

indicate that trunk muscles are unable to regain normal tonus and form (Fig. 2). Tetanic convulsions or chronic muscular rigor (or both) are associated with scoliosis and probably produce the fractured vertebrae of severely affected fish. The possible effects that Kepone may have on fish calcium metabolism, on the corpuscles of Stannius (because of their calcium-mediating role in some fishes), and on muscle contraction have not yet been evaluated.

The mechanism or mechanisms whereby different organochlorine compounds affect organisms are poorly understood. Human victims of Kepone poisoning have suffered tremors, nervousness (hyperkinesia), loss of memory, and slurred speech, among other effects (7). The human response syndrome suggests neurological lesions, some of which probably occur at higher nervous centers, as a result of Kepone poisoning. Tremors and other neurological-dependent responses in laboratory animals increased in severity with increasing Kepone concentration and duration of exposure (7). Hansen, *et al.* (5) observed the same correlation between concentration of Kepone, duration of exposure, and severity of scoliosis and related signs in fish. Our observations suggest that the severity of scoliotic effects in the sheepshead minnow is related to the duration of continuous exposure to a single low Kepone concentration (4  $\mu$ g/liter). Much higher concentrations of Kepone (2 to 400 mg/kg per day) are required to elicit neuropathological, reproductive, and tissue effects in birds or mammals (7).

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## Limbic System Interrelations:

### Functional Division Among Hippocampal-Septal Connections

**Abstract.** *Neuronal activity was recorded simultaneously from hippocampus and medial or lateral septum during classical conditioning of the rabbit nictitating membrane response. Although similarities exist between hippocampal and lateral septal patterns of activity, medial septal unit discharges indicate a different role during learning.*

Interrelations between hippocampus and septum have been a major focus of neurophysiological and anatomical investigation (1). Recent evidence implicates the hippocampal-septal system in learning (2). Our laboratory has recently reported dramatic changes in neuronal activity in the hippocampal formation during classical conditioning of the nictitating membrane response of the rabbit (3). We now relate unit activity of the medial and lateral septal nuclei to hippocampal neuronal plasticity using this paradigm.

Methodological details have been described previously (3). Two microelectrodes per animal were permanently implanted, one in the dorsal hippocampus (CA1 or CA3) and one in either the medial or lateral septum. After 1 week of recovery, animals in the conditioning group were given 13 blocks of trials per day, with eight CS-UCS (4) paired trials and one CS-alone (1-kHz, 85-dB, 350-msec tone) test trial per block. The UCS was a 100-msec air puff to the cornea, onset 250 msec after CS onset. Animals were given one, sometimes two, days of conditioning. Control animals received 13 blocks of unpaired CS and UCS presentations per day, with eight CS-alone and eight UCS-alone presentations, for 16 unpaired trials per block. Data from 19 conditioning and 8 control animals are reported here.

Multiple-unit activity (3) was recorded simultaneously from hippocampus and septum during all phases of training. Recordings were subsequently band-pass filtered, with a pulse-height discrimina-

tor set to pass only the larger units. Unit analysis consisted of computing (i) the mean and standard deviation of cell discharges occurring 250 msec prior to CS onset (pre-CS period) and (ii) the mean number of spike events during equal intervals after CS onset (CS period) and UCS onset (UCS period). A standard score was computed for each block of trials for the CS period and the UCS period relative to the pre-CS period (3). Poststimulus histograms of the total number of neural responses (per 15-msec time bin) in all three periods were also constructed for each block. Behavioral analysis consisted of an analog-to-digital conversion of the amplitude-time curve of nictitating membrane movement for each trial. At the completion of training, animals were anesthetized, current was passed through each electrode, and placements were verified histologically after perfusion.

Analysis of lateral septal neuronal records ( $N = 10$ ) revealed, in all but one case, the same pattern of unit activity seen in previously reported hippocampal results (3). Figure 1, A and B, shows the average nictitating membrane responses plus hippocampal and lateral septal poststimulus histograms from a typical animal at early and late phases of conditioning. Both hippocampal and lateral septal recordings show a rapid growth of unit activity in the UCS period early in training, long before behavioral conditioning (Fig. 1A). In addition, the pattern of unit firing, as represented by both poststimulus histograms, temporally precedes and parallels the amplitude-time

Table 1. Mean standard scores of unit activity in the CS period (CSP) and the UCS period (USP) computed from hippocampal (paired  $N = 11$ ; unpaired  $N = 5$ ), lateral septal (paired  $N = 10$ ; unpaired  $N = 4$ ), and medial septal (paired  $N = 9$ ; unpaired  $N = 4$ ) electrode site recordings during training trials.

