Feedforward and Feedback Connections Between Areas V1 and V2 of the Monkey Have Similar Rapid Conduction Velocities

P. GIRARD, J. M. HUPÉ, AND J. BULLIER
Institut National de la Santé et de la Recherche Médicale U371, 69500 Bron, France

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Girard, P., J. M. Hupé, and J. Bullier. Feedforward and feedback connections between areas V1 and V2 of the monkey have similar rapid conduction velocities. *J Neurophysiol* 85: 1328–1331, 2001. It is often assumed that the action of cortical feedback connections is slow and modulatory, whereas feedforward connections carry a rapid drive to their target neurons. Recent results from our laboratory showed a very rapid effect of feedback connections on the visual responses of neurons in lower order areas. We wanted to determine whether such a rapid action is mediated by fast conducting axons. Using electrical stimulation, we compared the conduction velocities along feedforward and feedback axons between areas V1 and V2 of the macaque monkey. We conclude that feedback and feedforward connections between V1 and V2 have comparable fast conduction velocities (around 3.5 m/s).

INTRODUCTION

Cortical areas of the visual system are usually arranged in a hierarchical manner with area V1 at the lowest level and the hippocampal formation at the highest (Felleman and Van Essen 1991). This sequential model is frequently interpreted as implying a progressive increase in latencies to visual stimulation for areas located higher and higher along the cortical hierarchy. Recent experiments have not confirmed this interpretation and showed many examples of cortical areas located at high hierarchical levels that have short latencies to visual stimulation (Nowak and Bullier 1997; Schmolesky et al. 1998). Reciprocal interactions between neurons activated simultaneously at different levels of the hierarchy are therefore possible. Consistent with these ideas are the recent findings from our laboratory (Hupé et al. 2001a,b) showing that the effects of feedback connections are delayed by less than 10 ms with respect to the beginning of the responses of neurons in low-order visual areas. Such a rapid action requires that the conduction times of feedback axons are sufficiently short to provide a rapid input, particularly in cases of areas V1, V2, and MT for which latencies to visual stimulation differ by less than 10 ms on average (Nowak and Bullier 1997).

The conduction times of feedforward and feedback axons have been compared in the rat (Domenici et al. 1995; Nowak et al. 1997; Shao and Burkhalter 1996), and these studies concluded that feedforward and -back axons have similar conduction velocities. However, the visual system of the rat and the monkey differ in several respects, and we decided to undertake a similar study in the monkey. Given the large amount of information on the timing of visual responses in areas V1 and V2 (Munk et al. 1995; Nowak et al. 1995), it was of particular interest to compare the conduction of feedforward and -back connections between these two areas. For comparison, we also measured the conduction times for intrinsic connections within area V1.

METHODS

Experiments were performed, along with other anatomical or electrophysiological studies, on five adult monkeys (*Macaca fascicularis*), one male and four females weighing 3–4.3 kg. Recording and maintenance procedures of the animals were done following those described in Hupé et al. (1998, 2001a).

Electrical stimulation was achieved with 75-μm-tip tungsten microelectrodes assembled in a triple- or double-electrode assembly. The tips delimited an equilateral triangle of 1.2–1.5 mm side. Cathodic current impulses (Neurolog system) were 0.2 ms in duration and were usually less than 1 mA (median, 0.7 mA). Stimulation pulses were monophasic and unipolar. Single units were recorded with tungsten microelectrodes (tip, about 10 μm) (Merrill and Ainsworth 1972).

We tried to position the tips of the stimulation electrodes midway through the cortical depth of V1 or V2 by recording the neural activity through the stimulating electrodes. Then the recording electrode was lowered in a cortical region in retinotopic register with the stimulated region. A good retinotopic register was mandatory to record antidromically activated neurons.

The latency was defined as the time between the beginning of the stimulation artifact and the foot of the spike. We first determined the stimulation threshold to evoke a spike and measured the latencies for this current. We used the minimum value in case of latency jitter.

Antidromic spikes were characterized with the usual criteria (Fuller and Schlag 1976): a latency jitter less than 0.1 ms, a collision test, the ability to follow 100-Hz stimulation for a short period, and a consistent threshold (i.e., that does not vary more than 0.1 mA).

