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Visual activity in macaque area V4 depends on area 17 input

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IT is known that some direct projections from the lateral geniculate nucleus terminate in area V4 of the macaque monkey. Retinal information can also bypass area 17 and reach V4 through relays in the superior colliculus and pulvinar. This raises the question whether area V4 is visually responsive in the absence of input from area 17. We tested this possibility by recording in area V4 while inactivating a region of area 17 by cooling. This led to a complete abolition of the visual responses of practically all the neurons whose receptive fields were included in the visual field region coded by the inactivated zone in area 17. In contrast, neurons whose receptive fields were outside this region remained visually responsive.

Key words: Extrastriate visual cortex, Inactivation, Cooling, Electrophysiology

Introduction

The mammalian visual cortex is made up of a number of functional areas which are thought to be responsible for much of the processing of visual information. In recent years, much research has been done in the macaque monkey, leading to the identification of several cortical areas beyond area 17 (also called V1). Among these areas are area V2, which surrounds area 17, area MT (Middle Temporal area buried within suleus STS shown in Fig. 1, below, also called V5), which is believed to be specialized for the processing of motion information, and area V4 which is involved in the processing of form and colour.[1–3] It is usually accepted that, in primates, visual information reaches extrastriate cortical areas via area 17. This is largely based on the traditional belief that the lateral geniculate nucleus (LGN) projects only to area 17. Although the bulk of the LGN projection does indeed reach V1, sparse direct projections have been demonstrated from this nucleus to areas V2 and V4.[4–7] Retinal information can also reach extrastriate cortex through relays in the superior colliculus and pulvinar. The question arises whether all visual responses beyond striate cortex depend on information relayed through area 17 or whether other pathways bypassing this area are functional and able to drive extrastriate neurons when area 17 is lesioned or inactivated. This question is of particular interest in view of the remarkable residual visual capacities of destriated macaque monkeys[8–10] and of the residual vision called blindsight in humans deprived of primary visual cortex.[11–14]

The question of the dependence of the visual responses of extrastriate neurons upon the activity of area 17 in primates was first addressed by Schiller and Malpeli[15] who showed that neurons in macaque monkey area V2 were silenced when V1 was inactivated by cooling, a finding which we subsequently confirmed.[16] In area MT, on the other hand, many neurons still respond to visual stimulation after ablation of area 17.[17] Furthermore, when area 17 is reversibly inactivated by cooling, the majority of MT neurons remain visually responsive.[17,18] This suggests that the visual responses of MT neurons after area 17 lesions are not due to a functional reorganization following the lesion but that afferents from areas other than area 17 provide an efficient input to most neurons in area MT.

The presence of residual visual responses in neurons of area MT demonstrates that inactivating area 17 does not silence the whole extrastriate cortex, as suggested by the lack of responses of neurones in V2. The interesting question is whether V2 or MT are exceptional in their dependence upon the visual responses of neurons in area 17. It is possible, for example, that neurons in V2 are silenced because this area is heavily interconnected with area 17 and is entirely dependent on it, whereas other cortical areas situated further along the chain of information processing may behave differently. Alternatively, it may be that area MT constitutes an exception among extrastriate areas by remaining active when area 17 is silenced. In order to decide between these two possibilities, we began an investigation of residual responses in extrastriate cortical areas during inactivation of area 17 by cooling. In this report, we present results concerning area V4. Whether visual activity remains in this area is of special interest since area V4 is a major processing center for form and colour information.

Materials and Methods

A full description of the experimental procedures has been provided in a previous publication[16] and only the main points are mentioned here. Electrophysiological recordings were made in four adult cynomolgus monkeys (*Macaca fascicularis*) paralyzed with pancuronium bromide (Pavulon, 0.08 mg $kg^{-1} h^{-1}$, i.v.) and anaesthetized with N_2O/O_2 (70/30%). Proper level of anaesthesia was assessed by monitoring heart rate and EEG. Additional analgesia was provided by a continuous infusion of Fentanyl

