

Engagement of visual fixation suppresses sensory responsiveness and multisensory integration in the primate superior colliculus

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Abstract

Neurons in the intermediate and deep layers of the superior colliculus (SC) often exhibit sensory-related activity in addition to discharging for saccadic eye movements. These two patterns of activity can combine so that modifications of the sensory response can lead to changes in orienting behaviour. Can behavioural factors, however, influence sensory activity? In this study of rhesus monkeys, we isolate one behavioural factor, the state of visual fixation, and examine its influences on sensory processing and multisensory integration in the primate SC. Two interleaved fixation conditions were used: a FIX condition requiring exogenous fixation of a visible fixation point; and a FIX-BLINK condition, requiring endogenous fixation in the absence of a visible fixation point. Neurons of the SC were influenced by fixation state, exhibiting both lower levels of sensory activity and reduced multisensory interactions when fixation was exogenously engaged on a visible fixation point. These results are consistent with active visual fixation suppressing responses to extraneous stimuli, and thus demonstrate that sensory processing and multisensory responses in the SC are not dependent solely on the physical properties of the sensory environment, but are also dynamically influenced by the behavioural state of the animal.

Introduction

Neurons in the intermediate and deep layers of the primate superior colliculus (SC) not only discharge in relation to saccadic eye movements (Wurtz & Goldberg, 1971; Sparks, 1978), but also exhibit sensory responses to visual, and in some cases auditory and/or somatosensory stimuli (Sparks, 1986; Jay & Sparks, 1987; Groh & Sparks, 1996; Wallace *et al.*, 1996). Studies in anaesthetized cats have shown that SC output neurons projecting to motor-related areas can carry integrated multisensory signals (Meredith & Stein, 1985; Meredith *et al.*, 1992), implying that the sensory processing performed within the SC could have behavioural consequences. This notion is supported by observations showing that the same physical factors (e.g. spatial/temporal disparity) that affect multisensory processing of neurons within the SC also affect orienting behaviours to multisensory stimuli (Stein *et al.*, 1989; Corneil *et al.* 2002). Furthermore, it is known that sensory activity of the SC can affect the motor output of the structure (e.g. Edelman & Keller, 1996; Dorris *et al.*, 1997; Frens & Van Opstal, 1998). However, little is known about how behavioural influences that precede the orienting response might affect the processing of incoming sensory and multisensory signals. In other words, how might the animal's current behavioural state affect sensory processing in the SC? Here we describe the influence of one orienting-related behavioural factor, fixation state, on unimodal and multisensory responses in the SC.

Control of orienting involves two alternating processes: acquisition of a new point of interest by means of a saccade and maintaining fixation on that location by suppressing unwanted saccades. Neural activity implicated in both processes is observed in the SC (for review see Munoz & Fecteau, 2002). Fixation neurons in the rostral SC are tonically active during fixation but pause during saccades (Munoz & Wurtz, 1993) whereas saccade-related neurons, located throughout the rest of the SC, are active immediately before and during a saccade (Wurtz & Goldberg, 1971; Munoz & Wurtz, 1995). It has been hypothesized that a network of inhibitory connections within the SC provides reciprocal inhibition between these two subpopulations of neurons to effectively control when we shift our gaze (Munoz & Istvan, 1998). The relative level of inhibition is dynamically controlled, can be quite subtle and depends greatly on the behavioural demands adopted by the animal. For example, 'actively' engaging fixation on a visible foveal stimulus (i.e. exogenously controlled fixation) suppresses the activity of SC saccade-related neurons (Dorris *et al.*, 1997), and decreases the probability that a stimulus appearing suddenly will initiate a reflexive saccade (Everling *et al.*, 1998). By contrast, maintaining stable gaze in the absence of a visible stimulus (i.e. endogenously controlled fixation) leads to the disinhibition of saccade-related neurons (Munoz & Wurtz, 1995; Dorris *et al.*, 1997), which could facilitate acquisition of a new stimulus.

In addition to being suppressed during visual fixation, many saccade-related neurons also show sensory activity (Sparks, 1986) and are capable of producing response interactions when their different sensory inputs are combined (Meredith & Stein, 1983, 1986; King & Palmer, 1985; Bell *et al.*, 2001). Therefore, we hypothesized that when behavioural state changes from endogenous to exogenous fixation, the

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sensory responses and multisensory interactions of SC neurons will be reduced. This hypothesis was tested by measuring the unimodal visual and auditory responses and multisensory interactions of neurons in the intermediate and deep layers of the SC from awake, nonhuman primates. Two fixation conditions were used: a fixation (FIX) condition, where stimuli were presented concurrently with a visible fixation point; and a fixation-blink (FIX-BLINK) condition, where the fixation point was briefly extinguished (Munoz & Wurtz, 1993). We found that sensory responses and multisensory interactions were weaker in the FIX condition compared to the FIX-BLINK condition, showing that exogenous fixation can suppress sensory and multisensory responses in the SC. Preliminary results from these studies have been presented in abstract form (Bell *et al.*, 2000).

