Thalamocortical (TC) neurones display fast oscillations (above 20 Hz, generally 30–80 Hz) due to their intrinsic properties and synaptic inputs. Direct depolarization of TC cells recorded from relay and intralaminar nuclei triggers fast membrane oscillations (Steriade, Curró Dossi, Paré & Oakland, 1991; Steriade, Curró Dossi & Contreras, 1993; Pedroarena & Llinás, 1997). The depolarization-dependent fast oscillations, which are transferred by TC neurones to neocortex, are controlled by mesopontine cholinergic nuclei and survive extensive lesions of the parallel cortical projection arising in nucleus basalis (Steriade et al. 1991), thus indicating that, at least under these experimental conditions, the cortical fast rhythms are generated in the bisynaptically activating brainstem-thalamic-cortical pathway. Besides the intrinsic fast oscillations induced by depolarizing current pulses, TC cells display spontaneously occurring fast oscillations that are ascribed to synaptic inputs arising in related areas of the cerebral cortex and/or afferent brainstem relay stations. Indeed, the configuration of fast events in TC cells recorded from cat ventrolateral (VL) nucleus of intact-cortex and decorticated cats under ketamine-xylazine anaesthesia revealed spontaneously occurring fast oscillations (mainly 30–100 Hz) in 86% of investigated cells. The fast depolarizing events consisted of excitatory postsynaptic potentials (EPSPs), giving rise to fast prepotentials (FPPs) in 22% of neurones, which eventually lead to full-blown action potentials. The frequency of fast events changed by factors of 2–5 in periods as short as 0·3–1·0 s.

1. Intracellular recordings from 216 thalamocortical (TC) neurones in the ventrolateral (VL) nucleus of intact-cortex and decorticated cats under ketamine-xylazine anaesthesia revealed spontaneously occurring fast oscillations (mainly 30–100 Hz) in 86% of investigated cells. The fast depolarization of TC cells triggered fast membrane oscillations (Steriade, Curró Dossi, Paré & Oakland, 1991; Steriade, Curró Dossi & Contreras, 1993; Pedroarena & Llinás, 1997). The depolarization-dependent fast oscillations, which are transferred by TC neurones to neocortex, are controlled by mesopontine cholinergic nuclei and survive extensive lesions of the parallel cortical projection arising in nucleus basalis (Steriade et al. 1991), thus indicating that, at least under these experimental conditions, the cortical fast rhythms are generated in the bisynaptically activating brainstem-thalamic-cortical pathway. Besides the intrinsic fast oscillations induced by depolarizing current pulses, TC cells display spontaneously occurring fast oscillations that are ascribed to synaptic inputs arising in related areas of the cerebral cortex and/or afferent brainstem relay stations. Indeed, the configuration of fast events in TC cells recorded from cat ventrolateral (VL) nucleus is similar to that of responses evoked in the same neurones by stimulating deep cerebellar nuclei or afferent cerebellothalamic axons (Steriade et al. 1991; Pinault & Deschênes, 1992; Sawyer, Young, Groves & Tepper, 1994). Some neurones in deep cerebellar nuclei oscillate in the fast frequency range (Jahnsen, 1986; Llinás & Mühlethaler, 1988; Mouginot & Gähwiler, 1995). Similar relations may exist in the visual system (Ghose & Freeman, 1992) where retinal and lateral geniculate (LG) neurones are synchronized within the frequency range of fast oscillations (Neuenschwander & Singer, 1996).

2. The spontaneous oscillations were similar to responses evoked in VL relay neurones by stimuli to the afferent cerebellofugal axons in brachium conjunctivum (BC) and were strikingly reduced or abolished after electrolytic lesion of BC axons.

3. The amplitude and duration of fast depolarizing events were significantly reduced during the descending phase of the inhibitory postsynaptic potentials (IPSPs) in TC cells, related to spontaneous spindles or evoked by local thalamic stimulation.

4. Averaged field potentials recorded from motor cortex and triggered by EPSPs and/or action potentials of intracellularly recorded VL cells demonstrated that both spontaneous and BC-evoked fast depolarizations in VL relay neurones were coherent with fast rhythms in cortical area 4.

5. These results show that, in addition to the thalamic and cortical generation sites of the fast (so-called gamma) oscillations, prethalamic relay stations, such as deep cerebellar nuclei, are major contributors to the induction of fast rhythms which depend on the depolarization of thalamic and cortical neurones and which represent a hallmark of brain activation patterns.

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synaptic activities in afferent projections to the thalamus may boost the intrinsic propensity of some TC cells to display fast oscillations. Here, we have investigated the intracellular patterns of fast oscillations in VL cells of intact-cortex and decorticated cats, as well as in preparations with lesioned cerebellothalamic inputs. The patterns of fast depolarizing events proved to consist of sequences of EPSPs and fast prepotentials (FPPs), which eventually lead to full-blown action potentials. We have compared the spontaneous events with those elicited by stimulation of cerebellothalamic axons in the brachium conjunctivum (BC) and we demonstrate the synchronization of fast events in the VL-cortical system, as well as the profound changes during spindle-related IPSPs in TC neurones.

