

intrauterine malnutrition may persist for a very long time, and perhaps be permanent and affect the next generation as well, with the implication that pathological disorders known to be associated with immunodeficiency, such as autoimmunity, frequent infections, and neoplasia, may be commoner in individuals with such perinatal history and in their children.

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## Response Plasticity of Lateral Geniculate Neurons During and After Pairing of Auditory and Visual Stimuli

**Abstract.** *Neurons of the lateral geniculate nucleus, responsive only to visual stimulation, show response plasticity during and after pairing of auditory and visual stimuli. Modal response histograms reveal a gradual decrement in the number of spikes at inter-stimulus pairing intervals of 0 and 100 milliseconds but not 500 milliseconds. This plasticity effect, limited to tonic units, may persist for 2 to 3 minutes after termination of click-flash pairing.*

Few studies have described plasticity or response modifiability of single visual units in the central nervous system of vertebrates as a result of either unimodal or cross-modal pairing of sensory stimuli (1, 2). We have determined the "conditionability" (plasticity or response modifiability) of units in the lateral geniculate nucleus of the cat as a result of pairing of auditory and visual stimuli. These units were differentiated by type of response (tonic or phasic) to visual stimuli. None were responsive to auditory stimuli before, during, or after stimulus pairing. Unit response modifiability was not of the classical conditioning type in which a response to an effective (unconditioned) stimulus is transferred to an originally ineffective (conditioned) stimulus. A period of pairing of auditory and visual stimuli did not cause lateral geniculate units, originally unresponsive to auditory stimulation, to become responsive; instead, the response to visual stimulation was gradually modified, and, in some instances, this response modification persisted for an appreciable period

of time after cessation of the pairing of the auditory and visual stimuli. The response modification during and after stimulus pairing consisted in a decrease of responsiveness, as shown by a reduction of the spike count of the modal peak of the peri-stimulus-time histogram (PSTH).

These results have a twofold importance, one, in demonstrating that unit response modifiability can be induced gradually in a specific sensory system during intermodal pairing of stimuli, and two, in showing that response plasticity may persist beyond the period of pairing of the auditory and visual stimuli.

Four cats prepared for repeated recording were employed in this study. Initially, each animal was anesthetized with halothane and an opening was made in the skull over which a metal cylinder 1 cm in diameter was mounted in dental acrylic. A microelectrode could be inserted via this cylinder into the lateral geniculate body. Three bolts mounted in the acrylic pedestal were inserted in a metal plate attached to the stereotaxic instrument and held the an-

imal's head rigidly and painlessly without the use of ear and eye bars. After recovery from surgery, each animal was used for several 3- to 5-hour recording sessions, spanning a 2- or 3-week period. Before each recording session the animal was anesthetized with halothane, the trachea was intubated with an endotracheal tube coated with lidocaine (Xylocaine), and the animal was placed on artificial respiration after infusion of gallamine triethiodide (Flaxedil) via an indwelling venous catheter. Thereafter, halothane anesthesia was discontinued. Pupils were dilated with 2 percent homatropine hydrochloride, and the nictitating membrane was retracted by topical application of 10 percent Neosynephrine.

Single unit activity was recorded from the lateral geniculate nucleus with stainless steel microelectrodes coupled with an emitter follower, the output of which was amplified by a Grass P-5 a-c preamplifier and recorded on FM tape by an Ampex SP-300 tape recorder. Unit responses were monitored on a Tektronix 565 oscilloscope and photographed by a Grass kymograph camera.

The animals were in an electrically shielded, dark, quiet room, facing a white, translucent, plastic hemisphere 30 cm in diameter. The cat's eye was 20 cm from the front surface of the hemisphere. The light flash (20  $\mu$ sec) was produced by a Grass PS-2 photostimulator, encased in a sound-attenuating box, which illuminated uniformly the entire surface of the plastic hemisphere. Miniature insert earphones in each auditory meatus, driven by square-wave pulses from a Grass S-4 physiological stimulator, furnished a 75-db click stimulus.