Materials and methods

Preparation of experimental animals

All procedures were approved by the Queen's University Animal Care Committee and were in accordance with the Canadian Council on Animal Care policy on the use of laboratory animals. Two adult male rhesus monkeys (*Macaca mulatta*), weighing approximately 6 and 8 kg, were used in this study. Animals were prepared for chronic experiments in a single surgical session. Details regarding the surgery have been published elsewhere (see Munoz & Istvan, 1998 for details). Animals were prepared for chronic experiments in a single surgical session under isoflurane anaesthesia. Briefly, animals were implanted with scleral search coils (to monitor eye position), a head restraint device, and a recording chamber allowing access to both the right and left SC. Animals were given a course of antibiotic (enrofloxacin) and analgesic (buprenorphine) treatment and monitored closely following surgery. They were given at least 2 weeks to recover before behavioural training and experimentation.

Experimental procedures

Monkeys were trained to maintain central fixation while peripheral visual and/or auditory stimuli were presented (Fig. 1). The onset of each trial was signalled by the removal of the background light and illumination of the fixation point (FP; 8.4 cd/m²) which the animal was required to fixate for 800–1500 ms, after which one of the two following fixation conditions was presented, for half the trials, the FP was visible continuously for the remaining 810 ms of the trial ('FIX' condition); for the other half of the trials, the FP disappeared for 310 ms before reappearing for an additional 500 ms ('FIX-BLINK' condition; Munoz & Wurtz, 1993).

Sensory stimuli consisted of visual, auditory, or combined audiovisual stimuli presented to the response field of the neuron being examined. Visual response fields were mapped using manually presented stimuli (described below). Visual test stimuli were electronically generated and consisted of moving (100–400°/s) rectangular bars of light of preset size (3.25° × 0.75°) and intensity (2.2–5.0 cd/m²). The auditory stimuli consisted of a white noise burst (100 ms duration, 44.0–78.0 dB, A-weighted), produced by small 4 cm, 8.0 Ω speakers suspended in front of the tangent screen, facing the animal. Previous studies have reported the strongest multisensory interactions for combinations of weaker stimuli (i.e. Principle of Inverse Effectiveness; Meredith & Stein, 1986; Wallace *et al.*, 1996). As such, we empirically adjusted the individual stimulus properties (e.g. intensity, direction, etc.) to evoke minimal response levels when presented alone, so as to maximize the potential for stronger interactions. In another study described elsewhere (Bell *et al.* 2001), we systematically manipulated the individual stimulus properties to investigate their influence on multisensory interactions in the awake, behaving nonhuman primate.

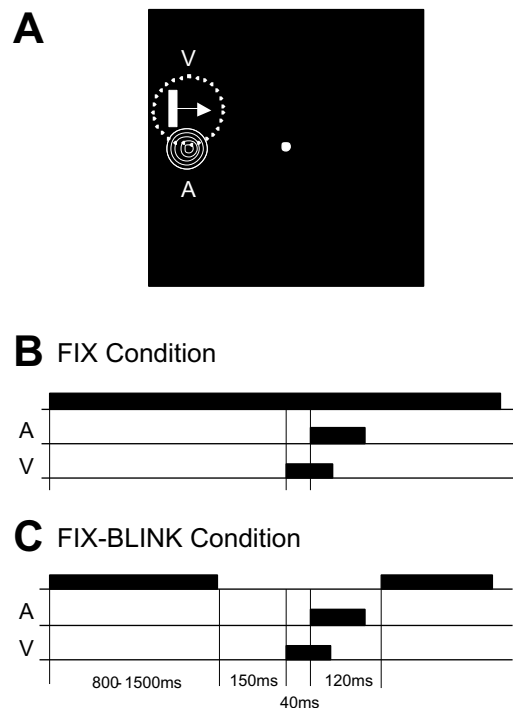


FIG. 1. Schematic representation of the multisensory fixation paradigm employed in this study. (A) Monkeys were required to fixate a central visual fixation point in the presence of visual (V) and/or auditory (A) stimuli. The paradigm included both the FIX condition (fixation point present for the duration of the trial (B)) and the FIX-BLINK condition (fixation point extinguished for a period of 310 ms during which time the peripheral stimuli are presented (C)).

For combined audiovisual stimulation, the stimuli were presented 150 ms (visual) and 190 ms (auditory) after FP disappearance in the FIX-BLINK condition and at the same interval relative to trial initiation with the same 40 ms visual–auditory asynchrony in the FIX condition. This 40-ms delay was introduced to account for differences in SC visual and auditory response latencies, thereby maximizing the likelihood of inducing multisensory interactions when the stimuli were combined (Meredith *et al.*, 1987). Furthermore, removal of the FP results in the disinhibition of SC neurons that peaks in effect approximately 200 ms afterwards (Dorris *et al.*, 1997; Munoz *et al.*, 2000). Thus, in the FIX-BLINK condition, the incoming sensory signals would arrive at the SC at approximately the same time as the SC reaches a minimal level of inhibition, thereby maximizing any potential effects. All trial types (i.e. FIX and FIX-BLINK, all stimulus conditions) were randomly interleaved within a block of trials. Monkeys were given a liquid reward if they maintained central fixation within 2° of the FP for the entire trial without generating any eye movements.

Recording techniques and response field mapping

Single neuron activity was recorded extracellularly in the SC with tungsten microelectrodes (Frederick Haer) having impedances of 0.5–5 MΩ at 1 kHz. Electrodes were driven by a hydraulic microdrive (Narishige MO-95) through stainless steel guide tubes held firmly in place by a Delrin grid placed inside the recording chamber (Crist *et al.*, 1988). Single-neuron activity was sampled at 1 kHz after passing through a window discriminator (Bak Electronics), which excluded action potentials that did not meet both amplitude and temporal constraints. Control of the behavioural paradigms as well as storage

of eye position and neural activity was achieved by a Pentium PC running a real time data acquisition software package (REX Ver. 5.4; Hays *et al.*, 1982). Eye position was sampled at 500 Hz.