Block	Hippocampus		Septum			
	CSP	USP	Lateral		Medial	
			CSP	USP	CSP	USP
Paired						
First	1.27	6.91	1.47	5.44	4.19	7.78
Last	5.42	15.90	5.02	13.29	1.63	4.00
Unpaired						
First	0.18	1.80	0.13	3.04	2.50	6.84
Last	0.33	3.22	1.34	1.81	0.29	5.40

course of the nictitating membrane response. As paired training proceeds and behavioral conditioned responses develop, increases in hippocampal and lateral septal activity occur in the CS period as well. Finally, responses during both lateral septal and hippocampal (3) UCS periods increase in magnitude throughout the course of paired training (Fig. 1B). Differences between hippocampus and lateral septum are evident only in the rates of growth of UCS period activity over trials on day 1. Across blocks, the hippocampal response shows a negatively accelerating trend, while the lateral septal response increases linearly.

In contrast to lateral septal findings, medial septal results ( $N = 9$ ) do not show parallels with the type of neuronal plasticity exhibited in the hippocampus (Fig. 1, C and D). Instead, medial septal neurons show evoked unit activity to

both tone and air-puff presentation. For the same measures from paired training on day 2, the hippocampal response has increased significantly and has shifted temporally into the CS period (Fig. 1D). The pattern of medial septal activity, on the other hand, has remained constant across blocks, the only change being a decrease in the magnitude of the evoked response to CS and UCS onsets.

Data from control animals ( $N = 8$ ) given unpaired CS and UCS trials indicates that, although unit increases of lateral septal conditioning animals are unique to the paired paradigm, neuronal responses seen in medial septal animals are not (Fig. 2). For blocks of air-puff-alone training trials from days 1 and 2 of unpaired training, there are reflex responses to the UCS presentation, yet there is no unit increase associated with nictitating membrane movement (Fig. 2,

A and B). For the tone-alone trials of the same blocks of unpaired training, there are no sensitization responses to the CS presentation and no evoked neuronal discharges associated with the stimulus occurrence (Fig. 2, C and D). Findings from the unpaired trials of lateral septal animals showed no change in unit activity across blocks during either CS- or UCS-alone trials and, in total, were equivalent to previously reported hippocampal control results (3). Although analysis showed large conditioning-versus-control differences for lateral septum, recordings from medial septum revealed identical paired and unpaired patterns of neural discharge. Unit responses in the medial septum are also elicited by unpaired air-puff and tone presentations (Fig. 2, E to H).

