INTRODUCTION

In the CNS, the dendrites of different neuronal types can receive thousands of synaptic inputs. The passive cable theory predicts that the sum of these inputs would be algebraic if they are electrically isolated or attenuated if they are electrically close (see Spruston et al. 1994, for review). Indeed, the proximity between synaptic inputs can lead to a change in the ionic driving force or to a shunt of the synaptic currents by decreasing the input resistance of the membrane. In addition to these passive properties, active membrane mechanisms can also influence the processing of information, and the final integration of synaptic inputs depends on nonlinear interactions dictated by the distribution and activation of voltage-gated channels in dendrites (see Yuste and Tank 1996, for review).

Although theoretical models aiming to understand passive and active integrations of different synaptic inputs exist (Jaslove 1992; Mel 1993; Softky 1994), reliable experimental tests of their predictions are sparse. In cortical structures, the summation of subthreshold excitatory synaptic inputs by pyramidal cells has recently been studied (Cash and Yuste 1998; Urban and Barriónuevo 1998), but there is still a lack of information about the integrative properties of other types of cortical neurons. In addition, most experiments have been done with extracellular stimulation, i.e., by activating simultaneously several different presynaptic fibers, or by mimicking synaptic inputs with local applications of exogenous glutamate (Cash and Yuste 1998; Langmoen and Andersen 1983; Skydsgaard and Hounsgaard 1994; Urban and Barriónuevo 1998). Under these conditions, the contribution of active mechanisms to the integration of synaptic potentials generated by the activation of unitary inputs is not easily resolved.

At excitatory glutamatergic synapses, the postsynaptic depolarization is primarily due to the activation of ionotropic \(\alpha\)-amino-3-hydroxy-5-methyl-4-isoxazole-propionate (AMPA) and \(N\)-methyl-d-aspartate (NMDA) receptors. The block of NMDA channels by magnesium ions at hyperpolarized potentials results in the marked nonlinear properties of these receptors. The integration of a given synaptic excitatory input will therefore be affected by the presence of nearby voltage-gated channels (see above) and also by the relative proportions of NMDA and AMPA receptors at these synapses (Thomson 1997; see Thomson and Deuchars 1995 for review).

The aim of the present work was to examine by means of paired recordings the characteristics of unitary excitatory connections between pyramidal cells and fast-spiking (FS) interneurons, a subpopulation of nonpyramidal cells (Cauli et al. 1997; Kawaguchi and Kubota 1993; McCormick et al. 1985). We first characterized the postsynaptic properties of excitatory postsynaptic potentials (EPSPs) and excitatory postsynaptic currents (EPSCs) mediated by glutamate receptors at pyramidal-FS interneuron connections.
dial cell to FS interneuron connections in layer V of rat motor cortical slices. We then analyzed how different excitatory inputs were integrated by FS cells. We found that the summation of excitatory synaptic responses was linear, and we could therefore estimate the number of pyramidal cells needed to be activated to make a FS cell fire.

METHODS

Slice preparation

Wistar rats (20 ± 6 postnatal day-old; range 14–35) were anesthetized by an intraperitoneal injection of Ketamine (65 mg/kg) and Xylazin (14 mg/kg) and decapitated. Brains were quickly removed and 300-μm thick parasagittal sections of cerebral motor cortex were prepared as previously described (Cauli et al. 1997). The slices were incubated for 1 h in a physiological extracellular saline solution containing (in mM) 121 NaCl, 2.5 KCl, 1.25 NaH₂PO₄, 2 CaCl₂, 1 MgCl₂, 26 NaHCO₃, 20 glucose, and 5 pyruvate and bubbled with a mixture of 95% O₂, 5% CO₂. For recordings, they were transferred to a chamber and perfused at 1–2 ml/min with the same physiological extracellular saline solution at 30–33°C.