To map the extent of a neuron's visual response field, a hand-held ophthalmoscope was used to back-project moving spots and bars of light onto the tangent screen while the monkey maintained central fixation. The visual test stimulus was then positioned so as to sweep through the area that evoked the largest response. Because previous studies have shown that auditory receptive fields in the primate SC tend to be very large (45–180° in the contralateral hemifield in primates; Wallace *et al.*, 1996), no attempt was made to map the extent of the auditory receptive fields and the auditory stimulus was instead placed in close proximity to the visual stimulus. A second speaker was positioned ipsilateral to the recording site to investigate the spatial dependency of multisensory interactions in the awake, behaving primate. These data are not considered for this paper and are instead described elsewhere (see Bell *et al.* 2001).

Data analysis

Before analysis, any incorrect trials (i.e. monkey-generated eye movements) were rejected. Sensory responses were convolved with a spike density function for each trial based on an exponential growth/decay function (Thompson *et al.*, 1996). This asymmetric activation waveform is physiologically more plausible for estimating response latencies than a Gaussian activation function, because a spike exerts an influence only forward and not backward in time. The spike density function was obtained by convolving each spike with the following function:

$$A(t) = \left[1 - \exp\left(\frac{-t}{\tau_g}\right) \right] \cdot \left[\exp\left(\frac{-t}{\tau_d}\right) \right] \quad (1)$$

where the activation level A varied as a function of t according to τ_g , the growth time constant (1 ms), and τ_d , the decay time constant (20 ms). These parameters were selected so as to mimic the characteristics of an excitatory postsynaptic potential. Using these probability spike density functions, each neuron was then analysed for stimulus-aligned activity. A sensory response was defined as a significant increase in activity following stimulus presentation over the baseline activity (mean activity 500–0 ms before stimulus presentation across all trials for

the given condition), assessed using a Wilcoxon rank sum test ($P < 0.05$). All classifications were later verified by the experimenter for consistency and accuracy. The magnitude of the sensory response was taken as the peak instantaneous firing rate of the neuron over the period from 0 to 300 ms following stimulus presentation on a trial-by-trial basis. These values were then averaged across all trials per given condition to yield the neuron's mean response magnitude. Response onset latency was defined as the time after stimulus presentation where the spike density exceeded baseline activity plus three standard deviations. The activity had to remain above this level for a minimum of 15 ms to be classified as a valid sensory response.

Multisensory interactions were identified statistically (Wilcoxon rank sum test; $P < 0.05$) by comparing responses to combined stimuli to those evoked by the best modality-specific stimulus. To determine the magnitude of the multisensory interaction, the following calculation was used:

$$\text{Interaction (\%)} = 100 \times (\text{CM} - \text{SM}_{\text{max}}) / \text{SM}_{\text{max}} \quad (2)$$

where CM is the mean peak response magnitude for all trials to combined visual and auditory stimulation and SM_{max} is the mean peak response magnitude of the strongest unimodal response (Meredith & Stein, 1986). Statistical significance for population data, comparing one condition to another, was assessed using a pair-wise Wilcoxon signed rank test ($P < 0.05$).

Results

Data from a total of 78 neurons were recorded in the intermediate and deep layers of the SC of two monkeys. Thirty neurons (39%) responded to unimodal visual stimuli, four (5%) responded to unimodal auditory stimuli and 34 (43%) responded to both unimodal visual and unimodal auditory stimuli, or were significantly influenced by the combined presentation of audiovisual stimuli (multisensory neurons). The remaining 10 neurons (13%) did not respond to any stimuli in either fixation condition and were not analysed further.

Manipulating the state of visual fixation (i.e. FIX or FIX-BLINK conditions) resulted in significant modulation of the sensory responses of 29% (20/68) of the neurons examined. Figure 2 shows the individual sensory responses recorded from one visual neuron in both fixation