Once a single lateral geniculate unit giving a stable response to light flash was located by audiometer and observed on the oscilloscope, it was classified as a tonic or phasic unit by its response to a steady spot of light, projected by an ophthalmoscope. After these preliminaries a "conditioning" procedure was initiated which consisted of three consecutive phases: (i) flashes alone (one per 2 seconds for 10 minutes); (ii) click-flash pairing (inter-stimulus intervals of 0, 100, or 500 msec) for 5 minutes; and (iii) flashes alone (one per 2 seconds) for 10 minutes. Seven successive PSTH's, each based on 40 stimulus presentations, were computed in each of phases 1 and 3 of the experiment, and three in phase 2. The PSTH's were computed by a Mnemotron computer of average transients (model 400B) with a bin width of 2.5 msec, covering a 500-msec epoch, and were plotted with a Moseley x-y plotter.

Of 53 units showing stable responses throughout phase 1 (flash alone), 33 were phasic units and 16 were tonic units, as judged by their previously determined response to steady light; for four the response pattern could not be clearly classified as phasic or tonic (3). Nine of the 16 tonic units showed response modifiability during the phase of click-flash pairing. Response modification consisted in a progressive reduction in the amplitude of modal discharge of the PSTH's during click-flash pairing (Fig. 1). This effect was obtained with interstimulus intervals of 0 or 100 msec, but not 500 msec. In four of the nine tonic units exhibiting response plasticity, this effect persisted for 2 to 3 minutes after cessation of the click-flash pairing (Fig. 1A) during phase 3 (flash alone). The other five units showed this effect only during the click-flash pairing phase, after which the modal discharge amplitude returned immediately to the level before pairing (Fig. 1B). In none of the instances in which the effect occurred were there any significant changes in latency of the modal spike discharge. Histological examination revealed that all tonic units manifesting plasticity were recorded from sites in either layer A or A<sub>1</sub> of the dorsal lateral geniculate nucleus.

During phase 1, none of the tonic units showed a habituation effect—that is, a progressive decrement in the modal response of the PSTH's—throughout the 280 flashes comprising the seven PSTH's of this phase. However, two of the 33 phasic units showed such an effect during phase 1. At the onset of phase 2, the PSTH's of these two phasic units immediately showed a marked, but incomplete, recovery of amplitude of the modal discharge. During the click-flash pairing the habituation effect was again seen, but marked recovery again occurred at the start of phase 3. Thus, the change in stimulation at the onset of phases 2 and 3 had a dishabituation effect. None of the phasic units showed the plasticity—that is, reduction of modal response amplitude during and after the click-flash pairing phase—described above for the tonic units.

In order to determine the composition of the modal spike discharge for the PSTH's that showed the plasticity effect, all of the single trial responses comprising the histograms during each of the phases of the conditioning procedure were recovered from the tape records and displayed on the oscilloscope screen. The number of individual spikes for each stimulation was determined, and the mean and standard deviation for each group of 40 responses were tabulated. During the portions of phases 2 and 3 in which the plasticity was seen, the

mean spike count for the modal discharge was significantly reduced. In all nine units for which there was a decrement in the amplitude of the PSTH (that is, reduced spike count), during phase 2, the differences in the spike count between phases 1 and 2 were statistically significant (two-tailed *t*-test for matched groups:  $P < .01$  for three cells;  $P < .05$  for six cells). These comparisons were based on the third group of 40 stimulations in phases 1 and 2.

Several previous studies have reported that visual responses of lateral geniculate units may be modified by stimulation of other sensory modalities (2, 4). Our results, however, indicate that pairing of nonvisual stimuli (clicks) with visual stimuli in a classical conditioning paradigm causes a gradual, decremental modification of response to visual stimulation only in tonic geniculate units and that this response modification may in some cases persist for 2 to 3

minutes beyond the period of click-flash pairing. The changes in response obtained as a result of this pairing demonstrate response plasticity rather than conditioning in the classical sense, which would be demonstrated only with the development of a response to the click stimuli previously ineffective in eliciting a response. Such response plasticity may indicate that tonic geniculate units play a role in intermodal associative processes.

