory counterparts. These results suggest that, rather than merely reflect different connectional arrangements, unisensory and multisensory neurons are likely to differ at the cellular level. Thus, it can no longer be assumed that the different populations of bimodal and unisensory neurons within a neural region respond similarly to a given external stimulus.

Keywords

Multisensory Integration; Parietal Cortex; Somatosensation; Vision; Neurophysiology

INTRODUCTION

Since the advent of multisensory neuronal recordings approximately a half century ago (Amassian and Devito, 1954; Horn and Hill, 1966), the bimodal neuron has come to represent the basic, if not iconic, unit of multisensory processing. These neurons, which show suprathreshold responses to stimuli from more than one sensory modality, also have the capacity to integrate multisensory information according to the parameters of stimulation. For example, stimuli in spatio-temporal coincidence tend to produce responses greater than any of the component stimuli presented alone (Meredith and Stein, 1986; Meredith *et al.*, 1987). Furthermore, the tendency for weaker stimuli to evoke higher levels of enhancement when combined demonstrated the inverse effectiveness principle (Meredith and Stein, 1986). The generality of these principles of multisensory processing, largely determined from studies of the cat superior colliculus, were supported by similar findings in cortex (Stein and Wallace, 1996; Wallace *et al.*, 1992).

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Within a given multisensory region, however, multisensory neurons coexist with unisensory neurons. Multisensory areas can exhibit an approximately 60:40 mixture of multisensory and unisensory neurons in most areas examined (e.g., Carriere *et al.*, 2006; Dahl *et al.*, 2009; Keniston *et al.* 2008; Jiang *et al.*, 1994) as well as in computer simulations of multisensory processing (Anastasio and Patton, 2003; Lim *et al.* 2011). Because these two types of neurons are physiologically distinguishable, it is logical to expect that one provides a function that the other does not. However, the question of functional differences between bimodal and unisensory neurons has largely been unexplored because multisensory investigations have almost exclusively examined bimodal neurons while the vast majority of studies of unisensory areas test only with the effective stimulus modality with the explicit exclusion of the others. Thus, missing from investigations of sensory neurophysiology are direct comparisons of multisensory and unisensory neurons. Therefore, the goal of the present experiments is to compare the functional properties of neurons that are demonstrably unaffected by multisensory stimulation (i.e., unisensory) with those that are.

To compare unisensory and multisensory neurons, the rostral posterior parietal cortex of the ferret (PPr) served as the experimental model. This region contains neurons that respond to either (unisensory) (Foxworthy and Meredith, 2011; Manger *et al.*, 2002) or both somatosensory and visual stimulation presented alone (bimodal) (Foxworthy *et al.*, 2012). Also, visual and somatosensory receptive fields in PPr are comparatively large, such that a standardized set of stimuli can activate a large proportion of sensory neurons within a spatially-distributed multiple single-unit recording penetration. In addition, the parietal cortex is well-studied in humans, monkeys and rodents and its behavioral role has been established in attention, rectification of spatial maps, goal-directed behaviors, and self-awareness (Alais *et al.*, 2010; Blanke, 2012; Calton and Taube, 2009; Kaas *et al.*, 2011; Nitz, 2009; Reep and Corwin, 2009; Save and Poucet, 2009). Last, because all eutherians studied reveal a multisensory visual-somatosensory region between visual and somatosensory cortical representations (Kaas, 2009; Manger *et al.*, 2002), the properties of bimodal/unisensory neurons observed in the ferret PPr can be generalized to a large number of species.

MATERIALS AND METHODS

All procedures were performed in compliance with the Guide for Care and Use of Laboratory Animals (National Institutes of Health, publication 86-23), the National Research Council's Guidelines for Care and Use of Mammals in Neuroscience and Behavioral Research (2003), and with prior approval by the Institutional Animal Care and Use Committee at Virginia Commonwealth University.

Surgical Procedures

Ferrets (male, adult $n=17$) were anesthetized (8mg/kg ketamine; 0.03mg/kg dexmedetomidine intramuscularly) and their heads were secured in a stereotaxic frame. Using aseptic surgical procedures, a craniotomy was made to expose the rostral posterior parietal (PPr) region, the caudal posterior parietal visual region (PPc) and the third somatosensory area (SIII) on the suprasylvian gyrus. Over this opening, a recording well/head supporting device was implanted using stainless steel screws and dental acrylic. After implantation, the animals were immediately transferred to the recording apparatus for data collection.

Electrophysiological Recording

For recording, the ferrets were secured to an immobile supporting bar via the cranial implant, such that their eyes and ears were not obstructed and no pressure points were

present. The animals were intubated through the mouth, ventilated (expired CO₂: ~4.5%) and immobilized (pancuronium bromide; 0.3 mg/kg initial dose; 0.2 mg/kg h supplement i.p.). Fluids (lactated Ringer's solution) and supplemental anesthetics (4mg/kg h ketamine; 0.5 mg/kg h acepromazine i.p.) were administered continuously with an infusion pump. Paralytics were necessary to prevent movement of the body and eyes during the lengthy and repeated presentation of somatosensory and visual stimuli at fixed locations. Heart rate was monitored continuously and, if heart rate rose over a sustained period of 5–10 minutes, additional supplemental anesthetics were administered. Animal temperature was continuously monitored and maintained at 38°C on a heating pad. The pupils were dilated with 1% atropine sulfate, the eyes were anesthetized with 0.5% proparacaine hydrochloride, and corrective contact lenses were placed on the corneas to adjust for refractive errors.

A 32-channel silicon probe (4 shanks 5mm long separated by 200 μ m, each with 8 recording sites separated by 200 μ m; impedance ~1 M Ω at 1kHz; NeuroNexus Technologies, Ann Arbor, MI) was positioned over the recording target according to sulcal and gyral landmarks described in published reports (Foxworthy and Meredith, 2011; Manger *et al.*, 2002). The probe was advanced into the cortex to a depth of about 1750 μ m using a hydraulic microdrive and allowed to stabilize for 30 minutes. Neuronal activity was recorded and digitized (rate>25kHz) using a TDT System III Workstation (TuckerDavis Technologies Alchua, FL) running MatLab software and stored for off-line analysis. The raw signal was bandwidth separated (at 0.5–5kHz) and denoised by a two-stage multiple linear regression function to reject signals common to all channels. Waveforms were then clustered by principal component feature space analysis and sorted into individual units using an automated Bayesian sort-routine. Spikes which failed to separate within a principal component cluster were marked as outliers and not included for further analysis. Also, spikes which had interspike intervals of less than 2ms were rejected. This technique has been used by our lab in single-unit evaluations of other cortical regions in the ferret (Keniston *et al.*, 2009; Allman *et al.*, 2009; Meredith *et al.*, 2012).

