BARBITURATE INFLUENCE UPON ORGANIZATION OF LATERAL GENICULATE RECEPTIVE FIELDS IN CATS

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Abstract. Under different levels of Nembutal anesthesia the spatio-temporal characteristics of receptive fields of cells in the lateral geniculate nucleus were investigated. All units decreased their maintained activity and bursts of spikes occurred spontaneously after administration of the anesthetic. The excitatory domains of the receptive fields were also changed by shortening of the cell’s sustained response and enhancement of the postinhibitory transient responses; the spatial extent of these domains being less affected. A qualitatively new excitatory “tertiary” domain appeared in the receptive field surround with a latency of 170–300 ms. These effects together with enhancement of the spatiotemporal extent of inhibitory domains suggest that the suppressive action of barbiturate takes place beyond the retina.

INTRODUCTION

The spatio-temporal organization of receptive fields (RFs) of the lateral geniculate nucleus (LGN) neurons (3, 22, 25), as well as of retinal ganglion cells (3, 21, 26) has been investigated previously. A number of more or less distinguishable domains have been demonstrated within the spatiotemporal image (contour plane) of the receptive field (22, 25). Variation of light adaptation level induced by change in background illuminations is followed by systematic reorganization of these domains (25). Such observation, as well as anatomy and the
results of experiments using electrical stimulation have led to several plausible models of LGN circuitry underlying the spatiotemporal extent and relative strength of particular domains in the single cell RF (22, 25).

Barbiturates are known to depress neuronal activity in such a way that an equilibrium between excitatory and inhibitory influences is shifted towards relative enhancement of inhibition (15, 24). Using the spatiotemporal RF analysis which is especially sensitive for expressing the subtle reorganization of domains (22, 25), we were interested mainly in searching for possible variations in the relative strengths of inhibitory and excitatory interactions between neurons due to administration of Nembutal.

**METHODS**

Seven adult cats weighing 2.0–3.7 kg were used. Pretrigeminal brain stem transections were performed under ether anesthesia. An atropine /neosynephrine mixture was applied to the eyes and refraction was corrected by +1D contact lenses. Single unit activity of LGN relay neurons was recorded with tungsten microelectrodes in animals paralysed using gallamine triethiodide. After conventional amplification action potentials were utilized to construct the contour planes. On such a contour plane (see Figs. 1–3) each spike is displayed as a dot corresponding to the location of the photic stimulus (ordinate) and the time lag from the onset of the stimulus (abscissa). The details concerned with surgery, visual stimulation, recording and analytical procedure as well as definitions of specific terms used, have been described elsewhere (25).

Single cell analysis consisted of gathering the contour planes obtained at two levels of light adaptation (at least 3 min of adaptation was allowed for each illumination level). After this had been accomplished, Nembutal (pentobarbital sodium, 50 mg/ml) was administrated intravenously in small dosage (0.2–0.3 ml) and analysis of the cell responses was repeated. Immediately after the drug had been infused the cell activity was arrested or rapid oscillations occurred. These phenomena usually disappeared after 2–3 min, therefore analysis of the cell response was started at 3 min after the drug administration.

Continuous recording of the electrocorticogram (ECoG) with two pairs of silver electrodes touching the dura above occipital and frontal cortices monitored the stage of anesthesia (20, 28). Recording of responses was repeated several times in different stages of anesthesia until the cell was lost or the ECoG became isoelectric. In two cases, however, this sequential procedure was disturbed during intermediate stage of barbiturate anesthesia, and the animal was allowed to return to a very
light level of anesthesia as revealed by ECoG monitoring. Such a control served as an indicator that receptive field modifications induced by Nembutal are reversible at least at the early and intermediate stages of barbiturate anesthesia (Fig. 1).