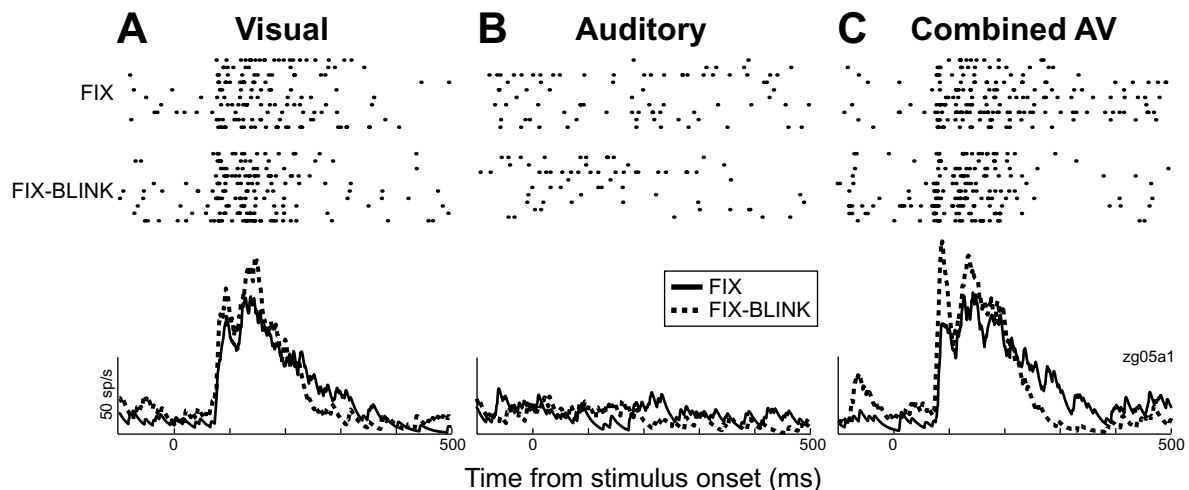


Fig. 2. An example of a visually responsive neuron recorded from the intermediate layers of the SC, exhibiting significantly weaker visual and combined audiovisual responses in the FIX (solid line) vs. the FIX-BLINK (dashed line) condition (Wilcoxon rank sum test; $P < 0.05$).

conditions. This particular neuron showed weaker visual (Fig. 2A) and combined responses (Fig. 2C) in the FIX condition (solid traces) compared to the FIX-BLINK condition (dashed lines), and did not display any auditory responses (Fig. 2B). This was true for the majority of significantly affected neurons (unimodal, $n = 9/34$; multisensory, $n = 11/34$), where 75% (15/20) had weaker responses in the FIX condition compared to the FIX-BLINK condition.

In addition to the individual neurons that showed a difference across fixation condition, a similar trend existed across the sample population; stimuli presented in the FIX condition evoked weaker responses than stimuli presented in the FIX-BLINK condition. Figure 3 shows individual sensory response magnitudes in the FIX condition subtracted from those in the FIX-BLINK condition for unimodal (black traces) and multisensory (grey traces) neurons. These differences are shown as cumulative probability plots, with each point representing the mean difference in activity for the two fixation conditions for a single neuron. Presenting the data in this format eases the comparison of the sample data across fixation condition. For example, points to the right

of the vertical 'zero' line denote responses of the designated neuron type (unimodal or multisensory) that were weaker during FIX than during FIX-BLINK conditions.

The most apparent trend from Figure 3 is that the combined audiovisual responses of multisensory neurons were weaker in the FIX than FIX-BLINK condition, and the significance of this trend was confirmed by a pair-wise comparison of response magnitudes (Fig. 3C; Wilcoxon signed rank test; $P < 0.009$). This trend for weaker responses in the FIX condition was also apparent for visual responses in unimodal and multisensory neurons and approached statistical significance (Wilcoxon signed rank test; $P < 0.09$ and $P < 0.08$, respectively). Importantly, although the differences in response magnitude across fixation condition were modest on a cell-by-cell basis, this analysis confirms that SC neurons as a population were less active in response to visual and audiovisual stimuli presented in the FIX condition.

It also appears that multisensory neurons might be more sensitive to fixation state than unimodal neurons, as evidenced by the rightward

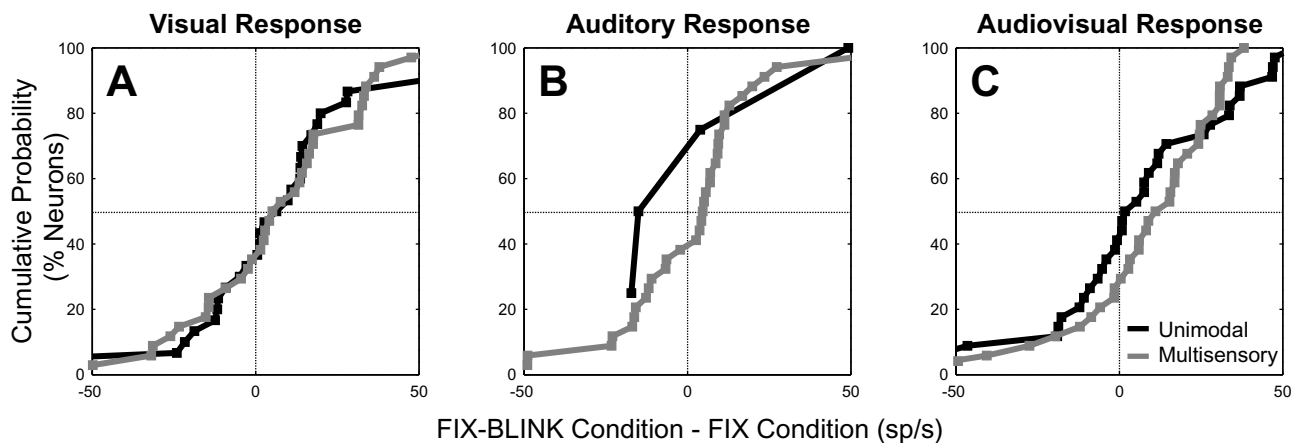


FIG. 3. The state of visual fixation influenced the magnitude of unimodal and combined audiovisual sensory responses. Cumulative probability plots for visual (A), auditory (B) and combined audiovisual (C) responses for unimodal (black traces) and multisensory (grey traces) neurons. Each point represents the arithmetic difference of the mean response magnitude for the FIX-BLINK from the FIX condition. Thus, a positive value indicates a stronger response in the FIX-BLINK condition and vice-versa. The ordinate axis indicates what percentage of neurons exhibited less than or equal to the corresponding difference in response magnitude indicated by the abscissa, ranked according to ascending value. For example, in C the unimodal neuron curve (shown in black) intersects the 50% cumulative probability at approximately the 0 sp./s change in response magnitude, indicating that 50% of the neurons examined had a difference of no more than 0 sp./s. The curve corresponding to multisensory neurons (shown in grey), by contrast, intersects the 0 sp./s change in response magnitude at approximately 25% cumulative probability, indicating that 75% of neurons exhibited greater than 0 sp./s difference in their response magnitudes.