Analysis of standard scores indicated that, although the relative amount of hip-

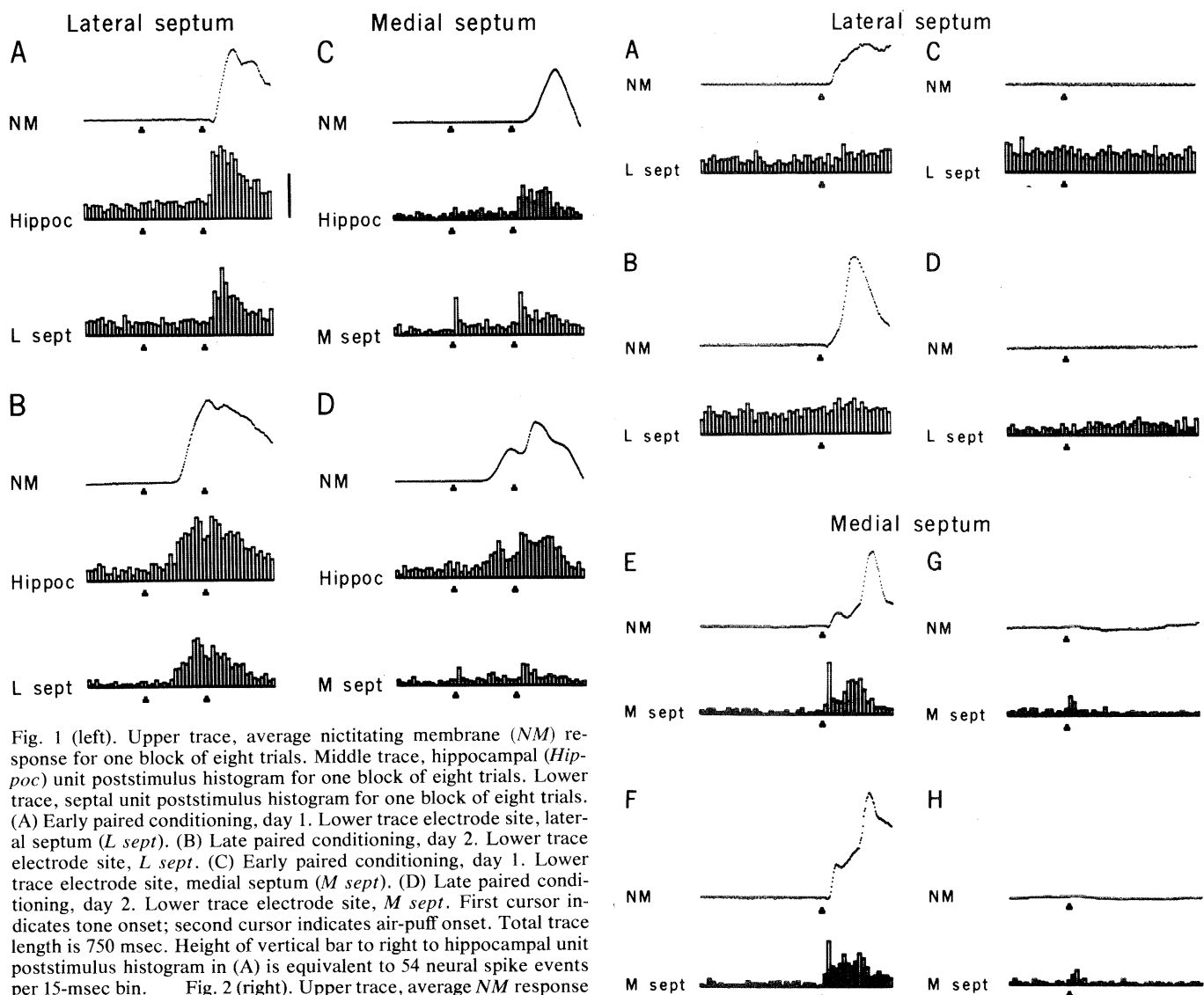


Fig. 1 (left). Upper trace, average nictitating membrane (NM) response for one block of eight trials. Middle trace, hippocampal (Hippoc) unit poststimulus histogram for one block of eight trials. Lower trace, septal unit poststimulus histogram for one block of eight trials. (A) Early paired conditioning, day 1. Lower trace electrode site, lateral septum (L sept). (B) Late paired conditioning, day 2. Lower trace electrode site, L sept. (C) Early paired conditioning, day 1. Lower trace electrode site, medial septum (M sept). (D) Late paired conditioning, day 2. Lower trace electrode site, M sept. First cursor indicates tone onset; second cursor indicates air-puff onset. Total trace length is 750 msec. Height of vertical bar to right of hippocampal unit poststimulus histogram in (A) is equivalent to 54 neural spike events per 15-msec bin. Fig. 2 (right). Upper trace, average NM response for one block of eight trials. Lower trace, septal unit poststimulus histogram for one block of eight trials. (A) Early block of UCS-alone trials, day 1. (B) Late block of UCS-alone trials, day 2. (C) Early block of CS-alone trials, day 1. (D) Late block of CS-alone trials, day 2. Lower trace electrode site (A to D), L sept. (E) Early block of UCS-alone trials, day 1. (F) Late block of UCS-alone trials, day 2. (G) Early block of CS-alone trials, day 1. (H) Late block of CS-alone trials, day 2. Lower trace electrode site (E to H), M sept. Early cursor indicates tone onset; late cursor indicates air-puff onset. Total trace length is 750 msec.