The mechanism underlying this response modification effect and the pathways mediating it are as yet unknown. However, it is possible that the clicks induce a gradual buildup of pre- or postsynaptic inhibition at the level of the lateral geniculate nucleus. With respect to possible pathways mediating this effect, it may be noted that the majority of inputs to the lateral geniculate are nonretinal in origin (5). Stimulation of various regions in the mesencephalic retic-

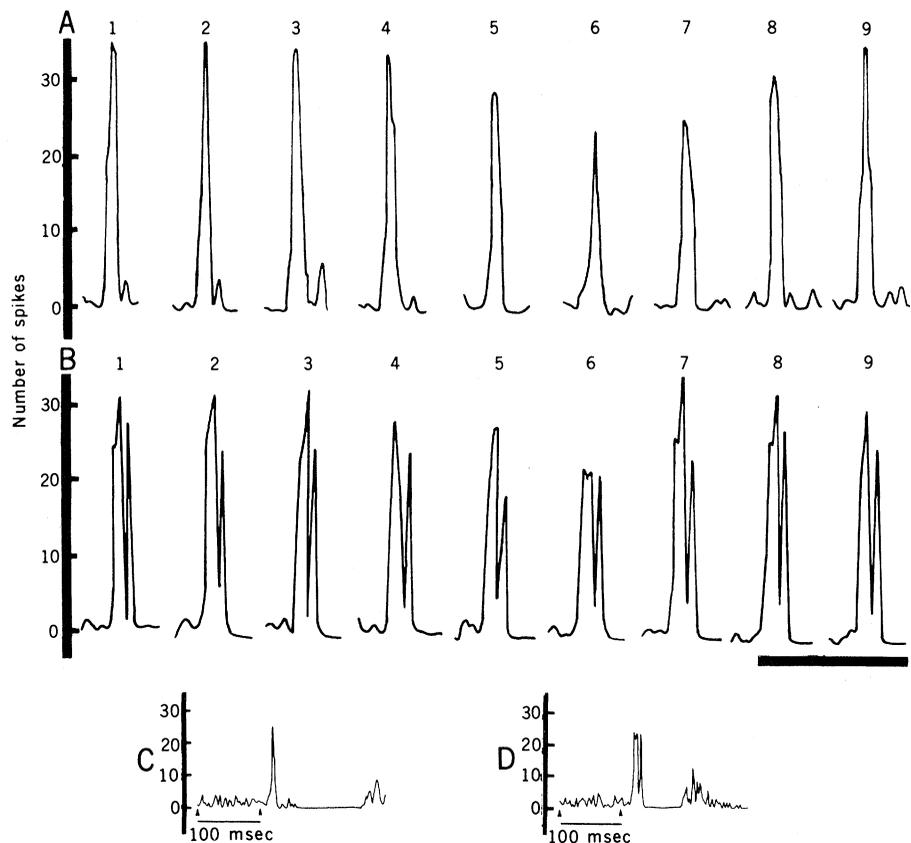


Fig. 1. Modal spike discharge of unit PSTH's for two lateral geniculate neurons (A and B) showing response plasticity as a result of click-flash pairing. Both neurons show a gradual response decrement during the click-flash pairing phase (A, 4 to 6; B, 4 to 6). In A this plasticity effect persists for 2 to 3 minutes after cessation of click-flash pairing (A, 7 and 8); in B the effect does not persist and the spike count returns to the preparing level immediately after cessation of pairing (B7). The flash occurred at the start of each trace; all traces were excerpted from 500-msec PSTH's. Traces A, 1 to 3, and B, 1 to 3, are the first three modal PSTH's of the preparing series of seven PSTH's in which visual stimulation was presented alone without appreciable change in spike count; A, 4 to 6, and B, 4 to 6, are PSTH's during click-flash pairing with 100-msec interstimulus interval; and A, 7 to 9, and B, 7 to 9, are the first three of seven PSTH's after cessation of click-flash pairing. The time calibration for A and B is 100 msec. Longer PSTH excerpts (C and D) corresponding respectively to A6 and B6 show the 100-msec interval between click stimulus (first arrow) and light flash (second arrow) and indicate that no response to click stimulus occurred. All PSTH's are based on 40 consecutive stimulations.

ular formation produces either inhibition or facilitation of the response of lateral geniculate units to visual stimulation (6). Also, a large proportion of visual cortical units are responsive to auditory stimuli (7). Thus, the auditory effect upon the visual response of lateral geniculate units might be mediated via either of these routes.