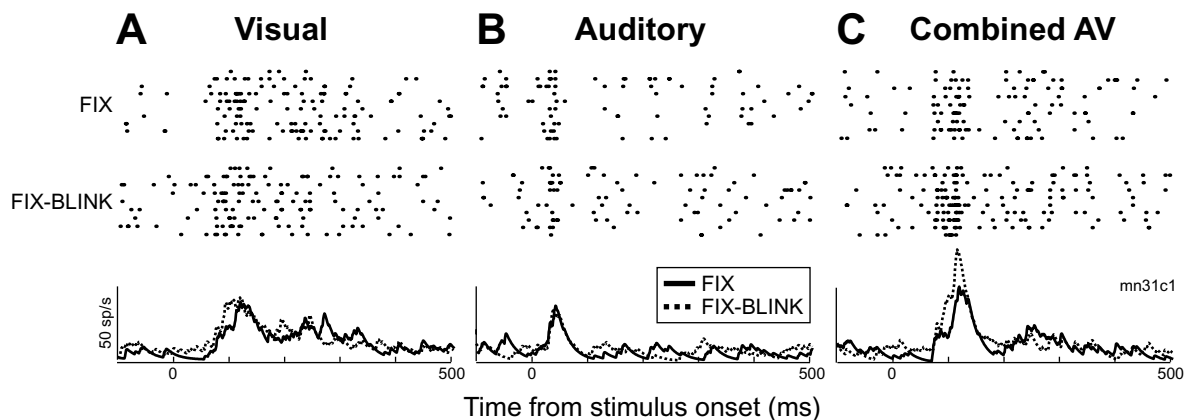


FIG. 4. An example of a multisensory neuron recorded from the intermediate layers of the SC, exhibiting a significant multisensory enhancement in the FIX-BLINK (+32%; Wilcoxon rank sum test; $P < 0.05$) but not the FIX condition (+11%; Wilcoxon rank sum test; $P < 0.20$).

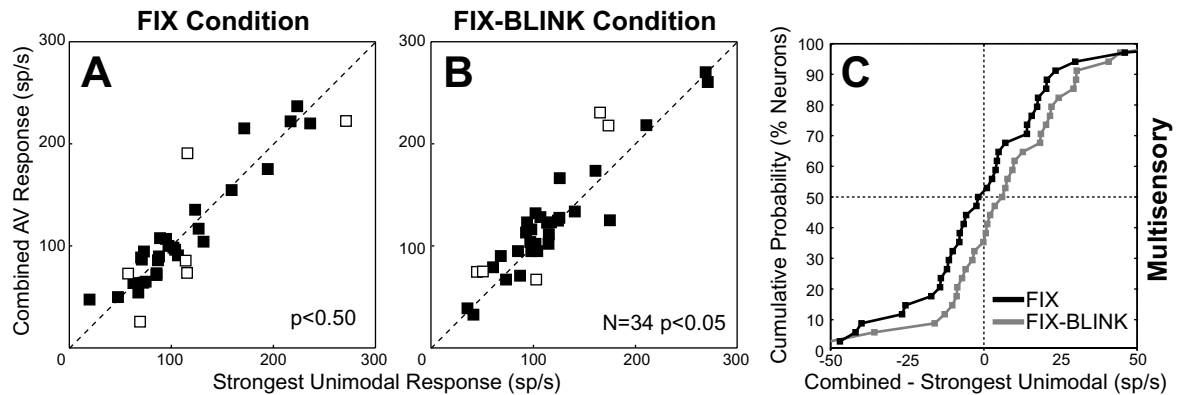


FIG. 5. The state of visual fixation influenced multisensory interactions. Comparison of the response magnitude evoked by audiovisual stimuli versus the strongest unimodal response for the FIX (A) and FIX-BLINK (B) condition. Open squares indicate neurons that exhibited statistically significant multisensory interactions. To further examine how fixation condition influenced multisensory processing, we subtracted the mean strongest unimodal response from the mean combined audiovisual response for each neuron and plotted the resulting values as a cumulative probability plot (same format as Fig. 3) for all multisensory neurons (C), documenting that multisensory responses were influenced differentially by the behavioural state.

TABLE 1. Sensory response latencies of neurons in the SC

Neuron modality	Latency (ms)	
	FIX condition	FIX-BLINK condition
Unimodal (visual response)	75 ± 3 (43–119)	72 ± 2 (43–127)
Unimodal (auditory response)	33 ± 4 (10–50)	32 ± 4 (8–45)
Multisensory (visual response)	76 ± 3 (33–136)	73 ± 3 (25–128)
Multisensory (auditory response)	34 ± 2 (8–96)	36 ± 2 (17–84)

*Data given as mean ± SEM (range).

shift of the grey line relative to the black line in Figure 3C. This possibility was further investigated by examining the effect of the state of visual fixation on multisensory interactions. Figure 4 shows a multisensory neuron that exhibited similar unimodal responses under both fixation conditions, but exhibited a significant response enhancement only in the FIX-BLINK condition with no significant interaction in the FIX condition. Significant multisensory interactions (i.e. response enhancement or depression) were seen in 32% (11/34) of the multisensory neurons examined (open squares; Fig. 5A and B).