**METHODS**

**Preparation**

Experiments were performed on thirty-four adult cats anaesthetized with ketamine–xylazine (10–15 and 2–3 mg kg\(^{-1}\), respectively, i.m.). In addition, all tissues to be incised and pressure points were infiltrated with local anaesthetic (lignocaine). Throughout the entire experiment, the depth of ketamine–xylazine anaesthesia was monitored by recording the sleep-like patterns of the electroencephalogram (EEG) and additional doses of anaesthetic (2–4 mg kg\(^{-1}\) ketamine and 0.5–1.0 mg kg\(^{-1}\) xylazine) were administered i.m. in response to the slightest change, i.e. diminished amplitude and increased frequency of EEG waves. In addition, the heart rate was continuously monitored by means of electrocardiogram and kept constant (acceptable range, 50–110 beats min\(^{-1}\)) by adjustment of the anaesthetic. Once the EEG indicated that anaesthesia induced sleep-like patterns, the animal was paralysed with gallamine triethiodide, mounted in a stereotaxic frame, and artificially ventilated keeping end-tidal CO\(_2\) within the range 3.5–3.8%. Body temperature was maintained at 37–39 °C. Glucose saline (5% glucose in 0.9% w/v NaCl solution, 10 ml i.p.) was administered 2–3 times during the experiments which lasted between 8 and 12 h. All experimental procedures were performed according to the national guidelines.

In five animals, the cerebral cortex was removed by section on the left side, where thalamic recordings were made. Histology demonstrated that all neocortical areas (sensory, motor and association) were ablated, only the perirhinal and prepiriform cortices were left intact, but these areas do not have connections with the VL nucleus (see Fig. 3 in Timofeev & Steriade, 1996). In four other animals, massive electrolytic lesions of cerebellothalamic axons in the brachium conjunctivum (BC), at the pontine level, were performed (1000 Hz, 0.5–1.0 mA) by using an oblique approach and conventional stereotaxic co-ordinates (Berman, 1968). In hemidecorticated animals, we recorded the EEG from the contralateral area 4. Stimulation of BC axone (at 2–3 mm posterior, 3.5 mm lateral and −1.5 mm dorsal, according to conventional stereotaxic co-ordinates, Berman & Jones, 1985) was delivered as single pulses (0.05–0.1 mA, 0.1 ms) or pulse trains at high frequencies (100–200 Hz).

**Analysis**

Statistical data are presented as means ± s.e.m. Two statistical tests were used. Student's unpaired \(t\) test for data with a normal distribution and a non-parametric Mann–Whitney \(U\) test for other types of data. The calculation of the depolarizing area of fast events was done by using the trapezoidal integration of IGOR Pro (WaveMetrics Inc., Lake Oswego, OR, USA). The peak of depolarization was taken as time 0 and the segments of calculations were taken in periods from −2 to +10 ms. Longer periods were not considered because of activations of secondary depolarizations during the ascending parts of spontaneous IPSPs (see Fig. 8E, right inset). The synchrony was determined by spike- and/or wave-triggered averages and by cross-correlograms.

**RESULTS**

**Database and neuronal identification**

The results are based on intracellular thalamic recordings from 154 VL neurones in intact-cortex animals and sixty-two VL neurones in the decorticated hemisphere (12 dual intracellular recordings). The neurones were selected from a larger database because they had long-lasting recordings with a stable membrane potential (\(V_m\)), more negative than −55 mV, and overshooting action potentials. The \(V_m\) of TC cells of intact-cortex hemisphere was −60.5 ± 1.7 mV and the apparent input resistance (\(R_{in}\)), measured by using short hyperpolarizing pulses, was 19.4 ± 1.1 MΩ. In the decorticated animals, the \(V_m\) was more negative (−62.5 ± 1.8 mV) and the input resistance higher (21.3 ± 1.0 MΩ). Although the \(V_m\) was more negative and the \(R_{in}\) higher in thalamic neurones from the decorticated hemisphere, we did not find statistically significant differences (\(P < 0.07\) for \(R_{in}\) and \(P < 0.06\) for \(V_m\)) between neurones recorded from the intact-cortex and decorticated hemisphere in the present neuronal sample.

TC cells in the VL nucleus were identified by their monosynaptic responses to BC stimulation and, in intact-cortex animals, antidromic invasion from area 4. BC-evoked responses were considered monosynaptic when characterized by constant latencies (1.2–2.0 ms in different cells) and...
ability to follow fast (100–200 Hz) BC stimuli (see Figs 9 and 11). In a sample of fifteen VL neurones, the latency of BC-evoked responses to the onset of EPSPs in VL cells was $1.6 \pm 0.3 \text{ ms}$, while it was $3.5 \pm 0.9 \text{ ms}$ when measured to the onset of the simultaneously recorded depth-negative (excitatory) field potential in cortical area 4. All of the VL neurones analysed showed basic electrophysiological properties typical of TC cells, namely: rebound spike bursts after hyperpolarizing pulses and/or biphasic IPSPs (see Figs 1, 4, 8 and 11) and clock-like delta oscillation (1–4 Hz) at a $V_m$ more negative than $-70 \text{ mV}$. The TC cells analysed in this study are different from local-circuit GABAergic cells as the duration of their action potentials (0.6–0.9 ms at half-amplitude) is much longer than that of action potentials fired by local interneurones (about 0.35 ms; Pape & McCormick, 1995), and rebound high-frequency spike bursts (see Fig. 11, After BC lesion) are rarely seen in local interneurones (McCormick & Pape, 1988), but when they do appear the intraburst frequency is much lower (130 Hz) than in TC cells (Williams, Turner, Anderson & Crunelli, 1996).