Paired recordings

Pyramidal-FS connections were examined by paired recordings as previously described (Angulo et al. 1999). Briefly, postsynaptic FS interneurons in layer V of the motor cortex were recorded with patch pipettes (resistance 3–5 MΩ) pulled from borosilicate glass tubing and filled with an internal solution containing (in mM) 144 K-gluconate, 3 MgCl₂, 0.2 EGTA, and 10 HEPES (pH 7.2–7.4, 300 mosM). In five experiments, we also included 4 mM ATP and 0.4 mM GTP. Postsynaptic FS cells were initially visualized using videomicroscopy with Nomarski optics under infrared illumination (Stuart et al. 1993) and later identified by the characteristics of their action potential discharges according to the procedure reported by Cauli et al. (1997). Only FS neurons with multipolar shapes and membrane potentials more negative than −60 mV were included in the sample. All membrane potentials were corrected for a junction potential of −60 mV.

After whole cell recordings were established, presynaptic pyramidal cells were impaled with sharp intracellular microelectrodes filled with 3 M KCl (resistance 40–80 MΩ) and identified by their characteristic action potential firing (Connor and Outtick 1990; McCormick et al. 1985). Unitary EPSCs and EPSPs were induced in FS cells by triggering action potentials in presynaptic pyramidal cells with depolarizing pulses (3 ms, 1.5 nA). Means of elicited synaptic responses were obtained by averaging the traces after the presynaptic action potential was aligned using automatic peak detection. The stability of the recordings during the time course of the experiment was tested by plotting the amplitudes of individual synaptic responses against time. Only connections showing stable EPSC or EPSP amplitudes and probabilities of response were further analyzed. From 50 to 100 traces were averaged to measure parameters of mean synaptic responses.

A Cs-glucuronate internal solution was used to minimize the voltage-clamp error in experiments aimed to study the current-voltage (I-V) curves of AMPA and NMDA receptor synaptic components of unitary EPSCs. However, to obtain the firing pattern of postsynaptic FS cells, the tip of the patch pipette was filled with the K-glucuronate internal solution (see above) and backfilled with a solution of the following composition (in mM): 125 Cs-glucuronate, 3 MgCl₂, 10 EGTA, 10 HEPES, 4 ATP, and 0.4 GTP (pH 7.2–7.4, 300 mosM). Spermereine (100 μM) was also included to maintain the voltage dependence of AMPA receptors (Bowie and Mayer 1995; Kamboj et al. 1995; Koh et al. 1995). The dialysis of the recorded cell with the Cs-glucuronate solution could be observed from the broadening of the action potentials after ~15 min of recordings.

Paired recordings were combined with extracellular stimulations (100 μs; 0.02–0.04 mA) using a monopolar electrode placed in layer III or V of the motor cortex to determine how the responses elicited by two independent excitatory inputs were integrated by FS interneurons. The position of the extracellular electrode and the stimulation intensities were adjusted to elicit pure excitatory responses; in our recording conditions, inhibitory synaptic currents were outwardly directed and thus could be distinguished from excitatory responses. The extracellular electrode was also used to establish the action potential threshold of FS interneurons. Stimulation intensities were increased until synaptic potentials induced in FS cells triggered an action potential. The threshold was measured when 50% of the responses elicited an action potential.

Data collection and analysis

Whole cell current-clamp (mode I-Clamp fast) and voltage-clamp recordings of postsynaptic FS cells were obtained using a patch-clamp amplifier (Axopatch 200A, Axon Instruments) and filtered at 5 or 2 kHz. Series resistances were monitored throughout the experiments and compensated only in experiments aimed to assess the independence of two inputs. Intracellular current-clamp recordings of postsynaptic pyramidal cells were obtained using an intracellular amplifier (Neuro Data, Instruments Corp.). Digitized data were acquired and analyzed using AcquisI software (Gérard Sadoc, CNRS, Gif-sur-Yvette, France).

Means of evoked unitary synaptic responses were obtained by averaging the traces after the presynaptic action potentials were aligned using automatic peak detection. Traces not showing postsynaptic responses larger than 150% of the noise level were considered as failures. The mean rise times (20–80%) of EPSCs and EPSPs were calculated by averaging the synaptic responses excluding failures. All statistical data are given as means ± SD.

