This demonstration of circulating factors, dependent upon the presence of complement and capable of producing a reversible synaptic blocking effect when applied directly to CNS tissue, may be significant in explaining the pathogenesis and clinical course of EAE and MS. However, the specificity of the demonstrated reaction in terms of the "demyelinative disorders" cannot be fully evaluated until the serums of patients with destructive but not essentially demyelinative lesions are examined.

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Visually Evoked Electrocortical Responses in Kittens: Development of Specific and Nonspecific Systems

Abstract. *Visually evoked electrocortical responses were differentiated ontogenetically in young kittens by age of onset, latency, and polarity. A long-latency negative wave, present by 4 days of age and abolished later by lesions of the superior colliculus and pretectal region of the midbrain, is attributed to the nonspecific sensory system. A short-latency, positive and negative, diphasic wave, developing by 10 to 15 days of age and blocked by lesion of the lateral geniculate body, is identified with the specific visual system.*

Recently there has been heightened interest in the structural, biochemical, and electrophysiological properties of the developing brain and its relationship to the ontogeny of behavior (*1*). Extensive investigations of the electrophysiology of the visual system have been made in adult animals, but there have been few studies of the maturation of electrocortical activity of the visual area in newborn and young animals, apart from electroencephalographic studies in human infants (*2*). Cross-sectional samplings, at different ages, of electrocortical responses to visual stimulation have been made in the rabbit (*3*) and kitten (*4*). These have revealed important changes in visually evoked potentials as a function of age.

Our interest has focused upon the significance of the time sequence of development of visually evoked responses in kittens as revealed in both longitudinal and cross-sectional studies from the time the kittens are a few days old, when the first response component appears, until they are 1 or 2 months old, when the evoked potential has attained essentially the form typical of the mature cat. The separation of early-developing and late-developing components of the evoked response in the natural course of the maturational process has made it possible to study the characteristics of the components separately as a function of age. Additionally, the separation of response components (by time of onset, polarity, latency, amplitude, and cortical distribution) at certain ages has made it possible to study the effect upon these components of selective midbrain and thalamic lesions.

The lesions were made on the basis of the hypothesis that an initially appearing wave of negative polarity, long latency, and widespread distribution is mediated by the nonspecific sensory system, and that a later-developing diphasic wave of positive and negative polarity, short latency, and more limited distribution is mediated by the classical, specific, visual projection system. The hypothesis appears to have been confirmed by our studies, in that lesions of the superior colliculus and pretectal region of the midbrain blocked the long-latency response, and lesions of the lateral geniculate body interfered with the short-latency response.

Forty kittens from 20 litters were studied at various ages; emphasis was placed on serial recordings. In the most extensive longitudinal sequence recordings were made repeatedly on the same kitten approximately every 5 days from the 4th to the 56th day of age. Both acute preparations (temporarily anesthetized for each recording) and chronic preparations (unanesthetized animals with permanently implanted electrodes) were used. In the case of the former the kittens were immobilized by light Nembutal anesthesia each time recordings were made. Brief flashes from a Grass PS-1 photostimulator were collimated and focused by an optical system and delivered monocularly. The eyelids were held open with a retractor, and the pupil was dilated with homatropine. Monopolar recordings (a mouthpiece served as grounded reference lead) and bipolar recordings were obtained bilaterally over two visual-response sites (shown in *1* of Fig. 2). In the chronic preparations screw electrodes were implanted in the skull over the same visual-response sites.

The sequence of development of the visually evoked responses was similar in cross-sectional and longitudinal methods of study.