After individual neurons were templated, their responses to sensory stimulation were determined. First, each neuron was assessed independently through the manual presentation of somatosensory (brush strokes, taps, manual pressure and joint movement) and visual stimuli (flashed or moving spots or bars of light from a hand-held ophthalmoscope projected onto a translucent hemisphere, 92cm diameter, positioned in front of the animal) to determine each neuron's responsiveness to somatosensory or visual stimuli and its receptive field(s). Electrode penetrations which contained a mixture of visual and tactile responses were considered to be in the PPr. Penetrations immediately rostral to this location that demonstrated only somatosensory responses were designated as being in SIII (Foxworthy and Meredith, 2011). Similarly, penetrations caudal to the PPr which exhibited only visual responses were defined as being in PPc (Manger *et al.*, 2002). Receptive field locations identified by manual stimulation were used to guide the placement of the subsequent electronically-generated, repeatable somatosensory and visual stimuli (described below). Auditory responsiveness was also evaluated using manually presented claps, hisses, whistles at different locations around the animal's head. However, auditory responses were not observed, so quantitative sensory testing progressed using only visual and somatosensory stimulation.

Electronically-generated, computer-controlled stimuli were used to acquire quantitative measures of neuronal functional properties in PPr, SIII and PPc. Stimulation parameters were kept as constant as possible (allowing for some minor adjustments due to preferred receptive fields in individual electrode penetrations) across different recording penetrations and among different animals. Somatosensory stimulation was produced by a calibrated 1 gram monofilament fiber moved by an electronically-driven, modified shaker (Ling, 102A)

that travelled 11mm and displaced hair or indented the skin on the contralateral side of the ferret's face at a velocity of 0.18 meters/second. Visual stimuli were projected onto the translucent hemisphere and consisted of a bar of light ($2 \times 20^\circ$) that moved ($70^\circ/\text{sec}$) $10\text{--}15$ degrees across the lower hemifield of the contralateral visual space in the nasal to temporal direction. These stimuli were presented separately and in combination. During combined presentations, the onset of the visual stimulus preceded that of the tactile stimulus by $\sim 40\text{ms}$ to compensate for the cortical latency disparity, such that the spike trains evoked by visual and somatosensory stimuli overlapped. The separate and combined presentations of stimuli were randomly interleaved to compensate for possible shifts in baseline activity, interstimulus intervals randomly varied between 3–7 seconds to avoid response habituation, and each stimulus or combination was repeated 50 times. In this way, a given recording penetration simultaneously sampled neuronal responses for each recording channel ($n=32$) to repeated visual, tactile, and combined visual-tactile stimulation. Operationally, (see Results) these stimulation parameters were appropriate to consistently elicit robust neuronal responses on a high proportion recording sites per penetration.

Once a recording session was completed, the animal was overdosed (Euthasol), perfused and fixed (4% paraformaldehyde). The cortex was blocked stereotaxically and serially sectioned in the coronal plane, mounted on slides and counterstained with cresyl violet. Sections containing recording sites were photographed using a light microscope and a scaled image of the recording probe was superimposed by aligning the depth and medio-lateral dimensions with the electrode tracks. This produced a scaled reconstruction of the tissue in relation to the recording probe. Individual recording sites localized in white matter, or not fully inserted into the cortex, were excluded from further analysis.

Data Analysis

To evaluate the neuronal responses to the somatosensory, visual and combined stimuli, custom software (MatLab) was used to compile and quantify single-unit spiking activity after the criteria of (Bell *et al.*, 2005). A neuronal response was defined as spiking activity which was >3 standard deviations from spontaneous activity, that lasted for 15ms duration, and ended when activity returned to baseline for at least 15ms. For each neuron, the following specific response features were analyzed:

Sensory category—Neurons were defined by their different patterns of responses to the quantitative sensory tests according to published criteria (Allman and Meredith, 2007; Allman *et al.*, 2008a; Allman *et al.*, 2009). Neurons showing suprathreshold activation to more than one sensory modality were defined as bimodal multisensory neurons. Neurons that exhibit suprathreshold activation in only one modality, but were significantly (paired t-test; $\alpha=0.05$) influenced by the presence of a stimulus from another modality were designated as subthreshold multisensory neurons. Those which showed suprathreshold activation by only one modality but were not significantly (paired t-test; $\alpha=0.05$) influenced by stimulation in other sensory modalities were defined as unisensory neurons. Neurons which were not activated by any sensory stimulus or combination were defined as unresponsive.

Response magnitude—The magnitude of response was calculated in terms of average number of spikes per trial for each stimulation condition (visual; tactile; visual-tactile) for each neuron. A response was defined as activity that was time-locked to the onset of stimulation and that rose >3 standard deviations above baseline activity for at least 15 ms.

Response duration—Onset of a response was defined as activity that rose >3 standard deviations from baseline activity for 15ms duration. Offset was the point where activity

returned to baseline for at least 15ms. Duration was defined as the time measured from response onset to offset.

Response latency—This was calculated as the time from the onset of the sensory stimulus to the beginning of a neuronal response.

Spontaneous activity level—The activity of the neurons in the absence of sensory stimuli was measured from spiking activity (spikes/second) captured from data records for the period of time 500ms prior to the onset of sensory stimulation.

Multisensory integration—Neurons classified as multisensory were further analyzed to determine if they demonstrated integrated responses to multisensory stimulation, which was defined as a response (average number of spikes/trial) to combined stimulation that was significantly different (paired t-test; $\alpha=0.05$) than that elicited by the most effective unisensory stimulus. Responses showing a significantly greater activation to multisensory stimuli versus that elicited by the most effective single modality stimulus were defined as showing response enhancement, those showing a significantly reduced activation to multisensory versus the best unisensory stimulus were classified as showing response depression. The magnitude of multisensory integration was calculated according to the method of (Meredith and Stein, 1986) using the formula: $(CM - SM_{max}) / SM_{max} \times 100 = \% \text{ Integration}$. In this equation, SM_{max} was the neuron's response to the most effective unisensory stimulus (average spikes/trial) and CM was the response to the multisensory stimulus.

After neurons were categorized as unisensory (tactile or visual) or multisensory (subthreshold or bimodal) using the criteria above, statistical tests were used to assess functional differences between the groups using two tailed t-tests (when only two groups were compared) and ANOVAs ($\alpha=0.05$) followed by Tukey tests (when multiple groups were compared; $\alpha=0.05$). Tests of linear correlation were used to assess the relationships between different functional properties. For variables which correlated with multisensory integration, the relative strength of these correlations was assessed using multiple regression analysis and subsequent comparison of beta weights (standardized multiple regression coefficients). All statistical analyses were performed using the software JMP Pro 9 (SAS Institute Inc., Cary, NC).