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## Temporal Pattern Shifts in Singing Birds: A Critique

Ficken *et al.* (1) have hypothesized that the red-eyed vireo (*Vireo olivaceus*) and the least flycatcher (*Empidonax minimus*) change their patterns of singing to avoid acoustic interference when they are breeding in the same habitat. We believe, however, that the data and analysis presented do not necessarily constitute a complete test of the hypothesis.

Ficken *et al.* used data from five pairs of birds in which the recording sequences contained from 43 to 519 songs of the flycatcher and from 59 to 512 songs of the vireo. Song initiation for each species of each pair was scored as either an interruption or not, and a  $\chi^2$  value was obtained for each bird. This test is quite appropriate if the assumption is made that each song produced by a single bird is temporally independent of all other songs produced by that same bird. Our major criticism is that there is likely to be a lack of temporal independence among songs within an individual's singing. Birds appear to sing in bouts of song; that is, there would be two major categories of silences, long intervals between singing bouts (between the last song of a particular bout and the first song of the next bout) and short intervals between songs within a bout. It is known that these latter intervals are rather constant (2). Thus a test of the hypothesis presented by Ficken *et al.* should recognize the three potential states of an individual bird as (i) singing within a bout, (ii) silent within a bout, or (iii) silent between bouts.

If one bird happens to start a bout while the other is between songs (within a bout), this one episode may be sufficient to ex-

plain the phase displacement during the rest of the bout. Bout occurrences then should constitute the data rather than individual songs. Because of the chance displacement mentioned above, it is important to know how Ficken *et al.* "selected" the five vireo-flycatcher pairs at Lake Itasca, Minnesota. Some individuals may have been singing out of synchrony with an individual of the other species, others may have been singing in synchrony, and still others may not have been singing at all. The occurrence of bout singing does not negate the possibility of acoustic avoidance; however, it does demand a different approach to the analysis. It seems necessary therefore to suggest the tentative nature of the conclusions presented.

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Contrary to the assertion by Planck *et al.*, we did not attempt to test the hypothesis that the vireo and flycatcher "change their patterns of singing to avoid acoustic interference." To dismantle the straw man, we repeat that we recorded the species singing together and found that song overlap occurred less frequently than would have been expected from the simplest quantitative model of singing. The results suggested to us that some mechanism to avoid overlap has evolved, but we do not even agree among ourselves as to the most likely mechanism.

The other assertion by Planck *et al.*, that the data may have been "selected" by recording only when no song overlap occurred, is easily answered: of course not. This is so obvious a potential bias that we did not even bother to mention in the original report that tapes were made opportunistically by R.W.F. and M.S.F. whenever possible.

The substance of the technical comment by Planck *et al.* is thus not a "critique" but rather an additional suggestion on the mechanism of overlap avoidance. R.W.F. and M.S.F. have data to indicate that the proposal of phase-displacement at the beginning of a bout, although clever, is unlikely. Contrary to the assertion of Planck *et al.*, neither species sings in a truly regular fashion; birds do not stay out of phase or even begin out of phase and drift slowly into phase. We are still investigating the problem and will consider the phase-displacement possibility quantitatively when a more propitious occasion arises.

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## Electrophysiological Correlates of Meaning: Vocalization Artifact

Johnston and Chesney (1) recorded the visual evoked potential from a frontal electrode in a choice reaction-time (RT) paradigm requiring a vocal response. They compared, by means of factor analysis, the wave forms evoked by a visual stimulus that was interpreted either as a letter ("B")

or number ("13"), depending upon the context in which the stimulus appeared. Their results indicated a consistent factor (in three of four subjects) that differentially loaded on "B" and "13" in the interval from 160 to 240 msec after stimulus presentation (the maximum time sample in