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8. If we estimate the rate of flow of receptors by dividing the receptor accumulation per day by the receptor content of the vagus per millimeter of nerve, we obtain a rate of 3.5 mm per day from the data in Fig. 2. This estimation assumes (i) that all the receptors are flowing, (ii) that there is no swelling of the nerve, (iii) that the flow rate is constant over the entire period of ligations, and (iv) that the ligation does not affect the flow rate. Previous experiments suggest that these assumptions may not be totally valid. For example, in studies of axonal transport of acetylcholinesterase, it was found that only 10 percent of the axonal enzyme was moving (*1*). Our microscopic studies suggest that some swelling occurs on the proximal side of the ligature. There is a technical limitation in that the grain density on the proximal side (Fig. 1 and 2) is somewhat beyond the limits of linearity compared to that on the distal side. For example, in an experiment with [^{3}H]naloxone with shorter exposures, the proximal to distal ratios were 10 or 12 to 1 (*9*), a result that could double our estimated rate. Thus, the actual concentration of radioactivity on the proximal side compared to that on the distal side is higher than the grain density would suggest in Fig. 2, and a more accurate estimate of the receptor flow rate could well be larger.
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Superior Colliculus: Control of Eye Movements in Neonatal Kittens

Abstract. *Activation of the neonatal cat superior colliculus can produce organized eye movements before visual stimuli are capable of activating visual neurons in the colliculus. These findings are consistent with the hypothesis that eye movement development precedes, and is necessary for, visuomotor integration.*

The ability to respond appropriately to visual cues (visuomotor integration) develops gradually with experience. Hein *et al.* (*1*) demonstrated that eye movements that produce image displacements across the retina are necessary for visuomotor development. Since central neurons responsive to visual stimuli (*2*–*4*) and the optical apparatus itself (*5*) require months to mature, the gradual association of visual stimuli and motor responses may be due, in large part, to the long maturational course of the sensory apparatus related to "seeing." The motor apparatus may already be functional in very young animals.

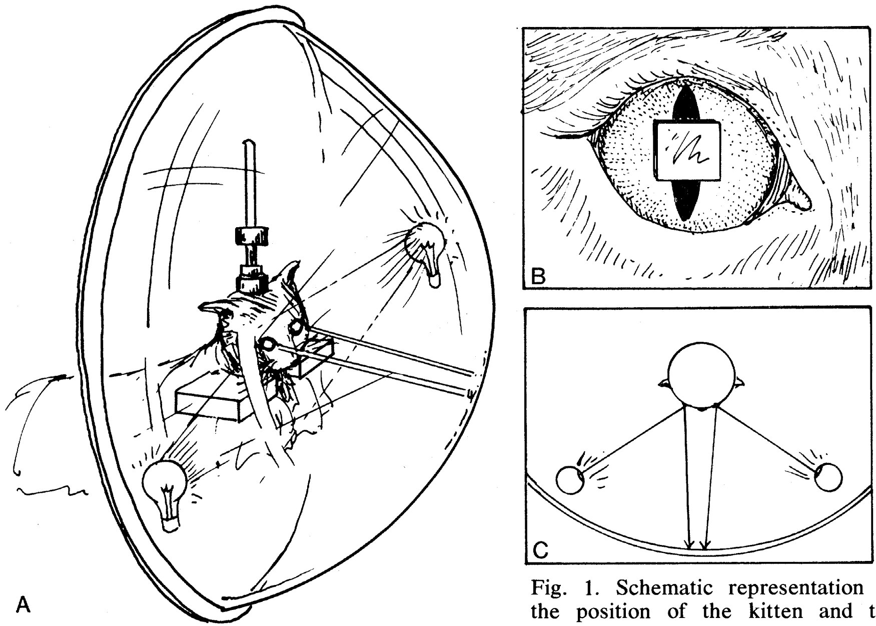

Fig. 1. Schematic representation of the position of the kitten and the apparatus. A permanent mounting bolt and hollow cylinder were implanted on the animal's skull. (A) The head was positioned at the geometric center of a translucent (not transparent, as drawn) hemisphere, and electrodes reached the superior colliculus through the hollow cylinder. (B) Small mirrors were fixed to the anesthetized eyes, and (C) beams of light, reflected from these mirrors, appeared as spots of light on the hemisphere. A pattern of 10° concentric circles was scribed on the hemisphere; eye movements caused movement of the light spots whose excursions were traced directly on the hemisphere's surface.