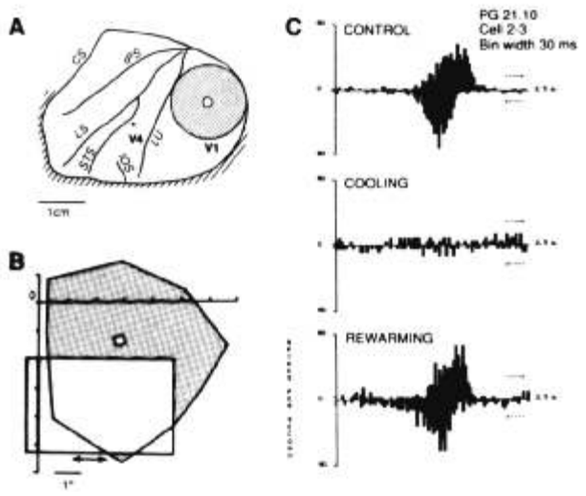

FIG. 1. (A) Experimental set-up. The circular stippled region on the opercular part of area 17 represents the cooling plate. The white circle in the center represents a hole through which a microelectrode is inserted to record in the deep layers of area 17. (B) Visual field. The vertical and horizontal axes represent the corresponding meridians and the point labelled 0 represents the projection of the fovea. The stippled region illustrates the extent of visual field coded in the region under the cooling plate (cooling perimeter). The small white square in the middle represents the receptive field (RF) of an area 17 neuron recorded through the central hole in the cooling plate. The large rectangle represents the RF of a V4 neuron recorded at the position of the black dot (near the prelunate gyrus) in A and whose response is illustrated in C. (C) Visual response of the V4 neuron whose RF is represented in B before (control), during (cooling) and after (rewarming) inactivation of the region of area 17 located below the cooling plate. Each set of post-stimulus histograms represents the response of the neuron to stimulation by a bar moving from left to right (upper histogram) and in the reverse direction (lower histogram read from right to left). Vertical scale bar: 60 spikes. Photic simulation was restricted by a mask to the part of the RF included within the cooling perimeter.

(0.14 mg $kg^{-1} h^{-1}$, i.v.). A large circular craniotomy was made over the opercular part of area 17. Cooling was applied through the dura with a circular copper plate which fitted in the craniotomy and was an extension of a Peltier cooling device. Cooling was achieved by passing a constant current and rewarming by inversing the direction of the current flow through the Peltier device. Visual responses of neurons in area 17 and V4 were tested once the temperature of the cooling plate had reached a steady value.

The experimental set-up is shown schematically in Fig. 1A. The circular stippled area on the surface of the operculum represents the location of the cooling plate applied to the cortical surface of area 17 (V1). The extent of visual field coded in the region of area 17 situated below the cooling plate was mapped electrophysiologically. This region, called the cooling perimeter, is shown by the stippled region in Fig. 1B. A circular hole through the center of the cooling plate allowed the passage of a microelectrode which was positioned at the border between the white matter and layer VI and was used to monitor the disappearance of visual responses of area 17 neurons during cooling. The receptive field of a neuron recorded by this electrode is shown by the small white square in the middle of the stippled region in Fig. 1B. Another microelectrode was used to record single units and multiunit activity on the part of V4 situated on the prelunate gyrus (Fig. 1A). Histological controls were performed on myelin-stained sections[19] to ensure that recordings were confined to area V4. The excitatory part of the receptive field of a V4 neuron is represented by the large rectangle in Fig. 1B. Although most of the units tested (74/85) had their receptive fields completely included in the cooling perimeter, in some recordings (eleven cases), the receptive fields of V4 neurons were only partially included in the cooling perimeter, e.g. as shown in Fig. 1B. In such cases, the responses were tested while restricting the photic stimulation to the cooling perimeter by masking the rest of the visual field. Responses of neurons were tested either by qualitative methods, i.e. listening to the multiunit activity on the audio monitor, or by quantitative recordings of visual responses (twelve cases; e.g. Fig. 1C). These two methods always gave the same unequivocal answer when used on the same neurons.

Results

Recordings were made at 85 sites in area V4 with receptive fields at least partially included in the cooling perimeter. Figure 1C illustrates the visual response of a V4 neuron whose receptive field is indicated by the large rectangle in Fig. 1B. The response of this neuron to a light bar moving back and forth across the portion of the receptive field included in the cooling perimeter is presented in the upper pair of histograms (control). The top histogram shows the response to the stimulus moving from left to right, whereas the lower histogram, read from right to left, shows the response of the neuron to movement in the opposite direction. The middle pair of histograms (cooling) shows the response of the neuron when activity in V1 is totally blocked by cooling. All visual response is abolished and spontaneous activity is raised slightly. The lower pair of histograms (rewarming) shows the response of the neuron after the temperature has returned to 37°C and i.e. when normal responses can be recorded in area 17.