RESULTS

Electrophysiological Recording Overview

To compare the functional properties of bimodal and unisensory neurons in the rostral posterior parietal cortex (PPr), multi-channel single-unit extracellular recordings (summarized in Fig. 1) obtained a total of 451 sensory responsive neurons. Of this sample, 50% (225/451) were bimodal neurons that were independently activated by visual and by somatosensory stimulation, while 36% were either unisensory visual (13%; 61/451) or unisensory tactile neurons (23%; 103/451). Examples of each response type are provided in Figure 2. Relatively few neurons activated by tactile (9%; 39/451) or visual (5%; 23/451) stimulation showed subthreshold multisensory responses. Recordings were also made in the adjacent somatosensory area SIII and the visual caudal posterior parietal cortex (PPc) where 78 tactile and 118 visual neurons were identified, respectively. Few subthreshold neurons (9%; 7/78 in SIII; 11%; 13/118 in PPc), and no bimodal neurons, were encountered these regions.

Bimodal vs. Unisensory: Spontaneous Rate

Figure 2 shows the spiking activity of simultaneously recorded bimodal and unisensory PPr neurons that includes periods of spontaneous discharge prior to the onset of stimulation. In these examples, the bimodal neuron had an average spontaneous rate of 24.9 spikes/second while the unisensory tactile and unisensory visual neurons had much lower spontaneous rates (13.7 spikes/second and 12.1 spikes/second respectively). These examples reflect the trend observed in the population of bimodal and unisensory neurons, as summarized in Table 1 and Figure 3A. Overall, bimodal neurons demonstrated an average spontaneous rate of 25 ± 0.93 spikes/sec that was ~ 1.4 times that of unisensory tactile (18 ± 1.38 spikes/sec) or unisensory visual neurons (14 ± 1.40 spikes/sec). An ANOVA ($F(2,386) = 25.6$; $p < 0.0001$) followed by post-hoc Tukey tests showed that bimodal neurons had a significantly higher spontaneous rate than unisensory visual and unisensory tactile neurons, while the unisensory neurons did not differ significantly from each other. In addition, data from individual recording penetrations (in which all neurons received identical stimulation and their responses were simultaneously recorded) followed the same pattern, where bimodal neurons showed higher spontaneous rates than their unisensory neighbors in all but one ($n=17/18$) penetration. In the overall sample, however, subthreshold multisensory neurons did not occur with sufficient frequency to be included in these and subsequent statistical comparisons (but see Multisensory Integration, below).

Bimodal vs. Unisensory: Response Magnitude

The response magnitude, or level, of evoked activity also varied among the different neuron types in the PPr. For example, the bimodal neuron depicted in Figure 2 responded to the tactile cue with an average 1.8 spikes/trial and to the visual cue with an average 1.9 spikes/trial, yet these identical stimuli evoked only 1.1 spikes/trial from the unisensory tactile neuron, and 1.4 spikes/trial in the unisensory visual neuron. These individual examples reflect the general trend observed in the overall PPr sample. On average, bimodal neurons generated a greater response magnitude to tactile (2.7 ± 0.15 spikes/trial) or to visual (2.7 ± 0.18 spikes/trial) stimulation than did their unisensory counterparts (tactile = 1.6 ± 0.22 spikes/trial; visual = 1.5 ± 0.27 spikes/trial), as summarized in Table 1 and Figure 3B. In fact, bimodal neurons' average responses were nearly 2x that of the unisensory neurons. These observations were statistically significant: t-tests showed that bimodal neurons had a greater average response magnitude to the same tactile stimulation compared to unisensory tactile neurons ($p < 0.0001$); and bimodal neurons had a greater response to the same visual stimulation compared to unisensory visual neurons ($p = 0.0003$). These same effects were also observed within the individual recording penetrations (in which all neurons received identical stimulation and their responses were simultaneously recorded), such that bimodal neurons showed higher average response values than their unisensory neighbors in all ($n=18/18$) penetrations.

Because the spontaneous activity of bimodal neurons was higher than that of unisensory neurons, their elevated response magnitude might only reflect their higher spontaneous rate of firing. To evaluate this possibility, the average spontaneous activity for a given neuron was subtracted from the response magnitude recorded for that neuron, and these adjusted values were then compared between bimodal and unisensory groups. However, this manipulation did not change the direction or significance of the results. With spontaneous activity subtracted, bimodal neurons still exhibited a greater average response magnitude to tactile stimulation compared to unisensory tactile neurons (t-test; $p = 0.0002$), and to visual stimulation compared to unisensory visual neurons (t-test; $p = 0.0045$). In summary, these results confirmed that the same visual or tactile stimulation evoked different response levels in bimodal and unisensory neurons of the PPr.

Bimodal vs. Unisensory: Response Duration

Given that bimodal neurons showed greater response magnitudes than their unisensory neighbors, one mechanism by which this change could be generated would be for the response duration of bimodal neurons to increase. Using the same visual and tactile responses described above, the response duration was measured for bimodal and unisensory PPr neurons. In the example provided in Figure 2, the response of the bimodal neuron had an average duration of 38ms to tactile stimulation while the unisensory tactile neuron exhibited an average duration of only 29ms to the same stimulus. With visual stimulation, however, the bimodal neuron revealed an average response duration of 38ms that was similar to that of the unisensory visual neuron (39ms). These examples mimic the trend seen in the overall sample, where bimodal neurons had a greater average response duration to tactile stimulation (39 ± 1.19 ms) than did unisensory tactile neurons (28 ± 1.72 ms), and this difference was statistically significant (t-test, $p < 0.0001$). In contrast, for visual stimulation, the average duration of response of all bimodal neurons (40 ± 1.70 ms) was similar to that of unisensory visual neurons (40 ± 2.54 ms), which was not significantly different (t-test, $p = 0.79$). These patterns for response duration were apparent within individual recording penetrations, where the duration of tactile responses was longer for bimodal than unisensory neurons in all but two penetrations ($n = 16/18$), while the duration of visual responses was essentially the same for bimodal and unisensory neurons in all penetrations.

Bimodal vs. Unisensory: Response Latency

The latency of response onset to tactile and to visual stimulation was compared between bimodal and unisensory PPr neurons, as listed in Table 1 and illustrated in Figure 3D. For the simultaneously recorded examples provided in Figure 2, the visual responses of the bimodal neuron (latency = 87ms) were much shorter than those of the unisensory visual neuron (98ms), but the tactile responses of bimodal (45 ms) and unisensory tactile (44 ms) neurons were essentially the same. These response latency patterns were reflected in the overall population. Bimodal neurons responded on average 17ms faster to visual stimulation (87 ± 4.24 ms) than did the unisensory visual neurons (104 ± 5.02 ms), and this latency difference was statistically significant (t-test; $p = 0.0116$). For responses to tactile stimulation, bimodal neurons exhibited an average response latency (51 ± 0.97 ms) that was similar to that measured for unisensory tactile neurons (53 ± 1.33 ms), and these values were not significantly different from each other (t-test, $p = 0.31$). These same patterns for response latency were evident within individual recording penetrations, where the average latency of visual responses was shorter for bimodal than unisensory neurons in all but one penetrations ($n = 17/18$), while the latency values for tactile responses were essentially the same for bimodal and unisensory neurons in all penetrations.