The AMPA receptor–mediated synaptic current was obtained by subtracting the insensitive 6,7-dinitroquinoxaline-2,3-dione (DNQX) or 2,3-dioxo-6-nitro-1,2,3,4-tetrahydrobenzoquinoxaline-7-sulphonamide (NBQX) NMDA receptor–mediated synaptic current from the control current. The rectification index (RI) of the AMPA receptors was calculated from I-V curves with the following expression (Angulo et al. 1997; Ozawa et al. 1991)

\[
RI = \left[ (I_{-28} - I_{rev}) / (I_{-72} - I_{rev}) \right] \left[ (I_{-28} - I_{rev}) / (I_{-72} - I_{rev}) \right]
\]

where \(I_{-28}\) and \(I_{-72}\) correspond to the currents at +28 mV and −72 mV, respectively, and \(I_{rev}\) to the experimental reversal potential. For statistical analyses the currents of the I-V curve obtained in the control solution (without DNQX or NBQX) were also included. In these cases, the I-V curve of the AMPA receptor component was obtained by measuring the EPSC amplitude at <0.5 ms after the beginning of the response to minimize the contamination by the NMDA receptor component. The chord conductances of the currents mediated by NMDA (g_{NMDA}) and AMPA (g_{AMPA}) receptors were calculated according to the expression \(g = f(V - E_{rev}) + 40 \text{ mV} \) and −60 mV, respectively.

The kinetics of AMPA and NMDA receptor components were determined by fitting the EPSCs with one or two exponential functions at different membrane potentials. When the decay was best fitted by two exponential functions, an amplitude-weighted decay time constant (\(\tau\)) of AMPA receptor–mediated synaptic currents was calculated by summing the two time constants, weighted by their fractional amplitude contribution. For comparison between cells, \(\tau_{NMDA}\) were determined by fitting the decay of the slow component of the EPSC recorded at holding potentials between +38 and +48 mV in control experiments (without DNQX or NBQX). Because the kinetics of the AMPA receptor current is faster than that of the NMDA receptor current, the contamination by the AMPA receptor component during the decay phase of the NMDA receptor component is negligible.
CNQX, DNQX, and NBQX were purchased from Tocris Cookson (Bristol) and the GYKI 53655 was a gift from Egis (Budapest).

**RESULTS**

The glutamate-mediated synaptic responses of neocortical pyramidal cell to FS interneuron connections were examined by using paired recordings \((n = 39)\). Presynaptic pyramidal cells were impaled with sharp intracellular microelectrodes, and unitary EPSCs and EPSPs were recorded in FS cells in the whole cell configuration with patch pipettes in layer V of the motor cortex (see METHODS).

Presynaptic and postsynaptic cells were first identified by the kinetics of their action potential firing. Figure 1A1 illustrates the firing behaviors of a pyramidal cell (top panel) and a FS interneuron (bottom panel), which were synaptically coupled. Presynaptic pyramidal cells showed slow action potentials and a strong and rapid accommodation of their action potential firing induced by depolarizing current pulses (see Connors and Gutnick 1990, for review). Postsynaptic FS interneurons had fast action potentials and limited accommodation of their action potential firing at all tested stimulation intensities (Cauli et al. 1997; Kawaguchi 1995; Kawaguchi and Kubota 1993). A detailed description of the firing kinetics and morphology of pyramidal-FS connections considered in the present work has been previously reported (Angulo et al. 1999).