Figure 1 shows a typical longitudinal sequence recorded at increasing age levels in the same kitten. The first response to appear over the visual cortex on the side opposite the eye stimulated (the contralateral visual cortex) was a single, long-latency wave of negative polarity with a peak latency of 165 msec. This is typically observed at 4 or 5 days of age. By 10 days of age the amplitude of this negative wave reached its maximum, and its latency diminished; also a shorter-latency negative wave usually preceded by a positive wave, as shown in Fig. 1, first appeared between 10 and 15 days of age. During the period from 10 to 30 days this shorter-latency, positive and negative, diphasic wave increased in amplitude and decreased slightly in latency to relatively stabilized values of 40 and 60 msec for its positive and negative peaks, respectively. Concurrently, the original long-latency, negative wave decreased in amplitude and latency until, at approximately 30 days, this wave appeared to coalesce with the shorter-latency negative wave and became relatively indistinguishable from it. The ipsilateral visual cortex (on the same side as the eye being stimulated) typically manifested the same electrocortical features as the contralateral visual cortex, but with delayed maturation of the response. The components of the ipsilateral response are slower to emerge and their peak latencies are slightly longer (about 4 to 5 msec) even after the adult-type pattern appears at 30 to 40 days.

In the chronic preparations (kittens with permanently implanted electrodes) in which recordings were made periodically without the necessity of anesthetization, evoked potentials averaged by computer were recorded over a span of ages and showed a similar developmental sequence of potential changes in response to binocular light flash during the first 30 days. Thereafter the evoked response had a form resembling that of an unanesthetized adult cat, a configuration in which a positive-negative-positive wave complex is followed by a slower negative component.

It is important to emphasize (see Fig. 1, "contralateral" tracing) that at 4 days of age only the long-latency negative wave is present, but that from day 10 to day 20 both short-latency and long-latency components are present and distinct; thereafter there is a gradual merging of the components. The fact that the short- and long-latency components are present, but separated, from 10 to 20 days of age led to our making lesions in the superior colliculus and pretectal region of the midbrain at this time in an attempt to eliminate the long-latency negative

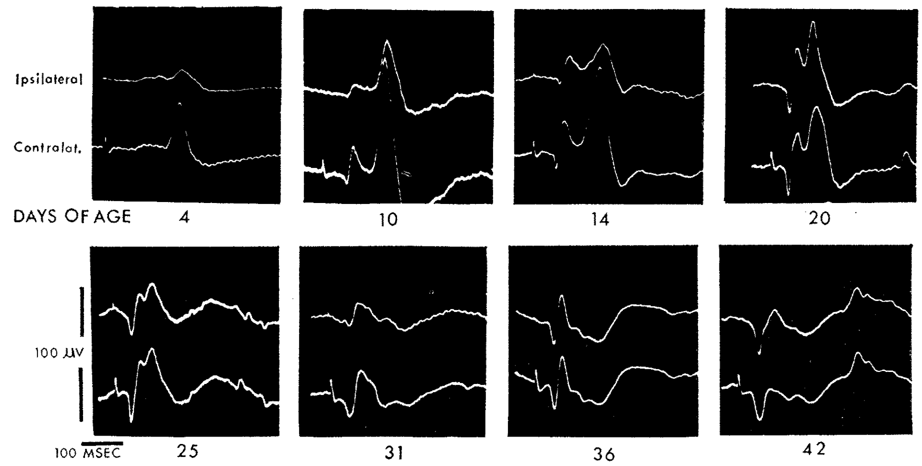

Fig. 1. Development of cortical potentials evoked by a light flash to the right eye in a kitten studied at successive age levels; the kitten was lightly anesthetized with Nembutal for each recording session. Monopolar recordings were made from the right (ipsilateral) and left (contralateral) visual cortex from leads 6 and 5, respectively, of Fig. 2, *I*. The light flash is indicated by an initial sharp upward deflection on the bottom trace. On day 4 only a long-latency wave of negative polarity is well developed in the contralateral tracing; it first increases in amplitude (day 10), then diminishes (days 14, 20, and 25), and steadily decreases in latency from day 4 to day 31. A diphasic (positive-negative) wave appears at day 10, increases in amplitude from days 10 to 25, and decreases slightly in latency from days 10 to 31. By day 31 the early-appearing negative wave has diminished in latency sufficiently to coalesce with the later-appearing negative wave of short latency, thereby resulting in a wave form similar to the visually evoked potential of a mature cat. In both Figs. 1 and 2 an upward deflection indicates negative polarity at the recording site.