Fig. 1. Left column, from top to bottom: the reorganization of the heterogeneous-ON receptive field induced by cumulative doses of Nembutal. Notation letters: PE, SE, PI, SI, T indicate respectively primary and secondary excitatory, primary and secondary inhibitory and tertiary domains. Ph, transient part of SE domain. Stimulus was a 0.5 × 1° bar of light, 5 cd/m². White and dark bars under the lowest contour plane indicate ON- and OFF-time of the stimulus, respectively. Adaptation to mesopic range was achieved by additional bar of light (0.5 × 2.5°), 0.7 cd/m², in the center of the RF, the whole screen being illuminated to 0.1 cd/m². Right column, ECoG recordings from frontal cortex concurrently with generation of contour planes. Consecutive doses of Nembutal and time between recordings are marked.

RESULTS

Eight LGN principal relay neurons and two optic tract fibers in seven cats were analyzed. The method used allowed us to record only one neuron per cat. On one occasion both a fiber and an LGN neuron
were recorded simultaneously with a single electrode; and another two units were recorded after animals had returned to an earlier anesthetic stage (see Methods). The sample of LGN-cell RFs consisted of 5 heterogeneous ON (Fig. 1, 2), 2 homogenous ON (Fig. 3) and 1 heterogeneous OFF fields according to the classification of Stevens and Gerstein (22). Both optic tract fibers exhibited heterogeneous ON type of receptive field.

The data obtained from one unit are shown in Fig. 1. Contour planes of the cell responses obtained during different levels of anesthesia, as reflected in the ECoG recordings, are grouped in the left side column of the Figure. The top contour plane represents the cell responses during desynchronized ECoG activity (top right) before any dose of the drug was administered. Four typical receptive field domains can be traced on this plane: primary excitatory (PE), primary inhibitory (PI), secondary inhibitory (SI), and secondary excitatory (SE). This arrangement fits the well known picture of an ON-center/OFF-surround receptive field, as previously described in unanesthetized animals (22, 25). The contour plane in the second row of Fig. 1 was obtained after an administration of 4 mg/kg of Nembutal, which evoked spindle activity in the ECoG (record to the right). Most units changed their spontaneous activity after the first drug infusion, exhibiting nonregular bursts of 2–5 spikes. Correspondingly slight changes can be observed on appropriate contour plane, i.e., bursts of spikes seen as thick dots in the middle of an SI domain. These specific bursts form a new, separate “tertiary domain” (T) as can be seen more clearly after an additional dose of 8 mg/kg (third row contour plane). This tertiary domain appears as a sparsely dotted region in the RF surround immediately following the SI domain, with a latency of 170 ms. Spontaneous firing of the cell dropped strongly at this stage of anesthesia and was still characterized by short bursts. However, the receptive field stimulation sometimes evoked prolonged bursts up to twenty spikes long (see Fig. 1). The other characteristic feature of the cell response under barbiturate action was phasic a like response (Ph) preceding the SE domain. These features of this contour plane suggest an enhancement of inhibition influencing the cell activity.

The animal was then allowed to return to a lighter anesthetic level e.g., the ECoG pattern returned to spindle activity like that observed after the first dose of Nembutal (see fourth frame in second row of Fig. 1). The appropriate contour plane resembles also in all respects that from the second row of Fig. 1.

The most pronounced changes evoked by Nembutal administration were noticed in the receptive field of the cell shown in Fig. 2. In the
Fig. 2. Two columns at left: contour planes of heterogeneous ON receptive field of single cell taken at two light adaptation levels (cd/m²) as indicated above. At right: ECoG recorded from frontal cortex at levels of anesthesia achieved by subsequent doses of Nembutal. Other explanations as in Fig. 1.