The result presented in Fig. 1 illustrates our general finding since, among 85 sites tested, 77 (91%) were completely silenced by inactivation of area 17. In all cases, visual activity returned after rewarming the cortex. Among units inactivated in V4, we identified neurons selective to the colour of the stimulus and neurons showing shape selectivity. Selectivity was tested before cooling area 17 and was also present after rewarming. In all other sites except one, in which a clear response was observed, only a weak residual response could be heard on the audio-monitor during cooling. With such poor responses, it was impossible to plot the extent of the receptive field, in contrast to the residual activity observed in area MT.[17,18] It is likely that these weak visual responses result from

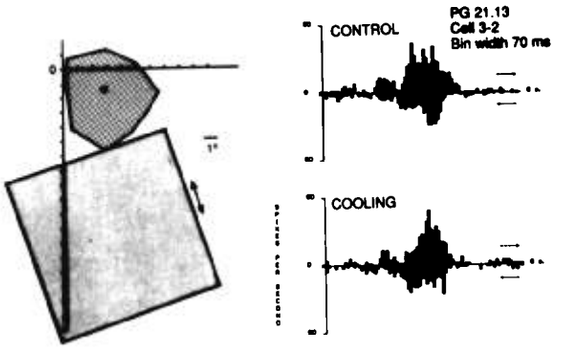

FIG. 2. Response of a V4 neuron whose RF is illustrated by the large gray square region on the left before (control) and during (cooling) inactivation of area 17 by cooling. The stippled region above corresponds to the cooling perimeter. Contrary to the neuron illustrated in Fig. 1 the response of this neuron, whose RF did not overlap that of the cooling perimeter, shows only a weak modification during cooling of area 17. Vertical scale bar: 60 spikes.

incomplete inactivation of area 17, especially in the case of two units whose receptive fields were located close to the border of the cooling perimeter. These two units were probably driven by area 17 neurons located close to the edge of the cooling plate, in a region which is more difficult to block because of the curvature of the cortical surface under the flat cooling plate.

We do not believe that the silence of V4 neurons results from a nonspecific cooling effect for the following reasons: 1) We measured the temperature at the site of V4 recording and found a value of 34°C. 2) Spontaneous activity was never abolished by cooling area 17. 3) The effect was remarkably specific, depending upon the position of the receptive field with respect to the cooling perimeter. In several instances of receptive fields partially included in the cooling perimeter (Fig. 1B), only the receptive field regions included in the cooling perimeter were responsive during inactivation of area 17, whereas the regions outside were responsive. In the case of some large receptive fields, during cooling of area 17, there was a 'hole' in the receptive field in the region corresponding to the cooling perimeter. 4) Unambiguous responses to visual stimulation were recorded from neurons whose excitatory regions of the receptive fields were situated outside the cooling perimeter, as illustrated in Fig. 2. This neuron was recorded in the same experimental conditions as those in Fig. 1, except that the penetration in V4 was located more dorsally and the RF was located outside that of the cooling perimeter. It is clear that the response of this neuron is barely affected by the cooling of area 17, in contrast to what was observed when the RF was located inside the cooling perimeter (Fig. 1).

Discussion

Our results show that inactivation of area 17 completely silences area V4, at least in the region representing central visual field. This suggests that not all extrastriate areas situated beyond V2 are active in the absence of an input from area 17. Since it is well documented that some neurons in the LGN project to the same region of area V4[4–6] as that recorded in the present study, it appears that either these neurons are silenced by inactivation of area 17 or that their input is not strong enough to drive neurons in V4.

Area V4 is of particular interest since it appears to play a pivotal role in what is called the ventral or occipito-temporal pathway of information transfer.[20] This pathway is principally made up of areas V2, V4, and inferotemporal cortex and is thought to be involved in the processing of form and colour information.[21] Our results and those of Rocha-Miranda and his collaborators,[22] showing loss of visual responses in inferotemporal cortex after area 17 lesion, suggest that the whole ventral pathway is silenced when it is deprived of input from area 17. This would suggest that the residual form and colour vision observed in monkeys deprived of area 17[8,10] may be subserved by other cortical or subcortical centers.

The pivotal role of area V4 in the ventral pathway is similar to that played by area MT in the dorsal or occipito-parietal pathway.[23,24] The presence of residual visual activity in MT[17,18] after inactivation of V1 suggests that the two visual pathways may be differently affected by the removal of input from area 17. Since activity in area MT in the absence of an input from area 17 depends on the integrity of the superior colliculus,[25] it is possible that the residual visual response observed in that area may be due to signals relayed from the superior colliculus and concerned with eye movements. Thus, the different effects of area 17 lesions on cortical areas involved in the dorsal and ventral pathways may be related to the importance of eye movements signals from the superior colliculus in the visuomotor processing occurring in the dorsal pathway.

Conclusion

When area 17 is inactivated, neurons in area V4 stop responding to visual stimulation. Activity in the ventral occipito-temporal visual pathway therefore appears to be entirely dependent upon input from area 17, in contrast to what is observed in some elements of the dorsal occipito-parietal pathway.

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