Characteristics of spontaneous fast oscillatory events in TC cells

During ketamine–xylazine anaesthesia EEG recorded from the cortical depth showed a slow oscillation (0.6–0.9 Hz) consisting of a long-lasting positive wave associated with cell hyperpolarization, followed by a sharp negative deflection associated with cell depolarization, leading to a brief sequence of spindle waves (7–14 Hz) and fast (> 20 Hz) rhythms (Fig. 1; see also Contreras & Steriade, 1995). The oscillatory cycle indicated by the box in Fig. 1 shows that the simultaneously recorded TC cell displayed a prolonged hyperpolarization during the depth-positive cortical EEG wave, followed by a sequence of IPSPs within the frequency range of spindles, leading to a postinhibitory low-threshold spike (LTS; Jahnsen & Llinás, 1984).

The fast spontaneous oscillations (above 20 Hz) were observed in 86% of TC cells ($n = 186$) from either intact-cortex (Fig. 1) or decorticated (Fig. 2) animals. In 119 neurones, the fast events were grouped, each group lasting

![Figure 1. Slow (<1 Hz) and fast (> 20 Hz) oscillations in the neocortex and thalamus of an intact-cortex animal](image)

Field potential recording from the depth of cortical area 4 (Depth EEG, area 4, uppermost trace) and intracellular recording from the thalamic VL nucleus (Intracellular VL, second trace from top). One cycle of slow oscillation recurring at 0.9 Hz is indicated by the box. Two periods (indicated by bars a and b) with fast depolarizing events in the VL cell are expanded below. Note that although in some cycles of the slow oscillation the fast activity is obliterated during hyperpolarization of the VL cell (related to the depth-positive EEG component), in other cycles the fast events overwhelm the prolonged hyperpolarization and diminish the occurrence probability of the postinhibitory rebound low-threshold spike (LTS). Here and in subsequent figures membrane potential ($V_m$) is indicated to the left of the trace (arrow).
1–2 s and repeating every 1–3 s. The temporal relations between the slow and fast oscillations in TC cells did not obey simple rules. Although in many instances the fast events were obliterated during the prolonged hyperpolarizing component of the slow oscillation (see 2nd and 4th (in box) oscillatory cycles in Fig. 1), in other cases fast events overwhelmed the hyperpolarization in TC cells and diminished the probability of a subsequent rebound LTS (see 1st and 3rd oscillatory cycles, marked a and b in Fig. 1). Thus, fast events could occur during the prolonged depth-positive EEG wave as well as during the spindle-related IPSPs (see Spindle in episode a).

Over a period as short as 0.3–1.0 s the frequency of fast events could change by a factor of 2–5. This is dramatically shown in Fig. 2, from an ipsilaterally decorticated animal.

![Diagram](image)

**Figure 2. Fast events appear in the thalamus of an ipsilaterally decorticated animal**

Depth-EEG from area 4 of the right hemisphere (top trace) and dual simultaneous intracellular recordings from two thalamocortical VL neurones (VL1 and VL2) in the left (decorticated) hemisphere (second and third traces from top). Cell VL1 displayed sequences of waxing and waning hyperpolarizing spindle waves, while VL2 displayed fast events grouped in sequences recurring at about 0.5 Hz (a frequency different from that of the cortical slow oscillation shown in the top trace, about 0.9 Hz). The period marked by the horizontal bar and arrow, activity from the VL2 cell, is expanded (fourth trace from the top), and three parts from this period (a, b and c) are further expanded below. Another period in c is further expanded in d.
where, during a 1 s epoch, cell VL2 displayed a group of depolarizing potentials starting at a frequency of 30 Hz (a), continuing at 90 Hz (b), and ending at 120–150 Hz (c and d). While frequency accelerations within grouped fast events were most often observed, in other instances high-frequency events were followed by lower frequency events (see 70 Hz followed by 25 Hz in Fig. 1b). Figure 2 also demonstrates that thalamic neurones devoid of cortical connections do not display a slow oscillation which is coherent with that seen in the intact-cortex hemisphere (see EEG from right area 4) and the fact that the fast oscillations in cell VL2 may avoid a neurone (VL1) recorded within the same nucleus.

Of twelve dual intracellular recordings from VL neurones performed simultaneously in decorticated animals, eight cell couples displayed coherent spindle oscillations, but four cell couples showed striking differences. One such couple is illustrated in Fig. 2 and shows that cell VL1 (a) exclusively displayed periodic spindle sequences with waxing and waning IPSPs, whereas cell VL2 (b) showed prolonged depolarizations, recurring with a slow rhythm (0·4–0·5 Hz) which was quite different from that of the cortical slow oscillation under ketamine–xylazine anaesthesia (0·9 Hz; see the EEG trace of the contralateral, intact-cortex hemisphere).