It is evident from Figure 5A and B that the types of multisensory interactions were biased by fixation condition. Neurons showing response enhancements in the FIX-BLINK condition (4/5; range, +25 to +66%) were absent or reduced in the FIX condition (range, -16 to +27%). Similarly, response depressions occurred predominantly in the FIX condition (4/6; range, -17 to -59%).

To further characterize how fixation condition affected multisensory processing across the population of multisensory neurons, we subtracted the magnitude of the strongest unimodal response from the combined audiovisual response for each fixation condition. These differences are shown in Figure 5C as cumulative probability plots, so that each point on the curve represents the mean difference in activity for the combined audiovisual and strongest unimodal response for a single neuron. From this plot, it becomes clear that multisensory neurons showed smaller differences between the combined and unimodal responses in the FIX condition compared to the FIX-BLINK condition (evidenced by the leftward shift of the black vs. grey lines), although this trend did not reach statistical significance in our sample ($P = 0.16$; Fig. 5C).

The state of fixation did not affect sensory response latencies ($P > 0.05$; see Table 1). The response latencies of unimodal (visual-

only, auditory-only) and multisensory neurons were essentially unchanged under the different fixation conditions. These ranges of response latencies compare favourably with those reported for SC neurons in anaesthetized cat (Meredith *et al.*, 1987) and monkey (Wallace *et al.*, 1996).

Discussion

Sensory responses and multisensory processing in the SC were both affected by the state of visual fixation. Stimuli delivered when fixation was exogenously engaged (FIX condition) resulted in weaker individual and combined audiovisual responses compared to when fixation was endogenously engaged (FIX-BLINK condition; Fig. 3). These effects were particularly evident for multisensory neurons (Fig. 5), highlighting the connective distinctions between unimodal and multisensory neurons that may supersede the sensory nature of their inputs (Meredith, 1999). Until recently, only changes in the spatial and temporal relationships of the sensory stimuli, or their physical parameters, have been identified as determinants of multisensory interactions (see Stein & Meredith, 1993 for review). Here, we show that a behavioural parameter unrelated to the stimuli, the state of visual fixation, has a subtle but consistent influence on both the magnitude of sensory responses and the relative strength of multisensory interactions.

The influence of fixation on SC neurons is believed to arise from both local circuits within the SC (Mize *et al.*, 1991; Behan & Kime, 1996; Meredith & Ramoa, 1998; Munoz & Istvan, 1998) as well as from projections from other brain areas (e.g. substantia nigra, Hikosaka & Wurtz, 1983; Wurtz & Hikosaka, 1986; cortex, Motter & Mountcastle, 1981; Segraves & Goldberg, 1987; Bender & Youakim, 2001). Exogenous fixation (e.g. FIX condition) has been shown to affect both fixation- and saccade-related neurons in the SC, resulting in modified saccadic reaction times (see Munoz *et al.*, 2000 for review). Similarly, active exogenous fixation suppresses unimodal visual, auditory, and somatosensory responses in the cat SC: an effect known to be a result of reduced excitability of the SC neurons and not simply because of decreased sensory input to those neurons (Guitton & Munoz, 1991).

The present results also have important implications regarding how multisensory integration is thought to function in behaving animals. In the initial studies of multisensory integration at the neuronal level, data from anaesthetized animals showed that a large proportion of neurons

in the SC were multisensory (55–60% in cat, Meredith & Stein, 1986; 28% in monkey, Wallace *et al.*, 1996) and that spatiotemporally coincident combined-modality stimuli could elicit responses that far exceeded the sum of the responses to the same stimuli presented alone (Meredith & Stein, 1986; Jiang *et al.* 2001). However, further work in nonanaesthetized cats (Wallace *et al.*, 1998; Populin & Yin, 2002) revealed a lower incidence of multisensory neurons as well as lower levels of response integration. The present study identified 43% of the sample as multisensory (note that criteria were more inclusive than Wallace *et al.*, 1996), but found significant multisensory interactions in only 34% of those neurons. Furthermore, the range of multisensory enhancement was consistently low (from 25 to 66%). One interpretation of these observations is that the awake animal is subject to additional inhibitory control over multisensory integration that is not evident in the anaesthetized preparation. Fixation-mediated inhibition, for example, is a generalized type of inhibition found across the SC and serves to suppress the powerful visual grasp reflex (Hess *et al.*, 1946; Ingle, 1973), preventing unwanted gaze shifts (Everling *et al.*, 1998). Without this type of generalized inhibitory control acting on SC neurons, sensory activity and multisensory interactions would presumably be much stronger resulting in the generation of excessive orienting movements.

Other factors are also likely to play a role in mediating the relative strength of multisensory interactions in awake animals. For example, in the present study, it was in the animal's best interest to attend exclusively to the FP and suppress any responses to the peripheral stimuli to avoid triggering a reflexive saccade. Consequently, sensory activity and multisensory interactions elicited by these peripheral stimuli would likely be attenuated under such behavioural constraints. By contrast, a study by Frens & Van Opstal (1998), which required monkeys to generate saccades to audiovisual targets, reported significant multisensory interactions in 90% of the saccade-related burst neurons they examined. This proportion of neurons with integrated responses is much higher than was previously reported for the anaesthetized primate (Wallace *et al.*, 1996) and our awake preparation, suggesting that because the stimuli had behavioural relevance (i.e. targets for rewarded saccades), their resulting sensory responses were augmented, which is consistent with similar observations on visual responses in the SC (Wurtz & Mohler, 1976).