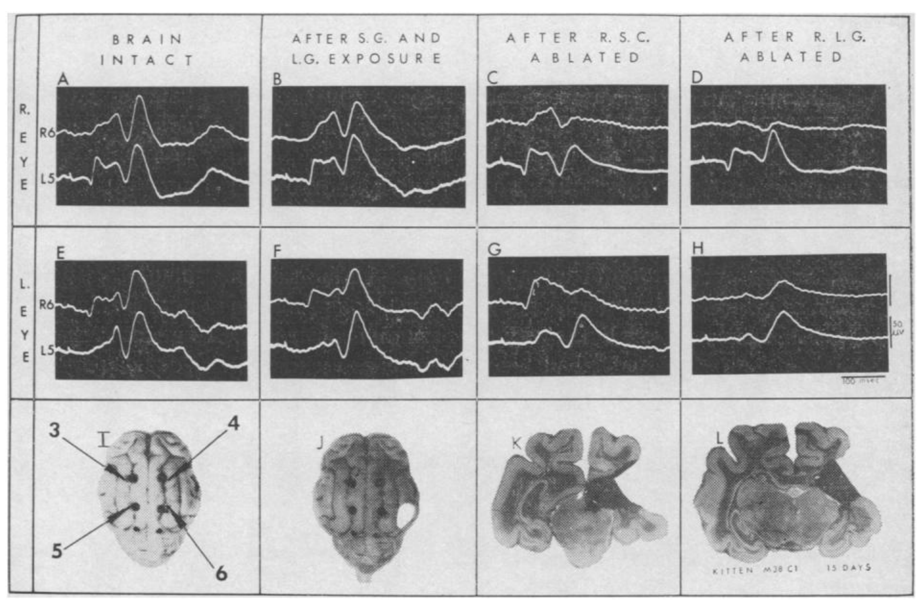

Fig. 2. Cortical potentials evoked in response to a light flash (first upward deflection on bottom trace) in a lightly anesthetized 15-day-old kitten; the flash was delivered to the right eye (R. eye) in records *A* to *D* or to the left eye (L. eye) in records *E* to *H*. Traces labeled *R6* and *L5* are from the right and left visual cortex, respectively, as shown in *I*. *A* and *E*, typical evoked responses from *R6* and *L5* with stimulation of the right and left eyes, respectively. *B* and *F*, control records, obtained after right posterolateral exposure (*J*) of superior colliculus (S.C.) and lateral geniculate body (L.G.) but before lesions were made in these structures. *C* and *G*, records after ablation of right superior colliculus (R.S.C.) as shown in *K*. *D* and *H*, records after subsequent ablation of right lateral geniculate body (R.L.G.) as shown in *L*. Ablation of the right superior colliculus blocks the long-latency negative wave from the right visual cortex (see *R6* in *C* and *G*). Ablation of the right geniculate body blocks the short-latency negative wave evoked from the right visual cortex by right-eye stimulation (see *R6* in *D*) and blocks the positive and negative wave complex evoked from the right visual cortex by left-eye stimulation (see *R6* in *H*).

wave believed to be associated with function of the nonspecific sensory system. Similarly, lesions of the lateral geniculate body were made in an attempt to remove the short-latency, positive-negative wave complex believed to be related to specific visual function. Lesions were made electrolytically by stereotaxic control and also by aspiration under direct observation.

Lesions in the superior colliculus and pretectal area in kittens aged 9, 13, 15, and 17 days in all cases abolished or markedly diminished only the long-latency negative wave associated with the nonspecific visual system. Lesions in the lateral geniculate body in kittens aged 13, 15, and 16 days in all cases removed or greatly diminished only the short-latency waves associated with the specific visual system.