The histograms of inter-event intervals (IEIHs) demonstrated the absence of any fixed or preferred frequencies for the fast oscillations. The group analysis of IEIs in a sample of ten VL neurones showed that 18·4 ± 2·9 % of IEIs were between 0 and 10 ms in duration; 48·6 ± 3·7 % were between 10 and 30 ms; and 33·0 ± 4·7 % were greater than 30 ms. One neurone of this sample is illustrated in Fig. 3A which shows 12·8 % of IEIs to be between 0 and 10 ms; 65·4 % between 10 and 30 ms; and 21·8 % in excess of 30 ms. The shortest IEIs were 5 ms (reflecting frequencies of 200 Hz). The fact that the majority of IEIs lasted between 10 and 30 ms indicates that the prevalent frequencies were 30–100 Hz. It should be emphasized that the frequency of depolarizing events changed by a factor of 2–5 in periods as short as 1 s (see again Fig. 2a–c in cell VL2). The amplitudes of depolarizing events were compared with the durations of IEIs and showed that IEIs separated by less than 13 ms were associated with lower amplitudes of fast depolarizing events than those of events separated by longer IEIs (Fig. 3B). We did not observe changes in amplitude at different $V_m$ levels (Fig. 3C) with the exception of very short episodes during spindle-related IPSPs (see below).

The effects of fast oscillations on the $R_m$ of TC cells and on their propensity to display LTSs were investigated by applying hyperpolarizing current pulses (100–200 ms) through the intracellular electrode. We measured in decorticated animals the $R_m$ during periods free of fast oscillations and during epochs with fast events ($n = 8$) and found that it decreased by about 27 % when hyperpolarizing current pulses were applied during fast events (22·7 ± 1·3 Ω in the absence and 16·8 ± 1·8 Ω in the presence of fast oscillations). Hyperpolarizing current pulses applied during epochs free of fast oscillations (Fig. 4A) triggered an LTS in isolation (Fig. 4A, 3) and, by increasing the duration and/or amplitude of current pulses, the LTSs were crowned by fast action potentials (Fig. 4A, 4–5), whereas no LTS was elicited by applying hyperpolarizing pulses with the same parameters during the fast oscillations. Besides, during the fast oscillations, depolarizing current pulses gave rise to more action potentials than in periods without fast events.

**Figure 3. Frequencies and frequency-dependent amplitudes of thalamic fast events**

_A_, inter-event interval histogram (IEIH, $n = 800$) shows the absence of a fixed frequency in fast depolarizing events in a VL cell. The great majority of IEIs were in the range 10–30 ms (reflecting frequencies between 30 and 100 Hz). _B_, plot showing the dependency of the amplitudes of fast events upon the IEI duration (abscissa, $n = 150$). Depolarizing events separated by less than 13 ms (dots, separated by dotted line) formed a group in which their amplitudes clearly diminished with IEIs. _C_, the amplitude of fast events did not depend on $V_m$. 

**Fast oscillations in cerebellothalamocortical pathway**

_J. Physiol._ **504.1** 157
Biphasic EPSP–FPP sequences build up fast spontaneous and evoked depolarizing events

In forty-eight of 216 VL neurones recorded from either intact-cortex and decorticated hemisphere, clear-cut differences between two components of the subthreshold depolarizing events could be observed. Figures 5–7 illustrate different aspects of the two subthreshold depolarizing events in spontaneously occurring and BC-evoked activities of VL cells, EPSPs and FPPs, eventually leading to full-blown action potentials. FPPs are defined according to criteria proposed for different neuronal types since the study of Spencer & Kandel (1961) on hippocampal cells (see Discussion).

The subthreshold depolarizations in the spontaneous activity depicted in Fig. 5 were EPSPs or sequences of EPSPs followed by FPPs (as in 1; see inflection marked by arrow). At slightly more depolarized levels, the EPSP–FPP sequence led to an action potential (2). The FPPs may be

Figure 4. Alterations in basic electrophysiological properties of TC cells during the fast oscillations

Amplitude and duration of depolarizing (1 and 2) and hyperpolarizing (3–5) current pulses as indicated by numbers on the traces which correspond to the protocol diagram (inset), in the absence (A) and presence (B) of spontaneously occurring fast oscillations. Resting $V_{m} = -60\text{ mV}$. Action potentials are truncated. Note in B the diminution of voltage deflections (3 and 4) triggered by hyperpolarizing current pulses and abolition of LTS during the fast oscillation (3–5).
confused with abruptly rising EPSPs; or, at hyperpolarized levels, with (partially) de-inactivated LTSs; or, in the case of FPPs with exceptionally high amplitudes, with initial segment (IS) spikes. Therefore, we attempted to differentiate these different components. Figure 6 illustrates the spontaneous activity of a VL cell at different $V_m$ values. At resting $V_m$ (−68 mV), this consisted of subthreshold depolarizations which occasionally gave rise to action potentials at a frequency of about 30 Hz. Under DC hyperpolarization, bringing the $V_m$ to −73 mV, half of the full spikes were obliterated and, instead, high-amplitude FPPs were seen on top of EPSPs, occasionally leading to action potentials that exhibited a clear-cut break between IS and somatodendritic (SD) spikes. Under further hyperpolarization (−78 mV), LTSs were observed, but their shape and duration were distinct from those of FPPs. Superimpositions of several traces (Fig. 6) revealed the four levels of depolarization: EPSPs, FPPs, and action potentials with both IS and SD components. The electrically differentiated records (Fig. 6) illustrate the rate of rise of the different components and show that the falling phase of FPPs (arrow) was considerably more rapid than in the case of a passive return to the former $V_m$. The intermediate depolarizing step between EPSPs and initiation of full-blown action potentials was similarly seen in 22% of neurones responsive to BC stimuli. Figure 7 depicts two such neurones displaying clear-cut inflections between EPSPs and faster events (arrows), eventually leading to action potentials at slightly more positive $V_m$ values, which were often reached towards the end of grouped fast oscillations (Fig. 7B, 3).