We previously demonstrated that visual cells in an area of the brain that plays a role in visuomotor integration (the superior colliculus) are not functional before 7 days of age and show a protracted developmental course thereafter (*2, 3*). On the basis of these observations we speculated that a structure such as the superior colliculus, whose role is normally to integrate sensory information and motor responses, might set the stage for visuomotor integration by developing the capacity to move the eyes even before visual sensation becomes a significant source of information (*6*). We now report that kittens are capable of some spontaneous eye movement even at 2 days of age and that electrical stimulation of the superior colliculus in the animals elicits eye movements with many of the same features seen in the adult (*7*).

Twenty-six kittens 2 to 77 days of age and six adult cats were studied. Prior to the experimental session, a stainless steel chamber was implanted on the skull over a cranial opening (*8*). Mounting bolts were fixed to the skull to provide an atraumatic means of securing the head during testing, and the entire assembly was held in place with anchoring screws and dental acrylic. On the experimental day, ketamine hydrochloride, a short-acting anesthetic, was administered, the animal was placed in a retaining bag, and the head was fixed to a stereotaxic headholder by the implanted bolts. The eyelids were opened when necessary, the eyes anesthetized with 0.5 percent proparacaine hydrochloride, and a small mirror was glued to each cornea. Light beams were reflected from the mirrors (Fig. 1) onto a translucent hemisphere so that two spots of light were clearly visible on this surface and moved as the eyes moved. The displacement of the light spots was exactly twice that of the eye movements in degrees of arc.

Testing began as soon as the anesthetic began to wear off and the animal moved either spontaneously or in response to tactile stimuli (*9*). A monopolar electrode approached the superior colliculus through the visual cortex in 0.5-mm steps. At each step, a 70-msec, 700-μA "search" stimulus consisting of 0.1-msec rectangular pulses at 200 pulses per second was delivered. When an eye movement was produced at a given locus, its threshold (*10*) was determined. The electrode was subsequently lowered in 0.25-mm increments, and movement thresholds were determined at these sites. Several stimulation series were conducted with various stimulus in-

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tensities at sites with the lowest eye-movement threshold. Electrolytic lesions placed at strategic loci in successful penetrations facilitated the later histological reconstruction of electrode tracks. At the end of an experiment, the animal was anesthetized with pentobarbital (40 mg per kilogram of body weight) and perfused through the heart with saline followed by Formalin. The brain was blocked and either frozen and cut into 40- to 50-μm sections or embedded in paraffin and cut into 20-μm sections; the sections were stained with cresyl violet.

A wealth of spontaneous saccadic and pursuitlike eye movements were observed in older kittens ($>$ 4 weeks of age, $N = 5$) and adult cats. Electrical stimulation of the colliculus in these animals evoked contralateral contraversive movements, and our earlier observations indicating an eye movement map in the intermediate and deeper laminae (11) were confirmed. Stimulation of medial sites produced upward movements, whereas stimulation of lateral sites produced downward movements. Stimulation of progressively more caudal regions produced progressively larger eye movements.

In contrast to the many saccadic eye movements exhibited by older kittens, the eyes of the seven neonatal animals ($\leq$ 1 week of age) were remarkably immobile. Slow drifts of the eyes were interspersed with long periods of immobility, and rapid movements were very rare. In some cases, a rapid eye movement was evoked by tactile stimuli, but usually this could not be repeated. This apparent absence of movement may have been due, in part, to the residual effects of the anesthetic. Yet a functional motor organization underlying eye movements was already laid down in these animals. Stimulating the oculomotor nucleus (later histologically verified) readily produced saccadic movements; functional connections between the superior colliculus and the extraocular motor nuclei were also present in these young animals.

Electrical stimulation of the superior colliculus produced saccadic movements in even the youngest (2 days of age, $N = 2$) animals studied (12). These movements (Fig. 2) had many of the same features as those of adult animals (11): they were conjugate and contraversive, with excursion length dependent upon stimulation intensity. Thus, stimulation of the left superior colliculus produced a deflection of the eyes to the right, and stimulation of the right colliculus produced eye movements to the left. The presence of a topographical organization at this developmental stage can be seen in Fig. 2 where stimulating homotopic loci in the two colliculi produced near mirror image eye movements. As in the adults, the threshold for eye movements dropped precipitously when the electrode reached the intermediate strata, and increasing stimulus intensity increased the length of the eye movement excursion.