For orthodromic spikes, the jitter is about 0.3–0.5 ms. Spikes from passing-by axons were rejected on the basis of their shape (sharp negative small-amplitude deflections).

At the end of the experiment, the animals were killed by an overdose of pentobarbital and perfused. In all cases, the positions of the recording and stimulation electrodes in the depth of V2 and in the operculum of V1 were examined on histological sections stained with cresyl violet. Confirmation of recording and stimulating sites has been obtained for all cases except for those excluded (see following text).

Present address and address for reprint requests: P. Girard, Centre de Recherche Cerveau et Cognition, CNRS-UPS UMR 5549, Université Paul Sabatier, 133 route de Narbonne, 31062 Toulouse Cedex, France (E-mail: girard@cerco.ups-tlse.fr).

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RESULTS

We applied electrical stimulation in V2 and recorded in V1 in two monkeys. The antidromic spikes obtained in this configuration travel along the feedforward projection from V1 to V2. In two other monkeys, electrical stimulation was applied in V1 and recording was performed in V2 (antidromic spikes correspond to the feedback connection from V2 to V1). A fourth monkey and one of those used for V2 stimulation were used for the study of horizontal connections within V1.

Antidromic activation

In the case of stimulation in V1 and recording in V2, we recorded 26 antidromic spikes and 271 orthodromic spikes. In the case of stimulation in V2 and recording in V1, we recorded 23 antidromic spikes and 84 orthodromic spikes. Figure 1 shows the distribution histograms together with the cumulative distributions of the latencies for both antidromic populations. The median latencies for feedback and feedforward are 1.25 and 1.1 ms, respectively (mean, 1.53 and 1.14 ms). Tests (Kolmogorov-Smirnov and Mann-Whitney *U*, $P = 0.272$ and $P = 0.084$, respectively) do not show any statistical difference between the two distributions.

A better comparison of the feedback and -forward pathways can be obtained with the conduction velocity since the distance between the stimulating and recording electrodes could vary from monkey to monkey or from penetration to penetration. We computed the conduction velocities using the latencies and the distances between the sites of electrical stimulation and recording as reconstructed from histological sections. Since we do not know the exact trajectory of fibers, we measured the distance along a straight line between the recording and the stimulation sites, on a three-dimensional reconstruction after histology. This procedure may underestimate the values of the corresponding conduction velocities since axons can follow more complicated paths and can therefore cover longer distances (Rockland and Virga 1989). Figure 2 shows the distributions of the conduction velocities for both populations. Note here that we study a smaller sample of feedforward axons than in Fig. 1. We excluded some cases because the position of one stimulation electrode suggested a possible contamination of the white matter. Excluded neurons have a mean conduction velocity of 5 m/s. Again statistical tests do not show any significant difference between both populations (Kolmogorov $P = 0.198$, *U*: $P = 0.417$). The median conduction velocities for feedback and -forward are 3.43 and 3.69 m/s, respectively (mean: 3.71 and 4.03 m/s).

We were able to find only one antidromic activation with intrinsic stimulation of V1, probably because we did not attempt to record and stimulate from iso-oriented domains that are preferentially interconnected. The latency was 1.3 ms and the conduction velocity 1 m/s. This incidental datum cannot be compared with other antidromic populations.

Orthodromic activation

Electrical stimulation tends to preferentially activate fast axons (Ranck 1975). We were therefore concerned that the small samples of feedforward and -back axons correspond only to the fastest axons. Hence we studied the distributions of orthodromically activated neurons that correspond to much larger populations and may therefore be less sensitive to sampling artifacts.