**Modulation of shape and amplitude of fast events during the slow oscillation and spindles**

The analysis of changes in patterns of spontaneous and BC-evoked fast depolarizing events during the slow oscillation and the subsequent sequence of spindles is important as the measurements of shapes and amplitudes of fast events may disclose those elements of low-frequency rhythms that are responsible for the striking reduction in synaptic transmission ofafferent signals through TC cells, which is known to be associated with the state of resting sleep (Steriade, 1970; J. Physiol. 504.159).

![Figure 5](image)

**Figure 5. EPSPs and FPPs build up spontaneously occurring fast depolarizing events in the thalamus**

Sections of the top trace (1—3) are expanded in the left panel below (somatic action potential is truncated) and further expanded in the right panel. Arrow marks inflection between EPSP and FPP. Note that at the more depolarized level (2), the EPSP–FPP sequence led to a somatic action potential.
Timofeev, Contreras & Steriade, 1996). The amplitudes and durations of fast events were considerably altered during various phases of the slow oscillatory cycle compared with control epochs free of low-frequency sleep rhythms (Fig. 8 and Table 1), especially during the descending phase of spindle-related IPSPs. The changes were as follows. (i) During the long-lasting hyperpolarization of TC cells, associated with depth-positive cortical EEG waves, the amplitude of spontaneously occurring fast events only slightly increased (by 10 %), but their duration (measured at half-amplitude) doubled (from 6.5 ms during control epochs to 13 ms during the hyperpolarization); consequently, the total area of depolarization increased by about 36 % (compare averages 1 and 2 in Fig. 8A; and see Table 1). (ii) By contrast, during the descending phase of spindle-related IPSPs that follow the slow oscillation, the amplitude

Figure 6. Differentiation of FPPs from EPSPs and IS spikes
Upper traces depict the spontaneous activity of a VL cell at resting $V_m$ (−68 mV, top left) and under hyperpolarizing current bringing the $V_m$ to −73 (top right) and −78 mV (second trace from top on left). Note decreased probability of full action potentials and their replacement by high-amplitude depolarizing events. The spontaneously occurring LTS at −78 mV (asterisk) is expanded (second trace from top on right) to show differences in shape and duration between LTS and FPPs. Lowermost traces: left, four levels of depolarizing event (EPSPs, FPPs, and IS and SD components of the full-blown action potentials) are illustrated (superimposition of 5 traces for each); right, electrically differentiated records illustrate that the rate of rise and decay of FPPs, occurring on top of EPSPs, is more rapid than that of the latter.
of fast events decreased by about 40%, their duration at half-amplitude decreased by 50%, and the total area of depolarization (see Methods) decreased by about 82% (compare averages 1 and 3 in Fig. 8A; and see Table 1); during the ascending part of IPSPs, the amplitude of fast events slightly decreased but their duration was exceedingly long. (iii) Similar results were observed by comparing BC-evoked fast events during the different components of the slow oscillation and subsequent spindles; in particular, the duration of BC-evoked fast events was greatly decreased during the descending phase of spindle-related IPSPs, which contrasted with their exceedingly long duration during the ascending phase of the same IPSPs (see Fig. 8B). Such changes were also observed during IPSPs evoked by local thalamic stimuli (not shown).

Synchronization of spontaneous and BC-evoked fast oscillations in the VL—cortical system

The coherence among fast oscillations occurring spontaneously or evoked by BC stimuli in thalamus and cortex was determined by: comparison between VL intracellular and area 4 field potentials, showing cortical activities delayed by intervals consistent with monosynaptic responses (Fig. 9); and autocorrelations, showing virtually identical frequencies in intracellular VL and field potential cortical activities, and EPSP-triggered averages (Fig. 10). These analyses were performed in fifty-seven simultaneous intracellular VL and field potential cortical recordings. In all but six cases, thalamic and cortical activities were found to be tightly synchronized, with time delays in area 4 potentials (compared with VL potentials) of 1.7–2.8 ms. The example

Figure 7. EPSP—FPP sequences in thalamocortical cells evoked by BC stimuli

A, BC stimulus evokes EPSP—FPP sequence (1, at −64 mV; arrow, inflection between the two events). At a more depolarized level (2, −62 mV) the same sequence led to a somatic action potential. B, three successive stimuli to BC evoked an EPSP (1, at −64 mV), an EPSP—FPP sequence (2, at −62 mV), and an EPSP—FPP sequence leading to action potential (3, at −58 mV).
in Fig. 9 shows VL responses evoked by pulse trains to the BC (5 stimuli at 100 Hz), repeated every second. The monosynaptic responses in the TC cell (with latencies of 1.5–1.6 ms) were followed after 1.8–2.4 ms by bisynaptic negative field potentials in the depth of projection cortical area 4 (arrows point to the expanded traces of two series of evoked responses). The close following of cortical field potentials after the monosynaptic EPSPs in TC neurones is also shown by averages of BC-evoked thalamic and cortical responses. Spontaneously occurring fast depolarizing events were in all respects similar to the BC-evoked responses (Fig. 9).