Figure 2 illustrates how both of these results were obtained in a 15-day-old kitten. The right eye (*A* to *D*) and the left eye (*E* to *H*) were stimulated separately with flashes of light; in each instance, only the tracing from the contralateral visual cortex showed a full complement of the components of the visually evoked response which have been observed at this age, including the long-latency negative wave of early origin and the positive-negative wave complex of shorter latency which appears subsequently. The short-latency positive component in a kitten of this age is usually absent or of low amplitude in the tracing from the ipsilateral visual cortex.

Columns 1 and 2 of Fig. 2 show typical visually evoked responses before (*A* and *E*) and after (*B* and *F*) operative exposure (*J*) of the fields where lesions are to be made. The control records (*B* and *F*) are not appreciably different from the initial records (*A* and *E*). Successive, two-stage ablations were made of (i) the right superior colliculus and pretectal region of the midbrain (*K*) and (ii) the right lateral geniculate body (*L*), by aspiration, under direct visual observation, through the lateral approach shown in *J*. In records *C* and *G*, made after removal of the right superior colliculus, the long-latency negative wave in the trace (*R*6) for the right visual cortex is abolished or markedly diminished but that in the trace (*L*5) for the left visual cortex is not. The short-latency, negative wave in *R*6 of *C*, and the positive-negative complex in *R*6 of *G* are relatively unaffected. In records *D* and *H*, after subsequent removal of the right lateral geniculate body, the short-latency negative component seen in *R*6 in *A*, *B*, and *C* and the short-latency positive-negative components seen in *R*6 in *E, F*, and *G* are removed only in the tracings (*R*6 in *D* and *H*) from the visual cortex on the side of the lesion.

Thus, a lesion of the right superior colliculus abolished or diminished the long-latency negative wave from the cortex on the side of the lesion when either eye was stimulated but did not affect the short-latency positive or negative components. A lesion of the right lateral geniculate body abolished the short-latency negative wave in the trace (*R*6) from the right visual cortex, with either right-eye (*D*) or left-eye (*H*) stimulation. Also, after this lesion, the positive wave component, which in *E, F*, and *G* occurred only in the trace (*R*6) from the visual cortex on the side opposite to stimulation, was absent from the trace (*R*6 in *H*) from the right visual cortex when the left eye was stimulated.

Therefore, the long-latency negative wave which appears first as the animal develops and which has been hypothesized to be a nonspecific sensory component, is blocked by a lesion of the superior colliculus and pretectal region. (It was not appreciably affected in several animals with only lesions of the lateral geniculate body.) Conversely, the short-latency positive-negative components are affected only by lesions of the lateral geniculate body and not by lesions of the superior colliculus and pretectum. Accordingly, these positive-negative components are attributed to the specific visual system.

Such a differentiation of electrocortical evoked responses into components associated with specific and nonspecific systems was aided by the serial recordings which reflected maturational changes and showed a separation of these system components at early ages. Further electrical and behavioral investigation of the visual modality in kittens is under way in an effort to clarify the development and interaction of specific and nonspecific visual systems, and to more clearly delineate their pathways and mechanisms.

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Facilitation: Electrical Response Enhanced by Conditional Excitation of Cerebral Cortex

Abstract. *Cats were conditioned to give a foot flexion in response to stimulation of the brain through implanted electrodes. The evoked electrical activity of an extracallosal interhemispheric pathway was much greater in the repeatedly stimulated direction than in the unstimulated direction in the brain. No difference in the two directions was observed in control animals that did not receive the unconditional foot shock.*

Changes have been reported in electroencephalograms (EEG) and evoked potentials obtained during short-term conditioning experiments. The report of Galambos and Sheatz (*1*) is especially noteworthy. Unfortunately, the reported changes in amplitudes of evoked potentials and in wave frequencies of EEG's as related to a conditioned behavior (temporary connections) were labile and not predictably persistent.

A new approach by John *et al.* (*2*), in which an analysis of correlation