Fig. 3. Reorganization of homogeneous ON receptive field of single cell obtained by changing light adaptation levels (two columns at left) and level of anesthesia (rows). Other explanations as in Fig. 1.
mesopic range of light adaptation (second column of Fig. 2) one can observe again a large tertiary domain built up from bursts of spikes and phasic OFF-responses (second column, second row — contour planes). These features could not be traced, however, when the receptive field was investigated at a scotopic level of light adaptation (first column of Fig. 2). At two adaptation levels diminution of both excitatory domains, PE and SE, can be observed. This was characteristic of most receptive fields investigated, especially after larger doses of the drug (more than 25 mg/kg accumulation). This suppression of excitatory domains, however, involves mostly a temporal extension of domains rather than their elongation in space, which is well illustrated in Fig. 3. The receptive field of this cell (Fig. 3) was investigated until only single spikes were recorded with ECoG electrodes. Even in this stage the spatial extent of the receptive field remained unchanged (first column, third row) although both spontaneous activity and sustained excitation in the center of the field, seen at the beginning of the experiment (first column, first row) was cut off completely. All the described changes under barbiturate influence were more pronounced in heterogeneous (Fig. 1, 2) than in homogeneous (Fig. 3) receptive fields.

We have investigated also two retinal ganglion cell receptive fields recorded from the optic tract. In both cases we could observe none of the changes described above. The retinal receptive field domains remained unchanged after the cumulative dose of 55 mg/kg of Nembutal when only single spikes could be recorded in the ECoG activity. The only feature which could be traced in both these units during deep anesthesia was a decrease in their spontaneous activity.

DISCUSSION

The most obvious finding in our sample of cells after barbiturate administration was depression of their maintained activity and appearance of bursts of action potentials. Similar effects have been found in many visual centers: retina (2), LGN (12), superior colliculus (11), visual cortex (17, 18) and also in different brain loci such as the midbrain reticular formation (23), thalamic (13) or caudate (6) nuclei. Burst activity of visual neurons has never yet been associated with particular spatiotemporal domains of neuronal receptive fields. In our data an additional, tertiary domain is found after Nembutal administration, and is mainly built from such bursts of spikes.

The other event found after infusion of the anesthetic agent was a shortening of the central sustained response and an apparent enhancement of the transient (phasic) surround response. Thus, responses of
cells become more transient than before barbiturate administration. Similar effects have been observed in the retina (11) and visual cortex (9) under gaseous anesthesia. It has to be stated that the anesthetic agent provides qualitatively different RF reorganization than changing the intensity of background light (25). Bear et al. (1) stated that "lateral geniculate receptive fields were little affected by barbiturate level". It is not clear, however, what the authors meant by "little". Moreover, they recorded a temporaly — averaged responses at several points in the receptive fields, and thus only the spatial, not the temporal dimension of spatiotemporal receptive field organization could be analyzed. In our sample the excitatory responses were correspondingly less affected, the main changes being obscured in more prolonged domains of the response.

It is well known that anesthetic agents depress neuronal activity. The mechanism of their action upon the nervous system remains unknown, however (15, 24). Many papers have shown that barbiturates enhance GABA-mediated pre and/or postsynaptic inhibition (4, 7, 19), but depression of synaptic action mediated by excitatory amino acids has also been suggested (15, 16, 24).

Our data suggest an enhancement of inhibition within the lateral geniculate receptive fields as an effect of Nembutal administration. Since retinal receptive fields were not affected, the source of inhibition seems to be extraretinal. This obviously needs more supporting evidence, as we recorded from only two retinal ganglion cells, and Mandl et al. (11) have found about half of their retinal ganglion cells to be sensitive to the level of anesthesia. They used, however, a different anesthetic agent but, similarly to our findings, observed that neurons in the superior colliculus were all more sensitive to the anesthetic level than were retinal ganglion cells (11). Others (2) have observed only a slight change in retinal ganglion cell receptive fields after Nembutal administration. It is well known that inhibition in receptive fields of lateral geniculate neurons is much stronger than in retinal ganglion cells (8, 27). Presumed interneurons have been localized both inside and outside the nucleus (5, 10). These interneurons have been shown to be rich in glutamic acid decarboxylase, which indicate that they are probably GABA-ergic (14). It is possible that they could be sensitive to barbiturate action.

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