Correlations Among Response Features

To evaluate whether response features of cortical bimodal and unisensory neurons might covary, data from the different response measures were examined for correlative relationships (Pearson's correlation). In Figure 4, response magnitudes for tactile and visual stimulation were plotted against spontaneous discharge rates. For responses to tactile stimulation, both bimodal ($r = 0.57$; $p < 0.0001$) and unisensory tactile ($r = 0.57$; $p < 0.0001$) neurons showed a significant positive linear correlation between spontaneous rate and response magnitude. Similarly, for responses to visual stimulation, both bimodal ($r = 0.39$; $p < 0.0001$) and unisensory visual ($r = 0.41$; $p = 0.0002$) neurons also showed a significant positive linear correlation between spontaneous rate and response magnitude. Thus, response magnitude tended to increase with increasing spontaneous rate for bimodal and unisensory neurons alike.

As shown in Figure 5, the relationship of the temporal variables of response duration and response latency was analyzed (Pearson's correlation). No significant correlation was found between tactile response latency and tactile response duration for either bimodal ($r=-0.08$; $p=0.33$), or unisensory tactile neurons ($r=-0.13$; $p=0.24$). For responses to visual stimulation, a significant negative linear correlation was found between visual response latency and visual response duration for bimodal neurons ($r=-0.34$; $p=0.0088$), but no significant correlation was found for unisensory visual neurons ($r=-0.29$; $p=0.65$). Thus, except for visual responses of bimodal neurons, there seemed to be little relationship between the temporal features of response latency and response duration.

Multisensory vs. Unisensory Areal Comparisons

Because the unisensory somatosensory (SIII) or visual (PPc) areas combine to provide a majority of the afferent input to the PPr (Foxworthy et al., 2012), comparisons of the functional properties of neurons between the different areas were also conducted. However, bimodal neurons were not observed in SIII or PPc, and too few subthreshold multisensory neurons were recorded for valid statistical evaluation, so only measures from unisensory tactile or unisensory visual neurons were available. As shown in Figure 6A and summarized in Table 1, the spontaneous rate of bimodal neurons in PPr (average 25 ± 0.93 spikes/sec) was about 1.4 times higher than that of the unisensory neurons in SIII (average 18 ± 1.82 spikes/sec) or PPc (19 ± 1.54 spikes/sec), which were statistically significant (ANOVA $F(4, 560) = 8.95$; $p < 0.0001$). However, the spontaneous activity of unisensory neurons from these same areas did not differ from each other (post-hoc Tukey tests). In other words, bimodal PPr neurons showed higher spontaneous rates than did any of the unisensory neurons examined within or outside the PPr.

When the response magnitude was compared between neurons in the PPr and its afferent regions (PPc and SIII), an interesting dichotomy was observed. The average response magnitude of bimodal neurons in the PPr (tactile = 2.7 ± 0.15 ; visual = 2.7 ± 0.18 spikes/trial) was similar to the responses of unisensory neurons in area SIII (2.4 ± 0.23 spikes/trial) and the PPc (3.1 ± 0.29 spikes/trial), as depicted in Figure 6B. However, the response of unisensory PPr neurons (tactile average = 1.6 ± 0.22 ; visual average = 1.5 ± 0.27 spikes/trial) was 1.5–2 times less than the unisensory responses obtained in areas SIII and PPc that are the major inputs to the PPr. These data show that responses of bimodal neurons in the PPr and unisensory tactile neurons in SIII did not differ statistically (ANOVA, post-hoc Tukey) from each other, and that both had a significantly higher magnitude of response than did the unisensory tactile neurons of the PPr ($F(2,396)=11.65$; $p < 0.0001$). Similarly, visual responses in the unisensory PPc did not differ significantly from those of bimodal neurons in the PPr, and both groups had a significantly greater magnitude of response than did unisensory visual neurons in the PPr ($F(2,388)=7.09$; $p = 0.001$). Thus, the responses of bimodal neurons in the PPr were similar in magnitude to those of unisensory neurons from its input regions of SIII and PPc, but unisensory PPr neurons exhibited lower response magnitudes than their input sources.

Measures of response duration were also examined between the different cortical areas. In response to tactile stimulation, SIII neurons (38 ± 1.78 ms) had a similar average response duration to PPr bimodal neurons (39 ± 1.19 ms), but were an average 10ms longer duration than unisensory tactile neurons in PPr (28 ± 1.72 ms). With visual stimulation, PPc neurons (52 ± 2.42 mean ms) had an average response duration that was 12ms longer compared to both bimodal (40 ± 1.70 ms) and unisensory visual neurons (40 ± 2.54 ms) in the PPr. These relationships are depicted in Figure 6C and the data summarized in Table 1. Statistical tests (ANOVA; post-hoc Tukey) showed that the response duration of SIII neurons and PPr bimodal neurons (to tactile stimulation) did not differ from each other, and that they were significantly longer than the average duration of unisensory tactile neurons in PPr

($F(2,396)=15.87$; $p<0.0001$). PPc neurons had a greater average response duration (to visual stimulation) than both bimodal and unisensory visual neurons in the PPr, which did not differ significantly from each other ($F(2,388)=8.06$; $p=0.0004$). Thus, the response duration of bimodal neurons in the PPr was similar to that of the unisensory neurons in area SIII, but PPc neurons showed a greater duration of response than either bimodal or unisensory neurons in the PPr.

Because areas SIII and PPc are the primary sources of projections to PPr (Foxworthy et al., 2012), it would be expected that response latency in the source areas would be shorter than that observed in the target. This expectation was confirmed by the data. The average response latencies to tactile or to visual stimulation were shorter in SIII (41 ± 1.25 ms) and PPc (67 ± 3.7 ms) than for both unisensory (tactile = 53 ± 1.33 ; visual = 103.6 ± 5 ms) and bimodal neurons (tactile 51 ± 0.97 ; visual 87 ± 4.24 ms) in the PPr. These results are illustrated in Figure 6D and summarized in Table 1. In response to tactile stimulation, SIII neurons responded, on average, 10ms faster than PPr bimodal neurons and 12ms faster than PPr unisensory tactile neurons. In response to visual stimulation, PPc neurons responded, on average, 20ms faster than PPr bimodal neurons and 37ms faster than PPr unisensory visual neurons. Statistical comparisons (ANOVA; Tukey tests) of SIII tactile response to both unisensory and bimodal PPr tactile responses showed that these differences were significant ($F(2,396)=28.32$; $p<0.0001$). Similarly, PPc responses to visual stimulation showed significantly (ANOVA; Tukey tests) shorter latency than both bimodal and unisensory visual neurons in the PPr ($F(2,388)=22.39$; $p<0.001$). Thus the average response latencies of afferent areas SIII and PPc were shorter than any of the neuron types measured in the PPr.

