Onset of Cross-Modal Synthesis in the Neonatal Superior Colliculus is Gated by the Development of Cortical Influences

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Wallace, M. T. and B. E. Stein. Onset of cross-modal synthesis in the neonatal superior colliculus is gated by the development of cortical influences. J Neurophysiol 83: 3578–3582, 2000. Many neurons in the superior colliculus (SC) are able to integrate combinations of visual, auditory, and somatosensory stimuli, thereby markedly affecting the vigor of their responses to external stimuli. However, this capacity for multisensory integration is not inborn. Rather, it appears comparatively late in postnatal development and is not expressed until the SC passes through several distinct developmental stages. As shown here, the final stage in this sequence is one in which a region of association cortex establishes functional control over the SC, thus enabling the multisensory integrative capabilities of its target SC neurons. The first example of this corticotectal input was seen at postnatal day 28. For any individual SC neuron, the onset of corticotectal influences appeared to be abrupt. Because this event occurred at very different times for different SC neurons, a period of 3–4 postnatal months was required before the adult-like condition was achieved. The protracted postnatal period required for the maturation of these corticotectal influences corresponded closely with estimates of the peak period of cortical plasticity, raising the possibility that the genesis of these corticotectal influences, and hence the onset of SC multisensory integration, occurs only after the cortex is capable of exerting experience-dependent control over SC neurons.

INTRODUCTION

The ability to respond to stimuli from different sensory modalities, and the ability to integrate the information from these different modalities, are characteristic properties of neurons in the superior colliculus (SC) (see Stein and Meredith 1993). Each multisensory SC neuron has multiple receptive fields that are in spatial register. As a consequence of this organization, multiple sensory stimuli (e.g., visual and auditory) originating from the same event will fall within the overlapping receptive fields of the same neuron, resulting in a substantially enhanced response (Meredith and Stein 1996). If, however, one of those stimuli is outside its receptive field, it can inhibit the neuron’s responses to the other stimulus (Kadunce et al. 1997). In a parallel manner, overt orientation and approach behaviors are facilitated by spatially coincident visual-auditory stimulus combinations, and depressed when these stimuli are spatially disparate (Stein et al. 1989).

Recently, however, it has been shown that multisensory integration is not an obligatory property of these neurons. In the adult, the cortex surrounding the anterior ectosylvian sulcus (AES), compromises the multisensory integrative capabilities of SC neurons (Wallace and Stein 1994) and the multisensory behaviors on which they depend (Wilkinson et al. 1996). Furthermore, early in life the responses of neonatal multisensory SC neurons to combinations of cues from different modalities typically are no different from their responses to those cues when presented individually (Wallace and Stein 1997). Thus the present study was initiated to determine if, as postulated (see Wallace and Stein 1997), the appearance of SC multisensory integration reflects the development of corticotectal influences, and, if so, what maturational changes these influences undergo.

METHODS

Procedures were conducted in accordance with the guidelines established by the Institutional Animal Care and Use Committee of Wake Forest University, are identical to those previously reported (Wallace and Stein 1994, 1997), and will be described only briefly. In anesthetized animals, multisensory SC neurons were isolated using extracellular recording techniques. The neuron’s receptive fields were mapped and its modality-specific and multisensory response profiles were quantitatively determined. The location, timing, and physical characteristics of the stimuli were varied in an effort to maximize multisensory response enhancement. The criterion for multisensory integration was a statistically significant (paired t-test) increase in the number of impulses evoked by a cross-modal stimulus combination (e.g., visual-auditory) over that evoked by the most effective (‘dominant’) modality-specific stimulus. When this criterion was reached, the magnitude of the resultant interaction for each neuron was calculated using the formula

\[
\% \text{ interaction} = \left[ \frac{(CM - SM_{max})}{SM_{max}} \right] \cdot 100
\]

where CM is the combined modality response and SM_{max} is the response to the most effective single modality. Modality-specific and multisensory responses were recorded before, during, and after cortical deactivation by cryoblockade (e.g., Wallace and Stein 1994). A deactivation-induced effect was a significant (t-test) decline in multisensory enhancement. Only cases in which postdeactivation responses returned to within 20% of control levels were considered for further analysis.

RESULTS

The responses of multisensory SC neurons (n = 104) were quantitatively examined in 37 neonatal animals ranging in age from 1–135 days postnatal (dpn). These data were compared with an adult data set (n = 78) previously collected (Wallace and Stein 1994). Prior to 28 dpn, multisensory SC neurons...
failed to exhibit multisensory integration and in all but 2 cases their responses were unaffected by AES deactivation.
The first neuron exhibiting multisensory integration was encountered at 28 dpn, and AES deactivation eliminated the neuron’s enhanced multisensory response without significantly affecting its modality-specific responses. This selectivity of AES deactivation for multisensory enhancement proved to be characteristic, with only 15/104 (14%) of the neurons examined showing effects on modality-specific responses. In this small group of neurons, these effects averaged a 28% reduction in one of the two modality-specific responses. These modality-specific effects did not change in either incidence or magnitude during development, were equivalent for integrating and non-integrating neurons and, as in the adult cat (Jiang et al. 1999), were not predictive of any AES deactivation-induced changes in multisensory responses. As development progressed, the proportion of integrating multisensory neurons grew; these neurons were almost invariably affected by AES deactivation, and they were often found in clusters (Fig. 1).