Figure 8. Alterations in amplitude and duration of fast events in TC cells during different phases of the slow oscillation and following spindles

A, one slow oscillatory cycle showing the epochs (1–3) from where averages (n = 40, shown below with corresponding numbers) of spontaneous fast events were computed. 1 is the control epoch before the initiation of the oscillatory cycle; 2 is during the depth-positive cortical EEG wave corresponding to the hyperpolarization of TC cell; and 3 is during the descending phase of spindle-related IPSPs (small arrows in A) that follow the slow oscillation (see EEG trace). B, BC-evoked fast events in another TC cell (under 0.5 nA depolarizing current; \(V_m\) without current was −68 mV). BC stimuli were applied at a fast rate (10 Hz) to detect differences between BC-evoked fast events during the descending and ascending phases of spindle-related IPSPs (see enlarged trace meets indicated by curved arrows).
Table 1. Characteristics of spontaneous and BC-evoked fast events during control epochs, depth-positive EEG component of the slow oscillation, and descending and ascending phases of the spindle-related IPSPs that follow the slow oscillation

<table>
<thead>
<tr>
<th></th>
<th>Spontaneous</th>
<th>BC-evoked</th>
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<tbody>
<tr>
<td></td>
<td>Duration</td>
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<tr>
<td></td>
<td>at Depolarization</td>
<td>at Depolarization</td>
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<td></td>
<td>Amplitude (mV)</td>
<td>half-amplitude (ms)</td>
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<tr>
<td></td>
<td>Amplitude (mV)</td>
<td>half-amplitude (ms)</td>
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<tr>
<td>Control</td>
<td>2.7 ± 0.3</td>
<td>6.5 ± 0.4</td>
</tr>
<tr>
<td>Depth-positive</td>
<td>3.0 ± 0.3</td>
<td>13.0 ± 1.4</td>
</tr>
<tr>
<td>Descending part of IPSP</td>
<td>1.6 ± 0.2</td>
<td>3.2 ± 0.3</td>
</tr>
<tr>
<td>Ascending part of IPSP</td>
<td>2.4 ± 0.3</td>
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</tbody>
</table>

Seven cells were analysed for both spontaneous and BC-evoked fast events. In each cell, the amplitudes, durations and depolarization areas of EPSPs (see Methods) were averaged (n = 40) during the different components of low-frequency sleep-like oscillations.

Figure 9. Thalamic responses to fast BC stimuli are faithfully reflected in the cortical area

Top two traces, simultaneous recordings of cortical field potentials from the depth of area 4 and intracellular activity of a thalamocortical VL neurone. The traces include five cycles of the spontaneous cortical slow oscillation (about 0.9 Hz) reflected in a VL neurone, as well as responses to four pulse trains (five stimuli at 100 Hz) applied to BC. Cortical and thalamic responses to two pulse trains are expanded below (bars, arrows). Bottom left, average of BC-evoked responses (n = 5). Bottom right, spontaneously occurring fast depolarizing events are compared with the BC-evoked events in a different period of recording.
The coherence between thalamic and cortical fast rhythmic events was demonstrated by different measures of synchrony. However, tight synchronization was only observed during short periods of time (less than 1 s) because of changing frequencies in one of the two (thalamic and cortical) sites of recordings. This is depicted in Fig. 10 in which, over a period of about 300 ms (horizontal bar below the intracellular trace), only half of it showed identical frequencies in the autocorrelations of intracellularly recorded activity of VL neurone and field potentials in area 4, as well as in the EPSP-triggered averages of these activities, with cortical depth-negativities following with a lag of about 1·5 ms the peaks of EPSPs in the TC cell. During the immediately adjacent half of this epoch, the fast frequencies were slightly different in the VL nucleus and area 4, and the EPSP-triggered averages no longer displayed evidence of synchrony. The synchrony of fast depolarizing oscillations in the VL—cortical system was further demonstrated by either averaged thalamic activities triggered by the peaks of depth-negative cortical field potentials or averaged cortical activities triggered by the action potentials of intracellularly recorded VL neurones (not shown).

![Figure 10. Synchronization of thalamic and cortical fast oscillations](image)

Upper four traces (from top to bottom), field potential recording from the depth of area 4 and digitally filtered trace (20—80 Hz), and filtered (20—80 Hz) intracellular activity from a VL neurone and real intracellular recording. Period marked by the horizontal bar is expanded below (arrow) with the three traces (from top to bottom) showing the filtered EEG, filtered intracellular, and real intracellular activities. Below are cellular (VL, continuous trace) and EEG (area 4, dashed trace) activity autocorrelograms and EPSP-triggered averages corresponding to the trace sections indicated by brackets and arrows. Note the synchronous thalamocortical activities in the left traces, and absence of such coherence between VL and cortical activities in the right traces.
Abolition of fast events in VL cells after lesions of afferent BC axons

The intracellular activity of the same TC cells could be recorded before and after massive electrolytic lesions of BC axons (n = 4). In all cases, the fast events recorded before BC lesions were dramatically diminished or abolished after the lesion. Figure 11 shows spontaneous fast oscillations (40–120 Hz) and VL responses evoked by fast (200 Hz) BC stimuli (left), and the disappearance of fast events after BC lesion (right).