We have shown that sensory processing and multisensory integration in the deeper layers of the SC are influenced by the state of visual fixation. These data provide experimental support for human studies that show that the impact of multisensory integration on behaviour is not simply determined by the temporal and spatial register of the stimuli, but is also modulated by contextual processes (e.g. Munoz & Corneil, 1995; Corneil & Munoz, 1996; Driver & Spence, 1998). These results underscore the importance of behavioural context when assessing the relationship between multisensory processing and its adaptive behavioural significance.

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Abbreviations

FP, fixation point; SC, superior colliculus.

References

- Behan, M. & Kime, N.M. (1996) Intrinsic circuitry in the deep layers of the cat superior colliculus. *Vis. Neurosci.*, **13**, 1031–1042.
- Bell, A.H., Corneil, B.D., Meredith, M.A. & Munoz, D.P. (2001) The influence of stimulus properties on multisensory processing in the awake primate superior colliculus. *Can J. Exp. Psychol.*, **55**, 123–132.
- Bell, A.H., Corneil, B.D., Meredith, M.A., Van Opstal, A.J., Abrahams, V.C. & Munoz, D.P. (2000) Multisensory integration in the superior colliculus of the awake behaving primate. *Soc. Neurosci. Abstr.*, **26**, 1221.
- Bender, D.B., Youakim, M. (2001) Effect of attentive fixation in macaque thalamus and cortex. *J. Neurophysiol.*, **85**, 219–234.
- Corneil, B.D. & Munoz, D.P. (1996) The influence of auditory and visual distractors on human orienting gaze shifts. *J. Neurosci.*, **16**, 8193–8207.
- Corneil, B.D., Van Wanrooij, M., Munoz, D.P. & Van Opstal, A.J. (2002) Auditory–visual interactions subserving goal-directed saccades in a complex Scene. *J. Neurophysiol.*, **88**, 438–454.
- Crist, C.F., Yamasaki, D.S., Komatsu, H. & Wurtz, R.H. (1988) A grid system and a microsyringe for single cell recording. *J. Neurosci. Meth.*, **26**, 117–122.
- Dorris, M.C., Paré, M. & Munoz, D.P. (1997) Neuronal activity in monkey superior colliculus related to the initiation of saccadic eye movements. *J. Neurosci.*, **17**, 8566–8579.
- Driver, J. & Spence, C. (1998) Crossmodal attention. *Curr. Opin. Neurobiol.*, **8**, 245–253.
- Edelman, J.A. & Keller, E.L. (1996) Activity of visuomotor burst neurons in the superior colliculus accompanying express saccades. *J. Neurophysiol.*, **76**, 908–926.
- Everling, S., Dorris, M.C. & Munoz, D.P. (1998) Reflex suppression in the anti-saccade task is dependent on prestimulus neural processes. *J. Neurophysiol.*, **80**, 1584–1589.
- Frens, M.A. & Van Opstal, A.J. (1998) Visual–auditory interactions modulate saccade-related activity in monkey superior colliculus. *Brain Res. Bull.*, **46**, 211–224.
- Groh, J.M. & Sparks, D.L. (1996) Saccades to somatosensory targets. II. motor convergence in primate superior colliculus. *J. Neurophysiol.*, **75**, 428–438.
- Guittin, D. & Munoz, D.P. (1991) Control of orienting gaze shifts by the tectoreticulospinal system in the head-free cat. I. Identification, localization, and effects of behavior on sensory responses. *J. Neurophysiol.*, **66**, 1605–1623.
- Hays, A.V., Richmond, B.J. & Optican, L.M.A. (1982) A UNIX-based multiple process system for real-time data acquisition and control. *WESCON Conference Proceedings*, **2**, 1–10.
- Hess, W.R., Burgi, S. & Bucher, V. (1946) Motor function of tectal and tegmental area. *Monatsschr. Psychiatr. Neurol.*, **112**, 1–52.
- Hikosaka, O. & Wurtz, R.H. (1983) Visual and oculomotor functions of monkey substantia nigra pars reticulata. II. Visual responses related to fixation of gaze. *J. Neurophysiol.*, **49**, 1254–1267.
- Ingle, D. (1973) Selective choice between double prey objects by frogs. *Brain Behav. Evol.*, **7**, 127–144.
- Jay, M.F. & Sparks, D.L. (1987) Sensorimotor integration in the primate superior colliculus. I. Motor convergence. *J. Neurophysiol.*, **57**, 22–34.
- Jiang, W., Wallace, M.T., Jiang, H., Vaughan, J.W. & Stein, B.E. (2001) Two cortical areas mediate multisensory integration in superior colliculus neurons. *J. Neurophysiol.*, **85**, 506–522.
- King, A.J. & Palmer, A.R. (1985) Integration of visual and auditory information in bimodal neurones in the guinea-pig superior colliculus. *Exp. Brain Res.*, **60**, 492–500.
- Meredith, M.A. (1999) The frontal eye fields target multisensory neurons in cat superior colliculus. *Exp. Brain Res.*, **128**, 460–470.
- Meredith, M.A., Nemitz, J.W. & Stein, B.E. (1987) Determinants of multisensory integration in superior colliculus neurons. I. Temporal factors. *J. Neurosci.*, **7**, 3215–3229.
- Meredith, M.A. & Ramoa, A.S. (1998) Intrinsic circuitry of the superior colliculus: pharmacophysiological identification of horizontally oriented inhibitory interneurons. *J. Neurophysiol.*, **79**, 1597–1602.
- Meredith, M.A. & Stein, B.E. (1983) Interactions among converging sensory inputs in the superior colliculus. *Science*, **221**, 389–391.
- Meredith, M.A. & Stein, B.E. (1985) Descending efferents from the superior colliculus relay integrated multisensory information. *Science*, **227**, 657–659.
- Meredith, M.A. & Stein, B.E. (1986) Visual, auditory, and somatosensory convergence on cells in superior colliculus results in multisensory integration. *J. Neurophysiol.*, **56**, 640–662.
- Meredith, M.A., Wallace, M.T. & Stein, B.E. (1992) Visual, auditory and somatosensory convergence in output neurons of the cat superior colliculus:

- multisensory properties of the tecto-reticulo- spinal projection. *Exp. Brain Res.*, **88**, 181–186.
- Mize, R.R., Jeon, C.J., Hamada, O.L. & Spencer, R.F. (1991) Organization of neurons labeled by antibodies to gamma-aminobutyric acid (GABA) in the superior colliculus of the Rhesus monkey. *Vis. Neurosci.*, **6**, 75–92.
- Motter, B.C. & Mountcastle, V.B. (1981) The functional properties of the light-sensitive neurons of the posterior parietal cortex studied in waking monkeys: foveal sparing and opponent vector organization. *J. Neurosci.*, **1**, 3–26.
- Munoz, D.P. & Corneil, B.D. (1995) Evidence for interactions between target selection and visual fixation for saccade generation in humans. *Exp. Brain Res.*, **103**, 168–173.
- Munoz, D.P., Dorris, M.C., Paré, M. & Everling, S. (2000) On your mark, get set. Brainstem circuitry underlying saccade initiation. *Can. J. Physiol. Pharmacol.*, **78**, 934–944.
- Munoz, D.P. & Fecteau, J.H. (2002) Vying for dominance: dynamic interactions control visual fixation and saccadic initiation in the superior colliculus. *Prog. Brain Res.*, **140**, 3–19.
- Munoz, D.P. & Istvan, P.J. (1998) Lateral inhibitory interactions in the intermediate layers of the monkey superior colliculus. *J. Neurophysiol.*, **79**, 1193–1209.
- Munoz, D.P. & Wurtz, R.H. (1993) Fixation cells in monkey superior colliculus. I. Characteristics of cell discharge. *J. Neurophysiol.*, **70**, 559–575.
- Munoz, D.P. & Wurtz, R.H. (1995) Saccade-related activity in monkey superior colliculus. I. Characteristics of burst and buildup cells. *J. Neurophysiol.*, **73**, 2313–2333.
- Populin, L.C. & Yin, T.C. (2002) Bimodal interactions in the superior colliculus of the behaving cat. *J. Neurosci.*, **22**, 2826–2834.
- Segraves, M.A. & Goldberg, M.E. (1987) Functional properties of corticotectal neurons in the monkey's frontal eye field. *J. Neurophysiol.*, **58**, 1387–1419.
- Sparks, D.L. (1978) Functional properties of neurons in the monkey superior colliculus: coupling of neuronal activity and saccade onset. *Brain Res.*, **156**, 1–16.
- Sparks, D.L. (1986) Translation of sensory signals into commands for control of saccadic eye movements: role of primate superior colliculus. *Physiol. Rev.*, **66**, 118–171.
- Stein, B.E. & Meredith, M.A. (1993) *The Merging of the Senses*. MIT, Cambridge, MA.
- Stein, B.E., Meredith, M.A., Huneycutt, W.S. & McDade, L. (1989) Behavioral indices of multisensory integration: orientation to visual cues is affected by auditory stimuli. *J. Cogn. Neurosci.*, **1**, 12–24.
- Thompson, K.G., Hanes, D.P., Bichot, N.P. & Schall, J.D. (1996) Perceptual and motor processing stages identified in the activity of macaque frontal eye field neurons during visual search. *J. Neurophysiol.*, **76**, 4040–4055.
- Wallace, M.T., Meredith, M.A. & Stein, B.E. (1998) Multisensory integration in the superior colliculus of the alert cat. *J. Neurophysiol.*, **80**, 1006–1010.
- Wallace, M.T., Wilkinson, L.K. & Stein, B.E. (1996) Representation and integration of multiple sensory inputs in primate superior colliculus. *J. Neurophysiol.*, **76**, 1246–1266.
- Wurtz, R.H. & Goldberg, M.E. (1971) Superior colliculus cell responses related to eye movements in awake monkeys. *Science*, **171**, 82–84.
- Wurtz, R.H. & Hikosaka, O. (1986) Role of the basal ganglia in the initiation of saccadic eye movements. *Prog. Brain Res.*, **64**, 175–190.
- Wurtz, R.H. & Mohler, C.W. (1976) Enhancement of visual responses in monkey striate cortex and frontal eye fields. *J. Neurophysiol.*, **39**, 766–772.