**Unitary AMPA and NMDA receptor–mediated postsynaptic responses at pyramidal-FS connections**

Unitary EPSPs were induced in FS interneurons by eliciting action potentials in the presynaptic pyramidal cells at a stimulation rate of 1 Hz (Fig. 1A2). Postsynaptic potentials were characterized by brief latencies (0.6 ± 0.2 ms, mean ± SD, \(n = 13\)) and fast rise times (0.76 ± 0.3 ms, \(n = 18\); see METHODS). At a membrane potential of −72 mV, the average amplitude and width at half-amplitude of the EPSPs had mean values of 2.1 ± 1.3 mV (0.35–5 mV) and 10.5 ± 3.7 ms (4.6–18.5 mV; \(n = 18\)), respectively. We did not find any correlation between the rise time and the EPSP amplitude or width at half-amplitude (data not shown), suggesting that the variability of the EPSPs was not markedly caused by cable attenuation of the responses over the dendrites of FS cells.

We then tested the effect of different glutamate receptor antagonists to identify the postsynaptic receptors underlying the unitary EPSPs at pyramidal-FS connections. Near the resting membrane potential of FS interneurons (−76 ± 5 mV; \(n = 38\)), the AMPA/kainate antagonist 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX; 10 μM) almost completely blocked the EPSPs (Fig. 1B1). In contrast, bath application of the NMDA antagonist α-(−)2-amino-5-phosphonovaleric acid (α-AP5; 50 μM) had only minor effects on the EPSPs (data not shown). This antagonist did not affect significantly either the amplitude or the width at half-amplitude of the EPSPs when the postsynaptic cells were depolarized to −60 mV (\(P > 0.05\), Wilcoxon \(t\)-test; Fig. 1B2). More depolarized membrane potentials were not tested in current-clamp because FS interneurons had a low action potential threshold (−55 ± 3 mV, \(n = 6\); see METHODS). These results indicate that, at subthreshold postsynaptic membrane potentials, NMDA receptors do not contribute significantly to the synaptic transmission at pyramidal-FS connections.

To further characterize the postsynaptic receptors involved at these connections, we studied the kinetics and voltage dependence of unitary EPSCs. Figure 2A illustrates the average unitary EPSCs of a FS interneuron at different membrane potentials. At a holding potential of −72 mV, the average EPSC excluding failures rose and decayed rapidly. In most of the connections, the decay was best fitted with a double exponential function showing a predominant fast component (Fig. 2B). For 16 connections, the rise time and amplitude-weighted decay time constant of the fast synaptic component had mean values of 0.29 ± 0.04 ms and 2 ± 0.8 ms, respectively (see METHODS). At this potential, 10 μM of the AMPA/kainate receptor antagonists NBQX or DNQX blocked 98 ± 2% of the synaptic currents (\(n = 5\); Fig. 2B). The selective antagonist of AMPA receptors GYKI 53655 (40–66 μM) also blocked 96 ± 1.9% of α-AP5–insensitive responses, confirming the predominance of AMPA receptors, as opposed to kainate receptors, at pyramidal-FS connections (\(n = 3\); data not shown).
postsynaptic response. A monoexponential fit of the EPSC decay was superimposed to the mean average of 106 responses at a holding potential of 72 mV. A biexponential fit of the average unitary EPSC recorded at +38 mV. Traces are averages from 50 to 106 responses. B: superimposed averages of the NMDA receptor–mediated component of the unitary EPSCs at different holding potentials (−72, −32, +28, and +48 mV) recorded in the presence of 2,3-dioxo-6-nitro-1,2,3,4-tetrahydrobenzoquinoxaline-7-sulphonamide (NBQX; 10 μM). Note the almost complete block of the EPSCs at −72 mV and the increase of the response at more depolarized potentials. C: peak current-voltage (I-V) relations of AMPA and NMDA receptor–mediated synaptic currents at the same pyramidal-FS connection. Note the inward rectification at positive potentials of the AMPA receptor–mediated currents and the region of negative slope at negative potentials on the I-V curve of the NMDA receptor–mediated responses. D: kinetics of the AMPA receptor–mediated component of the unitary EPSC. Average of 50 responses at holding potential of −72 mV. A biexponential fit of the EPSC decay was superimposed to the mean postsynaptic response. Numbers in parentheses represent the relative amplitude of the 1st (τ₁) and the 2nd (τ₂) exponential. E: kinetics of the NMDA receptor–mediated component of the unitary EPSC. Average of 106 responses at a holding potential of +48 mV. A monoeXponential fit of the EPSC decay was superimposed to the mean postsynaptic response.