Multisensory Integration of Multisensory Neurons in the PPr

The responses of individual unisensory neurons were not significantly changed by combined stimulation. On the other hand, bimodal multisensory neurons showed a range of changed responses to combined stimuli. The range of multisensory processing effects has been analyzed elsewhere in the brain (Avillac *et al.*, 2007; Stein and Meredith, 1993; Stein and Stanford, 2008; Stein and Wallace, 1996; Wallace *et al.*, 1992) and in synthetic neural networks (Lim *et al.*, 2011) with respect to the proportions of multisensory neurons, the share of multisensory neurons that exhibit multisensory integration, and the magnitude of multisensory integration generated. In the present study, of the 225 PPr neurons identified as bimodal multisensory, 105 (47%) generated responses to combined stimulation that met the statistical criteria for demonstrating multisensory integration. The magnitude of multisensory integration in bimodal PPr neurons ranged from -100 to 296% (avg. = 69%). Using another measure of integrative magnitude, the percentage of integrative neurons exhibiting super-additive responses (response to combined stimulation greater than the sum of the responses to the separate unisensory stimuli) was 32% ($34/105$).

Subthreshold multisensory neurons were infrequently encountered in all the regions studied. However, by definition (see Methods), all neurons of this type exhibited significant levels of multisensory integration (otherwise, they would be unisensory). For subthreshold PPr neurons that were activated by tactile stimulation, their spiking responses were significantly modified by combined stimulation (9% ; $39/451$) that ranged in magnitude from -100 to 238% (avg. absolute value = 22%). Visual PPr neurons which showed subthreshold multisensory effects (5% ; $23/451$) showed a range of multisensory integration from 35 to 217% (avg. = 55%). These subthreshold multisensory neurons tended to exhibit functional measures more akin to unisensory neurons than their multisensory counterparts. Specifically, tactile neurons with subthreshold multisensory responses had, on average, a spontaneous rate of 19.38 ± 2.25 spikes/second, a response magnitude of 1.58 ± 0.17 spikes/trial, a response duration of 29.89 ± 1.9 ms, and a response latency of 51.58 ± 1.16 ms. Visual neurons with subthreshold multisensory responses had an average spontaneous rate of

14.99±2.25 spikes/second, a response magnitude of 1.21±0.28 spikes/trial, a response duration of 36.03±3.4ms, and a response latency of 109.56±11.4ms. When compared with values from the other neuron types (see Table 1), all response measures of subthreshold multisensory neurons were similar to their unisensory counterparts, but these trends could not be statistically confirmed due to small numbers.

Correlations among Response Features and Multisensory Integration

To determine which response features of bimodal neurons might be predictive of their capacity to exhibit multisensory integration, the following correlations were tested. For the sample of bimodal PPr neurons that demonstrated multisensory enhancement and, separately, those that showed response depression, values for spontaneous rate or response magnitude were plotted against the measures of multisensory integration exhibited by those same neurons. These relationships are plotted in Figure 7. Spontaneous rate was found to have a significant negative linear correlation with the level of multisensory enhancement (Fig. 7A) (Pearson's correlation; $r=0.43$; $p=0.006$) and a significant linear correlation with the magnitude of multisensory depression (Fig. 7B) ($r = 0.43$; $p = 0.006$). In other words, bimodal neurons with lower spontaneous rates tended to exhibit greater levels of either multisensory enhancement or depression.

Next, the magnitude of response to separate tactile or visual stimulation was examined in relation to the level of multisensory integration generated by their combination. These relationships are illustrated in Figure 8. Specifically, the response magnitudes to separate tactile ($r=-0.47$; $p<0.0001$; Fig. 8A) or visual ($r=-0.34$; $p=0.0028$; Fig. 8B) stimulation showed a significant negative correlation with multisensory enhancement. Similarly, the response magnitudes elicited by tactile ($r=0.47$; $p=0.006$; Fig 8C) or visual ($r=0.51$; $p=0.0079$; Fig 8D) stimulation produced a significant, linear relationship with multisensory depression. Thus, the population behavior of bimodal PPr neurons indicates that there is an inverse relationship between response magnitude of the components of a multisensory stimulus and the levels of multisensory integration their combination evoked.

Because the relationship between response magnitude elicited by the components of a multisensory stimulus and multisensory integration was similar to that seen between spontaneous rate and multisensory integration, the relative strength of these factors to contributions to multisensory enhancement and depression were compared with a multiple regression analysis. This treatment demonstrated that, for bimodal PPr neurons, tactile responsiveness (standardized partial correlation coefficient $\beta = -0.44$, $p = 0.0035$) and visual responsiveness ($\beta = -0.10$, $p = 0.04$) were larger contributors to multisensory enhancement than spontaneous activity ($\beta = 0.046$, $p = 0.75$). Similarly tactile (standardized partial correlation coefficient $\beta = 0.35$, $p = 0.02$) and visual ($\beta = 0.60$, $p = 0.012$) responsiveness were larger contributors to multisensory depression when compared with spontaneous activity ($\beta = -0.27$, $p = 0.279$). In summary, both sensory response magnitude and spontaneous rate were correlated with the level of multisensory integration (both enhancement and depression), but sensory response magnitude was more predictive of the two.

DISCUSSION

Using neurons recorded from ferret multisensory cortex that were presented a standard set of visual, somatosensory and combined visual-somatosensory cues, the present study sought to compare the functional properties of bimodal and unisensory neurons. These comparisons demonstrated that bimodal and unisensory neurons within PPr cortex were distinct from one another on essentially all of the features examined. Specifically, when compared to the properties of unisensory PPr neurons, bimodal neurons had, on average, a significantly

greater spontaneous discharge rate, greater response magnitude, greater response duration to tactile stimulation and decreased response latency to visual stimulation. Similar results are apparent as ancillary observations in a few other reports. In the ferret medial rostral suprasylvian sulcus, bimodal neurons exhibited a level of spontaneous activity that was more than double that of unisensory neurons (Keniston *et al.*, 2009). In monkey ventral intraparietal cortex, the raw data/figures illustrate that response latency was shorter for bimodal neurons (average 78 ms) than for unisensory visual neurons (average 91.5 ms; Avillac *et al.*, 2007), although statistical comparisons were not made. It should be noted that in relation to results from awake macaques, the present ferret data was derived under anesthetized conditions which possibly acted to increase the overall latency measures. Nonetheless, because these results were derived from different cortical areas and different species, the observed distinctions between bimodal and unisensory neurons may represent a general property of the neocortex. Furthermore, since most studies of multisensory processing have focused almost exclusively on the integrative properties of multisensory neurons, the present findings represent a novel set of features by which bimodal and unisensory neurons can be distinguished.