Figure 3 shows distributions of orthodromic latencies for feedforward, feedback and local (in V1) connections. There are

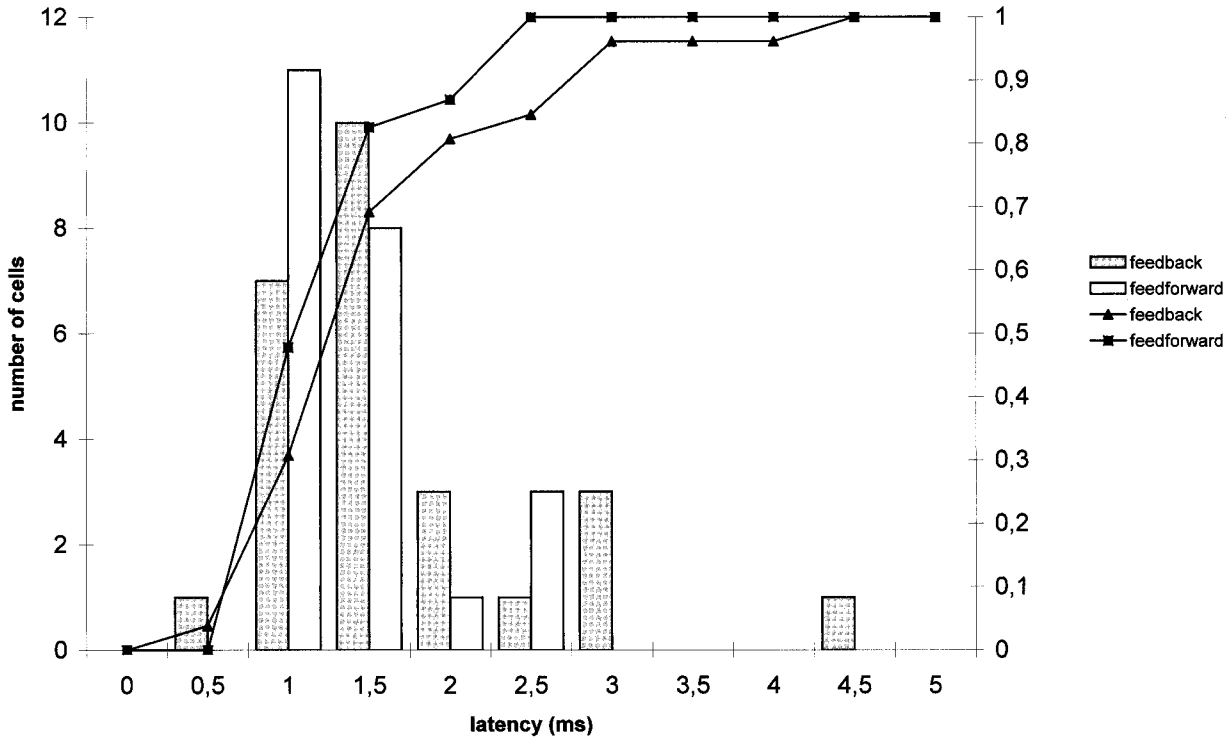

FIG. 1. Distribution and cumulative distribution of antidromic latencies of neurons in areas V1 and V2. All data from several monkeys are pooled together.