Despite these adultlike eye movement characteristics, many loci in the neonatal, but not in the adult colliculus, were ineffective in producing eye movements. Yet the eyes did move when the oculomotor nucleus was stimulated. In addition, thresholds for evoking movements were more than three times as high in neonates and the movements were smaller than those observed in adults. Neonatal eye movements rarely exceeded 10°, and were usually less than 5° of excursion even when current was two to six times threshold. In adults, movements were rarely less than 5° and often as large as 20° under the same stimulus conditions. In addition, in the kittens, the angle of eye movements on successive trials with identical stimuli was more variable than in adults. This sometimes made it appear that nonconjugate movements were evoked in neonates. These "immature" characteristics became less pronounced in older animals, and at 6 to 8 weeks of age, when the sensory responses of colliculus cells are mature (2, 3), these differences between kittens and adults had virtually disappeared.

Some of these age-dependent differences in eye movements may have been due to mechanical factors. The shape and size of the eye changes considerably during the first few weeks of life, and the extraocular muscles show

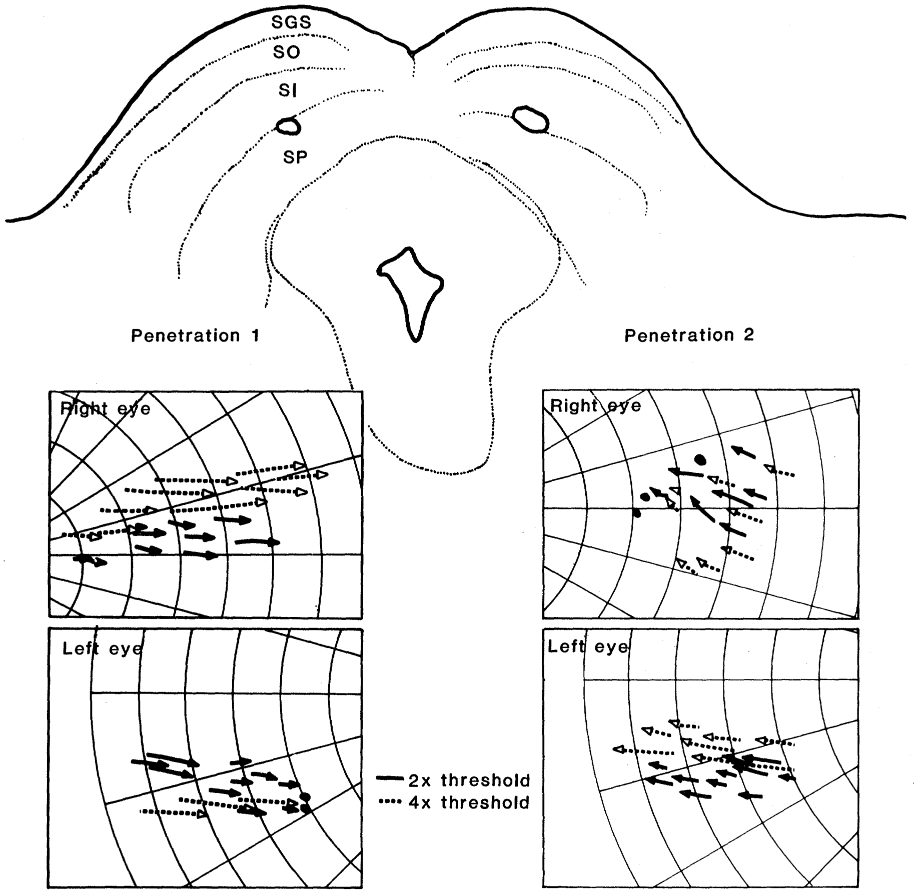

Fig. 2. Eye movements evoked by stimulation of the superior colliculus in a 2-day-old kitten. Stimulation of corresponding points in the left (penetration 1) and right (penetration 2) colluculi evoked contralateral contraversive eye movements. Eye movements are represented by arrows and are shown here as they appeared on the surface of the hemisphere (twice their actual size). Portions of the hemisphere map are shown here with concentric circles of the map at 10° intervals. The current intensities were multiples of the minimum current required to produce a detectable eye movement (10). Dots on the maps represent the position of the light spot during a trial in which no movement was evoked. The directions of evoked eye movements from the nearly homotopic stimulation sites in the two colliculi were approximate mirror images of one another. Stimulation sites are indicated by tracings of the marked lesions (ovals). Abbreviations: *SGS*, stratum griseum superficiale; *SO*, stratum opticum; *SI*, stratum intermediale; and *SP*, strata profunda.

dramatic changes in their contractile characteristics (*13, 14*). Furthermore, the optical axes are not fully aligned until after the second month of life (*14, 15*). Thus, the same neural output from the colliculus may produce large, coordinated movements between the two eyes in adults when the eyeballs and extraocular muscles are mature and smaller movements, which seem less coordinated, in the neonate. In addition, younger kittens will detoxify anesthetics more slowly than adults and some of these discrepancies might reflect the effects of the anesthetic (*16*). Consequently, the neural substrate for eye movements in the neonatal superior colliculus might be even more highly developed than could be demonstrated in these experiments.