Interestingly, AES deactivation effects on the youngest multisensory integrative neurons were comparable to those found in adults (Wallace and Stein 1994; Jiang et al. 1999). Thus despite a steady developmental increase in the incidence of neurons exhibiting adult-like multisensory integration (Fig. 2), neither the magnitude of their multisensory response enhance-
ment nor the magnitude of the effect of AES deactivation showed any age-dependent changes. Such a result suggests that for any given SC neuron, the functional AES link was established abruptly, so that the neuron was immediately rendered capable of adult-like multisensory integration (Fig. 2). That this functional transition was attributable to the onset of an AES-SC functional link was also consistent with the observation that AES deactivation eliminated the differences between the multisensory responses of the populations of integrative and nonintegrative neurons (Fig. 3).

DISCUSSION

These observations suggest that the development of the SC from a strictly modality-specific structure to a structure in which its neurons can respond to (but not integrate) multiple sensory modalities (see Stein et al. 1973; Wallace and Stein 1997) reflects the functional maturation of inputs from sources other than AES. However, the transition from this nonintegrative multisensory state to the adult integrative state appears to be intimately tied to the functional maturation of inputs from AES. It is not possible, in the absence of longitudinal recordings from the same neurons, to determine whether individual SC neurons pass through each of these developmental phases. Nevertheless, this seems likely, and provides a parsimonious explanation for why so many neonatal multisensory SC neurons fail to integrate cross-modal cues, but why so few such neurons are encountered in adults (Wallace and Stein 1997). Given that the incidence of recorded sensory neurons in the SC differs little from about 6 wk to maturity, despite major changes in the incidence of multisensory integrative neurons, there is little support for the possibility that integrative multisensory neurons remain inactive until they become fully capable of integrating cross-modal information.

The strikingly selective effect of AES deactivation on multisensory integration in neonatal SC neurons parallels the finding in adults, in which the majority of SC neurons have been shown to depend on influences from the AES for their multisensory integration capabilities but not for their ability to respond to individual cues from different modalities (Wallace and Stein 1994; Jiang et al. 1999). These observations support the hypothesis that the ontogeny of multisensory integration in the SC is, in large part, a reflection of the maturational onset of corticotectal influences from the AES (see Wallace and Stein 1997). Moreover, the data suggest that this event takes place in an abrupt, or “gate-like,” manner on any given SC neuron, and immediately provides that neuron with the capability to engage in multisensory integration. This helps explain the findings that the magnitude of multisensory interactions and the susceptibility of such interactions to AES deactivation remain relatively constant during development. The apparent abrupt onset of corticotectal influences from the AES onto multisensory (i.e., deep layer) SC neurons is not without precedent, as there is also an abrupt onset of corticotectal influences from primary visual cortex onto superficial layer visual neurons (Stein and Gallagher 1981). The small number of neonatal SC neurons that exhibited multisensory integration and in which this integration was unaffected by AES deactivation were likely dependent on influences from an adjacent region of association cortex, the rostral lateral suprasylvian cortex (Jiang et al. 1999).
FIG. 3. Nonintegrative and integrative multisensory neurons differed in their reactions to AES deactivation. Left: the multisensory responses of the population of nonintegrating neonatal neurons (pooled over age) is plotted as a function of their dominant modality-specific responses before (●) and during (○) AES deactivation. Note that the best fit to the data showed that there was no significant difference between the multisensory response of these neurons and their dominant modality-specific response (gray line, unity; ANOVA, \( F = 1.73, P > 0.05 \)), and that AES deactivation had no significant effect on their responses (repeated measures ANOVA, \( F = 2.34, P > 0.05 \)). Inset shows that the multisensory response was significantly less than the algebraic sum of the two modality-specific responses (gray line) and that, once again, AES deactivation had little effect on the response function. Right: in contrast, the multisensory responses of integrative neurons were significantly greater than their dominant modality-specific response (ANOVA, \( F = 45.6, P < 0.01 \)) and the sum of their modality-specific responses (ANOVA, \( F = 12.6, P < 0.05 \)). AES deactivation shifted these functions downward (repeated measures ANOVA, \( F = 61.2, P < 0.001 \) for main graph; \( F = 68.7, P < 0.001 \) for inset), rendering them indistinguishable from the functions for their nonintegrative counterparts (ANOVA, \( F = 1.93, P > 0.05 \) for main graph; \( F = 1.55, P > 0.05 \) for inset).

It is interesting to note that the AES, long considered an “association” area, does indeed play an associative role and appears to do so in two ways. It contains not only a substantial population of multisensory neurons that can integrate their multiple sensory inputs in much the same way as do SC neurons (Wallace et al. 1992; Jiang et al. 1994), but also a substantial number of corticotectal neurons (Stein et al. 1983) that mediate multisensory integration in the SC (Wallace and Stein 1994). It is surprising to note that these represent independent circuits. Multisensory neurons in AES do not project to the SC, whereas many of their modality-specific counterparts do (see Wallace et al. 1993).

Although AES corticotectal projections are already identifiable in newborn animals (McHaffie et al. 1988), apparently they are not functional in animals younger than four postnatal weeks. While little is known about the development of AES, the present data demonstrate that the maturational course of its functional influences on SC neurons corresponds well with the most sensitive period of structural and functional modifications of primary sensory cortex (e.g., Wiesel and Hubel 1965; Daw et al. 1992), a period that is essential to adapt cortex to the animal’s environment. Given that the responses of AES neurons are also plastic (Rauschecker and Korte 1993), it is intriguing to consider the possibility that AES corticotectal influences over any individual SC neuron are initiated only after these inputs are capable of modulating SC processes and SC-mediated overt responses in an adaptive fashion.

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