The mechanisms underlying these functional differences between bimodal and unisensory neurons remain to be identified. However, cortical neurons are not only heterogeneous in their distinctive discharge patterns, but also in morphology and the expression of voltage-gated ion channels (Bekkers, 2000; Storm, 2000; Sugino *et al.*, 2006). For example, in some neurons, the membrane current most closely associated with spontaneous activity results from hyperpolarization-activated channels (Chan *et al.*, 2004; Forti *et al.*, 2006) (Bennett *et al.*, 2000; Maccaferri and McBain, 1996; McCormick and Pape, 1990) while in other neuron types, spontaneous activity is dependent on a TTX-sensitive persistent sodium current that flows at voltages positive to -65mV (Bean, 2007; Bevan and Wilson, 1999; Do and Bean, 2003; Jackson *et al.*, 2004; Raman and Bean, 1997; Raman *et al.*, 2000; Taddese and Bean, 2002). Furthermore, layer 5 thick tufted neurons, which have distinctive membrane properties, exhibit both increased spontaneous activity as well as elevated response levels when compared with the other neurons in barrel (de Kock *et al.*, 2007) or visual cortex (Groh *et al.*, 2010). Whether any of these intrinsic factors are responsible for elevated spontaneous activity in bimodal neurons remains to be assessed.

In addition to the influence of intrinsic neuronal properties, extrinsic features such as connectivity are also likely contributors to the distinctions between bimodal and unisensory neurons. Indeed, there is a robust literature describing differential inputs to laminar-specific neuron types (e.g., (Krook-Magnuson *et al.*, 2012; Schubert *et al.*, 2007; Thomson and Lamy, 2007), and indications are that bimodal and unisensory neurons differentially distribute within and across the cortical laminae (Foxworthy *et al.*, 2012). This same study showed that layer 6 neurons in the PPr were most likely to be unisensory and were also the least likely to receive convergent inputs from afferent visual and somatosensory cortical areas. On the other hand, layer 2–3 neurons were highly likely to be multisensory as well as to receive convergent projections from the afferent visual and somatosensory areas. Thus, differential connectivity would appear to correlate with the unisensory and bimodal neurons identified in the PPr which, as a consequence, exhibit different activity levels.

During a recording session, because a single stimulus evoked different responses in the constituent bimodal and unisensory neurons of the region, these data suggest that multisensory and unisensory information is processed in parallel as it passes through the local cortical circuit. Although bimodal and unisensory neurons co-distribute within the PPr, bimodal neurons predominate in the layers 2/3 and 5, while unisensory neurons are the majority of neurons in layer 6 (Foxworthy *et al.*, 2012). The fact that layer 6 neurons to project to caudate and claustrum (for review, Thompson and Lamy, 2007), areas that are

both known for their multiple unisensory representations (Remedios *et al.*, 2010), indicates that unisensory signals are maintained through the output stages of the cortical circuit. Furthermore, the present study demonstrates that the response latencies for bimodal and unisensory neurons are significantly different, which is also consistent with the possibility of different and at least partially separate connectivity patterns. Alternatively, it might be possible for a multisensory circuit perhaps to filter-out the inputs from a weaker modality, but this condition has not yet been proposed or observed, and the data do not suggest that one modality has weaker effects in the PPr than the other.

These observations of co-extensive but distinct unisensory/multisensory functional features have serious implications for the interpretation of macroscopic measures, such as EEG, fMRI or computational models of multisensory processing. In all forms of multisensory study, establishment of response levels to unisensory stimulation is an essential baseline measure against which subsequent levels of multisensory integration are calculated. However, the present results demonstrate that it can no longer be assumed that a given unisensory stimulus evokes the same response from bimodal and unisensory neuronal subpopulations and formulae that predict multisensory response levels on the basis of group responses to single-modality stimulation should account for the lower level of activity elicited within the subpopulation of unisensory neurons. This issue is demonstrated by the following scenario based on the data from the present study. Unisensory visual neurons in PPr represented 13% of the sample and responded to visual stimulation with an average 1.5 spikes/trial, while somatosensory neurons represented 23% of the sample and responded to tactile stimulation with an average 1.6 spikes/trial. On the other hand, bimodal neurons represented 50% of the sample and exhibited an average of 2.7 spikes/trial to either visual or tactile stimulation while generating 4.5 spikes/trial to their combination. When these combined and unisensory responses are compared, the multisensory neurons generated 67% average response enhancement. However, when the proportions and values for unisensory neurons are included in the population response to combined stimulation, the population average drops to 3.2 spikes/trial, or 33% response enhancement, which is a 2-fold reduction of the estimate of multisensory processing. Thus, in a population response to multisensory stimulation, the presence of unisensory neurons and their low firing levels will result in an underestimation of the actual level of multisensory processing that occurs.

Given that the examined cortical regions are interconnected (Foxworthy et al., 2012), comparisons of response latency can provide an indication of their serial connectivity. As predicted by the anatomical observations, measures of tactile and visual latency indicate that both SIII and PPc regions were activated prior to the PPr. Furthermore, bimodal PPr neurons were activated, on average, earlier by visual stimulation than their unisensory counterparts in PPr, suggesting that bimodal neurons, at least in part, may occupy an earlier segment of the PPr cortical circuit. The mechanisms by which bimodal neurons might be recruited first within a local cortical circuit remain to be determined, but this observation is consistent with the large literature that documents the behavioral role of multisensory processing in reaction time facilitation. These latency data are also consistent with the hypothesis, mentioned earlier, that multisensory and unisensory signals are processed in parallel as they transit the circuitry of the PPr.

Correlates of Multisensory Integration and Inverse Effectiveness

Bimodal neurons have the capacity to integrate multisensory signals, while unisensory neurons, by definition, do not. For the population of bimodal PPr neurons, both response magnitude and spontaneous rate were correlated with the magnitude of multisensory integration generated across the sample. Specifically, bimodal neurons which exhibited vigorous sensory responsiveness to tactile or visual stimulation generated comparatively low levels of multisensory integration while other neurons that displayed low levels of sensory-

evoked activity tended to produce higher degrees of multisensory integration. Similarly, neurons with low levels of spontaneous activity tended to demonstrate the greatest degree of multisensory integration whereas different neurons with high spontaneous rates exhibited lower levels of multisensory integration. These relationships were observed for neurons that showed multisensory response enhancement (see also (Perrault *et al.*, 2003), as well as those demonstrating multisensory response depression. Moreover, although both response magnitude and spontaneous rate were inversely correlated with the magnitude of multisensory integration, response magnitude was the better predictor of multisensory integration (Perrault *et al.*, 2003; Stanford *et al.*, 2005). That similar functional features covary with both response enhancement and depression (and influence unisensory neurons *as well*), supports the notion that these contrasting effects actually fall along a broad continuum of response activity (Allman *et al.*, 2009).