The observation that eye movements can be elicited from the superior colliculus before cells in the colliculus can be activated by visual stimuli is consistent with the hypothesis advanced earlier: the development of eye-movement control systems precedes maturation of visual responses even in an area of the brain concerned with visuomotor integration. Since the motor responses seem to be necessary to "make sense" of the visual input (*1*), this developmental sequence seems appropriate. It is intriguing to consider what produces eye movements in these young animals in order to initiate the process of associating visual stimuli with motor responses, an association critical for normal visuomotor integration. This process may occur as the result of spontaneously generated eye movements or of eye movements initiated by vestibular stimulation (*17*). Another possibility is that tactile or auditory stimuli initiate eye movements via the superior colliculus. The different sensory modalities represented in the colliculus [visual, auditory, somatic, vestibular (*18*)] have been hypothesized to have access to the same motor outputs (*19*) that orient receptor organs (*11, 12*). Thus, stimuli from any of these sensory modalities may evoke organized eye, ear, or head movements. Since cells in the intermediate and deeper layers of the superior colliculus are responsive to tactile stimuli at birth and auditory stimuli at 5 days of age, these stimuli might initiate the eye movements, which, in turn, set the stage for later visual-motor associations.

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8. Young kittens received 0.1 to 2.5 ml of ketamine hydrochloride, and adults received either 1.5 to 2.5 ml of ketamine hydrochloride or 35 mg/kg of pentobarbital. Implantations were generally made 1 to 7 days before testing. In the youngest kittens, however (2 to 8 days of age), implantation occurred immediately before testing; all wounds and pressure points were extensively infiltrated with a long-lasting local anesthetic (Zyljectin) and then coated with a second anesthetic (Xylocaine jelly) before the head was secured for testing.
9. The testing session was variable in length. Despite the absence of painful wounds or pressure points, some kittens reacted to restraint by struggling or emitting stress vocalizations (more than a single meow). When such signs were exhibited, the experiment was abruptly ended. In some cases, only a single electrode penetration was made, in others two or more could be completed; young animals were studied for as little as 10 minutes and occasionally for well over 1 hour.
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Brain Events Underlying Detection and Recognition of Weak Sensory Signals

Abstract. *Through the use of a quantitative extension of signal detection theory, the brain events associated with the detection and recognition of weak acoustic signals were examined by recording brain event-related potentials. The early N100 component of the event-related potential varied only with detection, whereas the late P300 component varied with both detection and recognition. P300 amplitude accurately predicted recognition performance on a trial-by-trial basis. The results suggest that detection and recognition are partially concurrent processes in perception and demonstrate that the electrocortical events occurring during the perception of sensory stimuli are closely associated with both detection and recognition of these stimuli by the nervous system.*

Human observers are often required to detect the presence of weak sensory signals in the environment. Examining an x-ray for a suspected tumor, listening to sonar returns for the presence of a ship, and noticing a hidden obstruction on the highway are examples of signal detection, a phenomenon that has been extensively analyzed from the perspective of signal detection theory, or SDT (*1*). However, detection is only one aspect of the normal perception of weak sensory signals; the other is recognition or identification. A driver at night will not only notice a weak visual signal but will attempt to identify it as a relevant environmental stimulus, such as a tree, a child, or another automobile. Similarly, the radiologist and the sonar operator must also recognize as well as detect their targets. The relationship between detection and recognition, however, and the brain events mediating this relationship are not well understood. Two important questions are whether detection and recognition are independent processes and whether recognition can be predicted from detection or from the brain events subserving these aspects of perception. A related point of interest is whether detection and recognition are sequential or concurrent temporal processes.

We approached this problem by examining the event-related potentials (ERP's) of the brain, which provide a unique method for assessing dynamic properties of human cerebral function during cognitive processing. In pure signal detection, the amplitudes of both an early negative component, N100, and a late positive component of the ERP, P300, increase monotonically with in-