DISCUSSION

The main findings in this study are as follows. (i) Fast spontaneous oscillations (mainly 30–100 Hz) in cat VL relay cells consist of EPSPs and FPPs, eventually leading to full-blown action potentials. The spontaneous oscillations are similar to responses elicited by cerebellothalamic volleys and their incidence is diminished up to disappearance after lesion of afferent BC axons. (ii) The amplitude and duration of fast events are diminished during the descending phase of spindle-related IPSPs. (iii) Spontaneously occurring and

Figure 11. Abolition of fast depolarizing events in VL thalamus after lesion of cerebellothalamic pathway

Three episodes (1–3) of intracellular VL activity (paired traces: lower, real activity; upper, filtered between 20 and 10,000 Hz and enlarged five times) before (left column) and after (right column) BC lesion. Sections of trace in episodes 3 (marked by horizontal bar and arrow) are expanded and shown below. The expansion on the right shows a typical LTS burst following a prolonged hyperpolarization. Middle column, responses of VL cell to one BC stimulus (top) and five BC stimuli (bottom, 200 Hz) (arrowheads mark stimuli). Five experimental traces are shown in each case plus an averaged trace at the bottom.
BC-evoked fast events in VL cells are synchronized with field potentials recorded from the motor cortex. These data point to the induction of fast rhythms by specific afferents of TC systems and further indicate that spindles constitute the major element for the obliteration of fast incoming signals through the thalamus during sleep.

**Fast oscillations in TC cells**

The configuration and frequency of fast oscillations in the present study of VL neurones are similar to those previously described in intracellular recordings from the motor thalamus (Steriade et al. 1991; Pinault & Deschenes, 1992; Steriade, Contreras, Amzica & Timofeev, 1996b) as well as from the intralaminar centrolateral (CL) and lateral geniculate (LG) thalamic nuclei (Steriade et al. 1991; Nuñez, Amzica & Steriade, 1992b). Our data showed that the fast oscillations consist of EPSPs that give rise to FPPs in 22% of recorded neurones. FPPs have previously been recorded in TC cells (Maekawa & Purpura, 1967; Deschenes, Paradis, Roy & Steriade, 1984). Several features of the FPPs described in the present study are identical to those described in the original paper on these depolarizing events in hippocampal neurones (Spencer & Kandel, 1961): the falling phase of FPP was considerably more rapid than a purely passive decay would allow, IS—SD break occurred in association with FPPs, and FPPs were initiated at about 5—10 mV below the usual firing level (see Fig. 6).

In contrast to the fixed frequency of fast thalamic oscillations reported in experiments on rats under urethane anaesthesia, in which `single sharp peaks’ were found in autocorrelograms (Pinault & Deschenes, 1992), our data showed great variations in frequencies that could change by factors of 2—5 over periods as short as 0·3—1·0 s (see Figs 2 and 10). Such changes are congruent with similar phenomena reported from intracellular recordings of neocortical neurones where changes in frequency and amplitude of membrane fluctuations occurred within very short epochs, doubling with the progression of depolarization and decreasing after about 0·5 s, both in vivo (Steriade, Amzica & Contreras, 1996a) and in organotypic cultures (Plenz & Kitai, 1996). The dependency of fast oscillations on the depolarization of TC and cortical cells is in line with the assumption that, rather than being necessarily implicated in cognitive processes, the fast oscillations simply reflect the depolarization state of forebrain neurones, under the control of ascending activating modulatory systems (Steriade et al. 1996a).

The cerebellar origin of at least some fast depolarizing oscillations recorded from cat VL neurones is in keeping with previous results from rat VL cells (Pinault & Deschenes, 1992), as well as other relay thalamic nuclei. Thus, the thalamic source of such rapid rhythms is consistent with data from intracellular recordings of LG relay neurones where the frequency of spontaneous FPPs is accelerated to 40—50 Hz by photic stimuli and spontaneous fast events are suppressed after blockade of retinal inputs (Nuñez et al. 1992a).

The fact that fast oscillations in TC cells have been recorded in the present experiments after ipsilateral hemidecortication and have been strikingly reduced after BC lesions does not imply that the only sources of such events are prethalamic relay stations. On the one hand, intrathalamic operations may generate fast oscillations. Indeed, short-lasting hyperpolarizing current pulses reset and transiently increase the amplitudes of fast intrinsic oscillations in TC cells, thus suggesting that short IPSPs from thalamic GABAergic neurones may produce the same effects (Pedrosa & Linóa, 1997). Other candidates for the generation and synchronization of fast oscillations are a subset of intralaminar CL thalamic neurones discharging depolarization-dependent spike bursts with unusually high intraburst frequencies (900—1000 Hz) at about 40 Hz (Steriade et al. 1993). It is known that rostral intralaminar nuclei have widespread neocortical projections (Jones, 1985) and, thus, may impose the fast oscillations to various cortical areas. The synchronization of fast rhythms through intralaminar—cortical systems was hypothesized on the basis of magnetoencephalographic recordings (Linóa & Ribarya, 1993). On the other hand, corticothalamic neurones, as identified in cat association cortical areas 5 and 7 by antidromic invasion from the lateroposterior (LP) or intralaminar CL thalamus and receiving monoaminergic excitation from the same nuclei, have a high propensity to intrinsically generate fast rhythmic (30—40 Hz) spike bursts with high intraburst frequency (about 400 Hz) at given levels of depolarization (Steriade, 1997; M. Steriade, I. Timofeev, N. Dürmüller and F. Grenier, unpublished observations). Being part of a corticothalamocortical loop, such neurones are ideal candidates for transferring the fast oscillations to the thalamus and, after intrathalamic synchronization processes (Steriade et al. 1996b), to receive back these integrated rhythms.