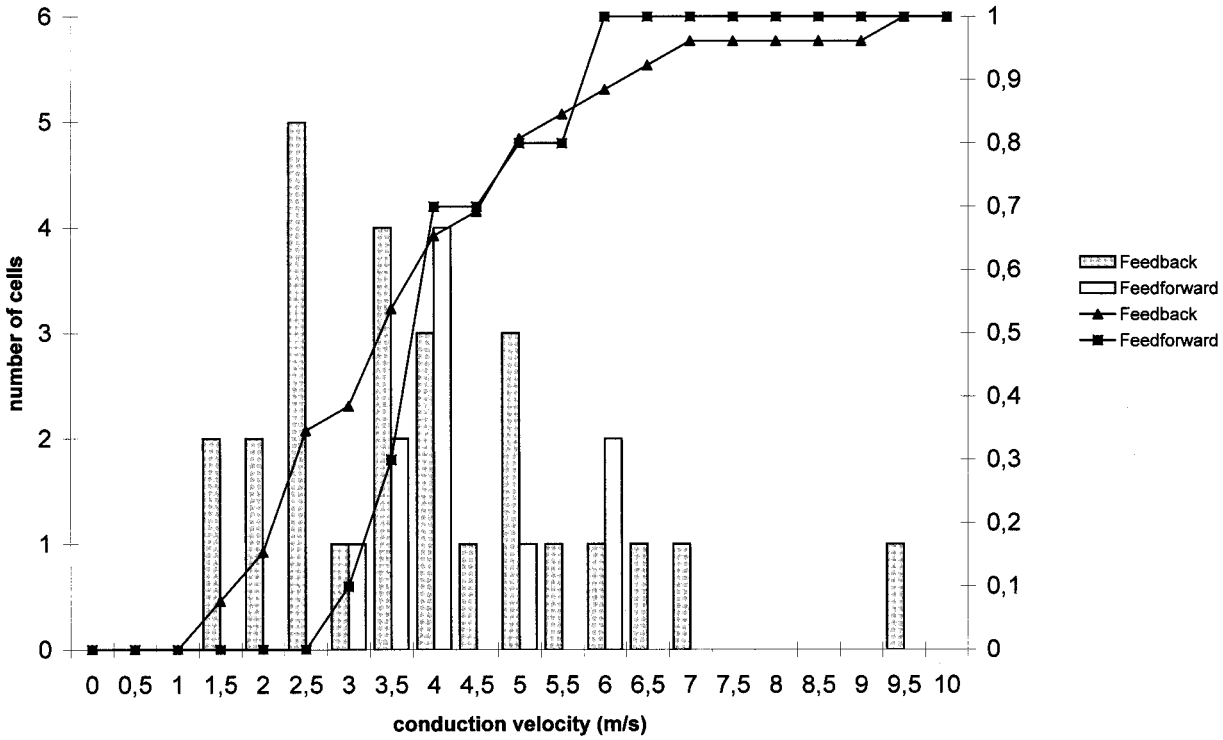

FIG. 2. Distribution and cumulative distribution of conduction velocities for feedback and feedforward axons.

marked statistical differences (Kolmogorov-Smirnov, Mann-Whitney U, $P < 0.0001$) between each population pair. The latency difference between feedforward and -back axons seems to be due to a trailing edge of long latencies obtained with V1 stimulation and recording in the deep layers of V2, a configuration that probably leads to polysynaptic activation.

Conduction velocities have been calculated for latencies less than 3.5 ms to avoid polysynaptic activation. The feedforward conduction velocities (not shown) are significantly slower than those of feedback (Mann-Whitney U, $P < 0.0001$; median, 2.24 and 3.74 m/s; mean: 2.4 and 3.8 m/s for feedforward and -back connections, respectively).

It is apparent in Fig. 3 that the horizontal connections return many large values (4–10 ms). This is even more surprising considering the fact that many recordings were done within a couple of millimeters away from the stimulation electrode. Some of these orthodromically activated neurons with long latencies showed a very small amount of jitter, suggesting