The described relationships between groups of highly (or weakly) responsive neurons and multisensory integration also correspond with a fundamental property demonstrated by individual multisensory neurons. Termed the “inverse effectiveness principle,” individual multisensory neurons tend to exhibit higher levels of multisensory integration when the separate components of the stimulus are minimally effective, while in the same neuron lower levels of integration tend to result from the combination of highly effective stimuli (Avillac *et al.*, 2007; Kayser *et al.*, 2005; Meredith and Stein, 1986; Perrault *et al.*, 2003; 2005; Wallace *et al.*, 1996). The present study demonstrates that this principle extends to a population response of bimodal neurons to a single set of stimuli. Specifically, bimodal PPr neurons, as a group, exhibited a range of activity and in response to a given stimulus or stimulus combination (see also Meredith *et al.*, 2011a; Perrault *et al.*, 2005). Some PPr neurons demonstrated low levels of response to separate visual and somatosensory stimulation and generated proportionally large magnitudes of multisensory integration, while other neurons were more highly activated by the separate-modality stimuli and generated lower levels of multisensory integration when those same stimuli were combined. Thus, the present results showed that bimodal neurons in a given cortical region are specifically tuned to different functional levels (or modes, see Perrault *et al.*, 2005) that collectively contribute to a population-wide expression of inverse effectiveness. In addition, this group inverse effect was observed for bimodal neurons showing multisensory response enhancement as well as for those that generated response depression. To our knowledge, these are the first indications that inverse effectiveness applies to expressions of multisensory response depression.

When compared with multisensory response enhancement, multisensory depression has received far less investigative attention. Perhaps the most extensively examined model of multisensory response depression is found in the higher level somatosensory area SIV of the cat anterior ectosylvian sulcal cortex (Clemo and Stein, 1983; Dehner et al., 2004). Area SIV receives a robust crossmodal projection from an adjoining auditory region, the auditory field of the anterior ectosylvian sulcus (FAES). Surprisingly, the expected result of such somatosensory-auditory convergence in SIV was rarely observed: few bimodal neurons were identified (Clemo and Stein, 1983; Dehner et al., 2004). However, when somatosensory stimulation was paired with activation of auditory FAES, nearly 70% of the neurons demonstrated significantly suppressed responses. This response depression was found to be GABA-A mediated, because application of the antagonist bicuculline methiodide blocked the suppressive effects (Dehner et al., 2004) and projections from auditory FAES were identified in synaptic contact with dendrites of inhibitory interneurons within SIV (Keniston et al., 2010). Thus, GABA-mediated inhibition has been demonstrated within a circuit known to elicit multisensory response depression. It is also widely known that inhibitory inputs to cortical pyramidal neurons almost uniformly occur on the soma and initial segment, where they potentially act to suppress spiking activity arriving from the

dendritic arbor. Given these features, the mechanism underlying inverse effectiveness of response depression may be something as simple as the possibility that a “unit” of inhibition is more effective in reducing weak excitatory responses than strong ones. The present observations support this notion, since a single stimulus level was used here to induce suppression yet a wide range of response depression was observed within the sample population. This also seems to make intuitive sense behaviorally, since highly effective stimuli that have a high likelihood of generating a behavioral response would be less suppressed than a less effective stimulus. Ultimately, depressive inverse effectiveness might even act like a filter that improves signal by preferentially reducing low-magnitude, neural “noise.”

Response variation to standardized stimulation

The present study has shown that a single external stimulus produces different responses in populations of bimodal and unisensory neurons of the PPr. Specifically, a given unisensory stimulus (visual or somatosensory) elicited, on average, a significantly larger response in bimodal than in unisensory neurons. It is also important that a single set of combined stimuli (visual and somatosensory) produced a wide range of responses, from enhancement to depression, in bimodal neurons. These observations indicate that cortical bimodal neurons have distinct operational modes, much like that demonstrated for the brainstem (Perrault *et al.*, 2005). Importantly, because these operational modes of multisensory neurons are independent of the stimulus features that are involved, (Perrault *et al.*, 2005), it is unlikely that the present observations in cortical neurons would be substantially different if a larger or different set of stimulation parameters had been employed.

In addition to representing part of the multisensory response continuum that occurs between enhancement and depression, bimodal neurons that did not integrate multisensory information raise an important conceptual issue. Non-integrating bimodal neurons, despite having the ability to represent information from different sensory modalities, appear to respond to multisensory stimulation as they would to their preferred unisensory stimulus. Accordingly, it has been suggested (Sabes, 2011) that at least for some bimodal neurons, there is *competition* for representation of a particular sensory modality rather than integration. Alternatively, bimodal neurons with different integrative capacities may occupy distinct locations and perform distinct functions within a local circuit. This notion is supported by recent evidence (Foxworthy et al., 2012) that demonstrated a predisposition for supragranular neurons to generate multisensory response enhancement while infragranular neurons were more evenly distributed in their production of either enhanced or depressed responses. Furthermore, the magnitude of the integrated multisensory responses (both enhanced and depressed) increased with increasing laminar depth. Because each cortical layer exhibits a distinctive connectional pattern (both inputs and outputs), these data suggest that integrated multisensory information is processed and relayed in a laminar-dependent fashion.

Summary and Conclusions

While bimodal neurons have long been regarded as unique in their ability to integrate responses to multisensory stimuli, the present study has revealed a novel set of features that also distinguish bimodal from unisensory neurons. When tested with a standard set of stimuli (visual, somatosensory and combined), bimodal cortical neurons exhibit significantly higher spontaneous discharge rates and greater magnitudes of response than did their unisensory neighbors. In response to these same stimuli, the population of bimodal neurons exhibited a range of responses that included both enhancement and depression, as well as maintained the multisensory principle of inverse effectiveness. In addition, because functionally distinct bimodal and unisensory neurons co-exist within a given cortical region,

these results support the postulate that multisensory cortex operates as a parallel processor of multisensory and unisensory signals. Ultimately, these results have serious implications for the interpretation macroscopic studies of multisensory processing, such as fMRI, EEG and computational simulations, because it can no longer be presumed that a given sensory stimulus evokes the same responses from multisensory neurons and their unisensory counterparts.

Acknowledgments

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ABBREVIATIONS

PPC	caudal Posterior Parietal Cortex
PPR	rostral Posterior Parietal Cortex
SIII	Somatosensory area III

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Figure 1.

Summary of recording penetrations. The lateral view of the ferret cortex indicates the three brain regions examined: somatosensory area III (SIII), the multisensory rostral posterior parietal cortex (PPr), and the visual caudal posterior parietal cortex (PPc). The expanded view shows the approximate location of all the recording sites as well as the orientation of the electrodes. Scale bar = 1mm.

Figure 2.

Sensory responses of PPr neurons. Responses of typical bimodal (A), unisensory tactile (B) and unisensory visual (C) neurons in the PPr are depicted. All of the responses depicted here were elicited by the same set of visual and somatosensory stimuli (indicated by the traces at top; V=visual, T=tactile), and were recorded simultaneously. In (A), the bimodal neuron responded to visual and tactile stimulation presented alone and its response to combined stimulation was significantly greater than that elicited by either separate stimulus. In part (B), the unisensory tactile neuron did not respond to the visual stimulus, but was activated by the tactile stimulation presented alone; this response was not significantly altered when the visual-tactile stimuli were combined. In part (C) the unisensory visual neuron was activated by a visual stimulus presented alone but was not significantly influenced by the presence of the tactile stimulus alone or in combination. Raster: 1 dot = 1 spike; 50 trials. Histogram: 10ms time bins.