pocampal and lateral septal unit activity increases progressively over training for conditioning animals only, medial septal neuronal responses decrease across trials for both paired and unpaired groups (Table 1). For both the lateral septal and medial septal responses, a  $2 \times 13$  analysis of variance was computed for paired versus unpaired standard score measures over all blocks of trials. Consistent with the interpretation of medial septal activity as sensory evoked responses, analysis of variance failed to reveal any significant differences between groups in paired and unpaired conditions for either period, on either day. Moreover, responses during both paired and unpaired CS periods ( $P < .05$ ) and UCS periods ( $P < .01$ ) showed a significant across-block decrement on day 1. Lateral septal trends were also confirmed, with the between-groups effect significant for the UCS period on both days ( $P < .01$ , day 1;  $P < .05$ , day 2), and the CS period differences reaching significance ( $P < .05$ ) by day 2.

Although many studies have indicated septal involvement in learning (2), our findings now argue for a distinction between possible roles of the medial and lateral septal nuclei. Neuronal records obtained from the lateral septum are completely consistent with anatomical descriptions of that area as a primary efferent projection site for hippocampal pyramidal cells (1). These results further support an association between hippocampal function and learned behavior (3), as most aspects of hippocampal cellular response correlated with nictitating membrane conditioning are also seen at the level of the lateral septum. On the other hand, our findings imply that the medial septum may function in an afferent capacity with respect to the hippocampus, at least in this learning paradigm, responding primarily to stimulus onsets. This implication is supported by anatomical evidence (1) and is in accordance with characterizations of medial septal activity as "arousal" in nature (5).

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## Event-Related Brain Potentials: Comparison Between Children and Adults

**Abstract.** *Event-related brain potentials in response to tachistoscopically presented stimuli were recorded from adults and children. Rare, nontarget stimuli (both novel and easily recognized) elicited different brain potentials in children and adults, while equally rare, target stimuli elicited similar potentials in children and adults.*

Although the averaged event-related brain potential (ERP) has been studied in infants and children (1), ERP wave forms with latencies later than 250 to 300 msec have seldom been examined. Shelburne (2), studying children aged 8 to 12 years found late positive waves (latency, 450 to 600 msec) in response to the last letter of three-letter words that were presented one letter at a time, tachistoscopically. Symmes and Eisengart (3), however, studying children aged 5 to 11 years, found large negative waves (latency, 520 msec) in response to colorful pictures of cartoon figures and familiar objects such as toothbrushes and keys; they did not report finding P3 waves or any other late positive waves. It is unclear whether the different waves found in these two studies reflect differences in subject populations, tasks, stimuli, or attention or arousal levels. Furthermore, no comparisons of such late waves in children with those in adults have been reported.

In an effort to compare late waves elicited in normal children to those of adults, I presented four categories of visual stimuli to ten children (age 6 to 8 years) and ten adults (age 23 to 35 years) (4). The results show that novel and easily recognized stimuli that are nontargets (that is, not counted by the subject) and deviate from an ongoing sequence of background stimuli elicit very long latency negative and positive waves in

children (termed Nc and Pc waves); in contrast, such stimuli consistently elicit P3 waves in adults. However, in response to equally infrequently presented but target stimuli (those counted by the subject), P3 waves similar to those seen in adults are recorded in children.

Each subject reclined in an easy chair 2.5 m from a viewing screen. Slides were flashed onto this screen at regular intervals of 1250 msec; each flash lasted 80 msec and subtended 2.3° of visual angle. Subjects fixated their eyes on a dot at the center of the viewing screen during slide presentations.

Four types of visual stimuli were used in different phases of this experiment: (i) slides bearing the letter A, each subtending a visual angle of 0.5° and having a luminance of 1.8 log cd/m<sup>2</sup>; (ii) slides bearing the letter B with the same visual angle and luminance as A slides; (iii) slides bearing any letter from C to Z, each subtending a visual angle of 0.2° and having a luminance of 1.3 log cd/m<sup>2</sup> (termed dim); and (iv) slides bearing novel stimuli, each consisting of a different, quasi-random, unrecognizable color pattern, subtending a visual angle of 2.3° and having a luminance of 1.2 log cd/m<sup>2</sup> (5).

Before the recording session began, each subject was shown a sample 20-slide sequence of A's and B's and was told that the slides would be presented in