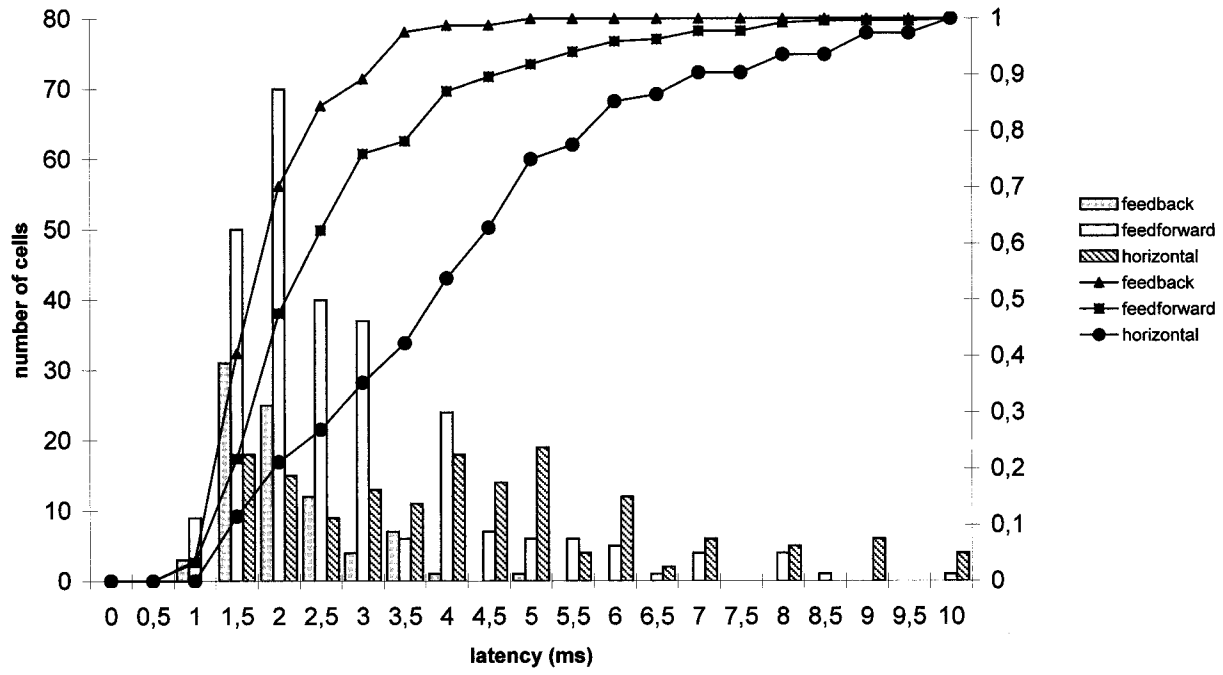

FIG. 3. Distribution and cumulative distribution of latencies for orthodromic activation.

direct monosynaptic activation. From the orthodromic activation, local connections have a median conduction velocity of 0.33 m/s (mean, 0.6). Conduction velocities are slower for neurons located in the upper layers of area V1. The median velocity is 0.3 m/s for the upper half of V1 and 1 m/s for the lower half (mean, 0.46 and 0.90 m/s; Mann-Whitney: $P < 0.0001$).

DISCUSSION

The obvious conclusion to be drawn from these data is that feedback and feedforward cortical connections have comparable conduction velocities. The median conduction velocity is about 3.5 m/s, which means that information travels rapidly along both pathways.

This result is best obtained with antidromic activation, and it is crucial to be sure that we stimulated axon terminals in the gray matter and did not inadvertently stimulate the white matter between V1 and V2. From Nowak and Bullier (1996), it could be inferred that we stimulated a sphere of 1.5-mm diam when thresholds were less than 1 mA. Hence for most cases, stimulation was restricted to the gray matter (about 2 mm). We think we can rule out white matter stimulation when thresholds were more than 1 mA because, with such intensities, we could not elicit any antidromic activity when the visual field representations of V1 and V2 were not in register. Some units have been discarded (see preceding text, Fig. 2) that could have been driven by direct stimulation of the white matter; indeed their thresholds were lower than those of other antidromically activated axons.

Conduction velocities are within the range predicted from the sizes of axons of feedforward and feedback connections (Rockland and Virga 1989, 1990), assuming a multiplication factor of 5.5 between fiber size and conduction velocity (Nowak and Bullier 1997). A previous study (Movshon and Newsome 1996) reported antidromic latencies between 1 and 3 ms when stimulating MT and recording in V1. Although this corresponds to higher conduction velocities (3–10 m/s), because of the larger distance between V1 and MT, it is interesting to note that, despite this difference, the conduction times from V1 to V2 and to MT are very similar. This is in keeping with reports that latencies to visual stimulation are similar in V2 and MT (Nowak and Bullier 1997; Raiguel et al. 1989). Thus the first stages of processing in the visual cortex appear to be temporally compact despite large differences in axonal lengths. In contrast with the rapid conduction of feedforward and feedback axons, most of the horizontal fibers appear to be slow conducting as indicated by the long latencies recorded within V1 (Fig. 3). This probably results from the fact that most local connections correspond to nonmyelinated axon collaterals of pyramidal cells that are likely to have conduction velocities in the 0.1 m/s range. Such slow conduction velocities may explain the slow wave of surround effects reported in the monkey with optical imaging methods (Grinvald et al. 1994) and in the cat with intracellular recordings (Bringuier et al. 1999).

Present addresses: J. Bullier, Centre de Recherche Cerveau et Cognition, CNRS-UPS UMR 5549, Université Paul Sabatier, 133 route de Narbonne, 31062 Toulouse Cedex, France; J.-M. Hupé, Center for Neural Science, New York University, 4 Washington Place, New York, NY 10003.

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