Figure 3.

Functional properties of bimodal neurons are distinct from those of unisensory neurons in the PPr. Each panel (A–D) shows a dot plot (individual neuron data=dot; population mean=horizontal line) with a summary bar graph (mean $\pm$ se) below; significant differences are indicated by an asterisk. (A) The rate of spontaneous activity for bimodal (Bi) neurons was significantly greater than that of unisensory tactile (Uni T) or unisensory visual (Uni V) neurons. (B) The response magnitude of bimodal neurons was significantly greater to tactile or visual stimulation than that of unisensory tactile or visual neurons, respectively. (C) The average response duration of bimodal neurons to tactile stimulation was significantly greater than that of unisensory tactile neurons, but the bimodal visual response duration did not

differ significantly that of unisensory visual neurons. (D) The response latency to tactile stimulation did not significantly differ between bimodal and unisensory tactile neurons, but bimodal neurons did have significantly shorter average response latency than unisensory visual neurons.

Figure 4.

Correlations of spontaneous rate and response magnitude for bimodal and unisensory PPr neurons. The scatterplots shows the relationship between spontaneous rate and response magnitude for bimodal neurons (black dots) and unisensory neurons (gray symbols). The lines indicate line of best fit for bimodal (black) and unisensory (gray) neurons. (A) With tactile stimulation, both bimodal and unisensory tactile neurons showed a significant positive linear correlation between spontaneous rate and response magnitude. (B) For visual stimulation, both bimodal and unisensory visual neurons showed a significant positive linear correlation between spontaneous rate and response. See text for statistics.

Figure 5.

Response latency correlated with response duration for visual but not for tactile responses in bimodal neurons. The scatterplots show the relationship between response latency and response duration for bimodal neurons (black dots) and unisensory neurons (gray symbols). The lines indicate the line of best fit for bimodal (black) and unisensory (gray) neurons. (A) For tactile stimulation, no significant correlation was found between tactile response latency and tactile response duration for either bimodal (black dots, black line) or unisensory tactile neurons (gray dots, gray line). (B) With visual stimulation, a significant negative linear correlation was found between visual response latency and visual response duration for bimodal neurons. On the other hand, no significant correlation was found for these measures in unisensory visual neurons. See text for statistics.

Figure 6.

Functional properties of neurons in areas SIII, PPr, and PPc. Each panel (A–D) shows a dot plot (individual neuron data=dot; population mean=horizontal line) with a summary bar graph (mean $\pm$ se) below; significant differences are indicated by an asterisk. Differences among data from PPr neurons already illustrated in Figure 3 are not depicted here. Data from unisensory tactile neurons of SIII are displayed on the left side of the graphs; data from the unisensory visual neurons of the PPc are displayed on the right side of the graphs. (A) The spontaneous rate of bimodal (Bi) neurons in PPr was found to be significantly higher than that of any other group. (B) Average response magnitudes were found to be similar between bimodal PPr neurons and the unisensory neurons of SIII and PPc. However, the average magnitude of SIII neurons was significantly higher than that of the unisensory tactile (Uni T) neurons in PPr, and PPc neurons had a significantly greater response

magnitude than the unisensory visual (Uni V) neurons of the PPr. (C) Visual neurons of the PPc had a greater duration of response than either the bimodal or unisensory visual neurons within the PPr. The somatosensory neurons of SIII on the other hand, had similar average response duration to PPr bimodal neurons, but had a significantly greater duration than the PPr unisensory tactile neurons. (D) Both SIII and PPc neurons had shorter response latencies, to tactile and visual stimulation respectively, than either the bimodal or unisensory neurons of the PPr.

Figure 7.

Spontaneous rate correlates with levels of multisensory enhancement and depression in bimodal PPr neurons. The scatterplots show the relationship between spontaneous rate and the magnitude (percent) of multisensory enhancement (A) or multisensory depression (B) for bimodal neurons that met the criteria for demonstrating multisensory integration. The lines indicate the lines of best fit. (A) The spontaneous rate of bimodal neurons showed a significant negative linear correlation with the magnitude of multisensory enhancement generated by these same neurons in response to combined stimulation. (B) The spontaneous rate of bimodal neurons showing multisensory depression demonstrated a significant linear correlation with the magnitude of multisensory depression. In either condition (enhancement or depression), lower spontaneous levels correlated with higher levels of integration. See text for statistics.

Figure 8.

Single-modality response level correlates with magnitude of multisensory enhancement or depression. The scatterplots show the relationship between sensory response magnitude and the magnitude (percent) of multisensory enhancement (A, B) or multisensory depression (C, D) for bimodal PPr neurons (1 dot=1 neuron). The lines indicate the line of best fit. (A) The relationship of tactile response magnitude to multisensory enhancement showed a significant negative relationship, whereby bimodal neurons with weaker tactile responses tended to generate higher levels of multisensory enhancement. (B) A significant negative linear relationship was found between visual response magnitude and multisensory enhancement. Thus, bimodal neurons with lower visual responses tended to generate higher levels of multisensory enhancement. (C) The relationship of tactile response magnitude with multisensory depression showed a significant linear relationship, such that bimodal neurons with weaker responses to tactile stimulation tended to show more negative (deeper) levels of multisensory depression. (D) A significant linear relationship was found between visual response magnitude and multisensory depression, where bimodal neurons with relatively low visual responses tended to show more negative (deeper) levels of multisensory depression.

Table 1

Category	Stimulus					
	Tactile			Visual		
	Spontaneous rate	Magnitude	Duration	Latency	Magnitude	Duration
PPr Bi	25.12 ± 0.93	2.67±0.15	39.4±1.19	50.8±0.97	2.69±0.18	40.4±1.70
PPr Uni T	18.27 ± 1.38	1.56±0.22	28.4±1.72	52.5±1.33	NA	NA
PPr Uni V	13.68 ± 1.40	NA	NA	NA	1.50±0.27	39.6±2.54
SIII Uni T	17.72 ± 1.82	2.35±0.23	38.5±1.78	40.7±1.25	NA	NA
PPc Uni V	19.41 ± 1.54	NA	NA	NA	3.12±0.29	51.5±2.42
						66.5 ± 3.7

Response measures of parietal cortical neurons from areas PPr, PPc and SIII. Bi=bimodal; Uni T= unisensory tactile; Uni V=unisensory Visual. Spontaneous = spontaneous rate in spikes/second measured for 500ms prior to stimulation onset; Magnitude = sensory response in average number of spikes/trial; Duration = average response duration in milliseconds; Latency = average time from stimulus to response onset in milliseconds; '±' = standard error; NA=not applicable.