**Gating of fast depolarizing events during spindle-related IPSPs in TC cells**

The synaptic transmission of afferent signals through the thalamus is obliterated during the state of resting sleep. It was shown by means of field potentials from the cat VL nucleus that the thalamus is the first relay station where blockade of incoming information occurs when falling asleep. The postspindle potentials evoked by stimulation of afferent cerebellar fibres diminish in amplitude or virtually disappear during drowsiness, well before behavioural sleep is fully developed, in spite of no concomitant alteration in the presynaptic deflection that monitors the magnitude of cerebellofugal volley (see Fig. 9 in Steriade, Iosif & Apaetol, 1969). Spindles are oscillations that mark the early stage of sleep, so it was therefore of interest to investigate the fluctuations in amplitude and duration of fast depolarizing oscillations during the brief sequence of spindles that follow the slow oscillation under...
ketamine-xylazine anaesthesia especially since we showed previously that the BC-evoked EPSPs are not changed during the long-lasting hyperpolarizing component of the slow oscillation (Timofeev et al. 1996). In that study, the prolonged hyperpolarization prevented TC cells transferring signals of prethalamic origin to the cortex, but the amplitude and duration of BC-evoked EPSPs did not change. This result, which was unexpected because observations in behaving animals demonstrate a striking reduction in TC responsiveness from the very onset of sleep (Steriade et al. 1969), was interpreted as being due to the fact that the timing of testing stimuli is crucial and we hypothesized that BC-evoked responses may be altered during the following spindle sequence. The present results demonstrate that the amplitude of BC-evoked EPSPs diminishes by about 40 %, and the duration by 50 %, during the hyperpolarizing phase of spindle-related IPSPs. It is known that TC cells display an important increase in membrane conductance during the GABA-mediated IPSPs (Crunelli, Haby, Jassek-Oerschenfeld, Leresche & Pirchio, 1989) which build up spindles in TC neurones (Andersen & Anderson, 1968; Deschênes et al. 1984; Nuñez, Curro Dossi, Contreras & Steriade, 1992b; Bal, von Krogh & McCormick, 1995). Thus, inhibition of afferent information through the thalamus critically depends on spindle oscillations.

The reciprocal relations between the fast depolarizing events and various components of the sleep oscillations in TC cells were quite complex; in some instances the fast oscillations were suppressed during the long-lasting hyperpolarization of the slow oscillation, as also noticed with the fast rhythms originating in corticothalamic networks (Steriade et al. 1996a,b), whereas in adjacent slow oscillatory cycles the fast depolarizing oscillations succeeded in overwhelming the prolonged hyperpolarizing phase of the slow oscillation (see Fig. 1). Predictably, however, the fast oscillations diminished the Rm in TC cells and prevented the rebound LTS de-inactivated by membrane hyperpolarization (Fig. 4). This suggests that the coupling between thalamus and cortex through the rebound spike bursts of TC neurones during sleep may be disrupted by trains of high-frequency afferent signals.

Coherent fast oscillations in TC systems during brain activation

Diffuse brain activation, consisting of the blockage of low-frequency high-amplitude oscillations coupled with the induction of fast rhythms, is produced by brainstem and forebrain modulatory systems exerting their actions upon the thalamus and cerebral cortex. Besides these generalized systems, activation of brain electrical activity can be elicited by specific sensory or motor projections acting on circumscribed regions in the thalamus and cerebral cortex. Bremer's (1935) claim that the cerebral tone is maintained by sensory projections was supported by experiments performed in his laboratory by Claes (1939), showing that sleep spindles selectively appear over the visual cortex following bilateral section of optic nerve. Similarly, stimulation of interpositus or dentate cerebellar nuclei produces an activation pattern, including fast activity around 40 Hz, that is transmitted through the VL thalamus and is confined to the motor cortex, whereas stimulation of the fastigial nucleus induces much more diffuse fast rhythms because the thalamic relay of fastigial nucleus is the ventromedial (VM) nucleus projecting more diffusely over the cortex (Steriade, 1995).

The present data show, by means of a series of analyses including EPSP- and spike-triggered averages, that fast depolarizing events in VL cells are synchronized with EEG field potentials recorded from the motor cortical area 4. In general, the coherence of fast rhythms decreased with distance and became weaker over distances of 5–7 mm in the cat cerebral cortex (Steriade et al. 1996a). However, the synchronization of fast oscillations was also observed among different thalamic nuclei (Steriade et al. 1996b), even between specific and intralaminar nuclei that are not linked by known direct projections (Amzica, Neickelmann & Steriade, 1997); the synchronization process is probably mediated in such cases by neocortical areas. In the present study, the synchronization between thalamic and cortical fast oscillations occurred over short periods, generally less than 1 s duration, and was thus different from the long-range coherence of low-frequency (< 15 Hz) sleep rhythms (see Steriade et al. 1996a). Thus, the so-called specific projection pathways, with access to circumscribed thalamic and cortical fields, contribute to the generation of brain activation patterns.