As shown in Fig. 2C, the I-V plot of the AMPA receptor EPSCs showed a pronounced inward rectification with a RI of 0.38 ± 0.1 (n = 9, see METHODS). The fast kinetics and the inward rectification of this EPSC component was consistent with the activation of calcium-permeable AMPA receptors lacking GluR2 subunits (see Jonas and Burnashev 1995, for review; Angulo et al. 1997; Lambolez et al. 1996).

At positive holding potentials, unitary EPSCs showed an additional slower component (Fig. 2A, inset). This component was insensitive to NBQX (Fig. 2B) and had a mean rise time of 7 ± 0.5 ms and a decay time constant of 52 ± 9 ms (n = 4; Fig. 2E). The I-V plot of the average slow EPSC had a region of negative slope between −60 mV and −20 mV (Fig. 2C), characteristic of NMDA receptor–mediated currents (Mayer et al. 1984; Nowak et al. 1984).

We estimated the relative proportion of NMDA and AMPA receptor–mediated synaptic components by calculating the ratio of gnMDA(+40 mV)/gAMPA(−60 mV), which was 19 ± 1% (n = 3; see METHODS).

These results indicate that calcium-permeable AMPA receptors and NMDA receptors are present at pyramidal-FS connections. However, when the membrane potential of the interneuron is below the action potential threshold, synaptic transmission is mainly mediated by AMPA receptors.

Integration of excitatory inputs in FS interneurons

We previously reported that either depression or facilitation of synaptic currents can occur at pyramidal cell to FS interneuron connections when pairs of presynaptic action potentials are applied (Angulo et al. 1999). We therefore tested how unitary EPSPs triggered by train of moderately high-frequency presynaptic action potentials were temporally integrated at connections showing paired-pulse depression (Fig. 3A) and paired-pulse facilitation (Fig. 3B). At both types of connections, we observed a limited temporal summation of unitary EPSPs when presynaptic action potentials were delivered every 15 ms at a stimulation rate of 0.2 Hz (Fig. 3). The rapid time course of unitary EPSPs prevented significant temporal summation at these connections. Together with the small mean amplitude of unitary EPSPs, the lack of substantial temporal summation indicates that several presynaptic pyramidal cells must fire simultaneously to induce the discharge of a FS interneuron.

We therefore determined how FS cells integrate the responses elicited by two independent inputs by combining paired recordings with extracellular stimulations using a monopolar electrode placed in layer III or VI of the motor cortex.

We first tested the independence of these two inputs in voltage-clamp mode using two different procedures. First, as shown in Fig. 4A, the EPSC induced by the extracellular stimulation (extracellular EPSC) and the EPSC elicited by the activation of the presynaptic pyramidal cell (unitary EPSC) were first elicited alternately and then simultaneously. The predicted sum of the two EPSCs elicited alternately was com-

![Image](https://via.placeholder.com/150)
pared with the experimental sum obtained by simultaneous stimulation of the two inputs (Fig. 4A2). The independence of both inputs was assumed when there was <10% difference between the amplitude of the predicted and the experimental sum of the EPSCs ($n = 5$; Fig. 4A2). However, this protocol could lead to exclusion of cases where nonlinear summation of independent inputs arises from a large shunt of the membrane caused by one of the inputs. Therefore the independence of the inputs was tested in six other experiments with a second protocol. The paired-pulse response characteristics of the unitary EPSC were first examined using pairs of single action potentials elicited in the presynaptic pyramidal cell by applying two short depolarizing current pulses separated by 50 ms (Fig. 4B1; top light traces). In all tested pyramidal-FS connections, the amplitude of the first EPSC (EPSC1) was larger than that of the second EPSC (EPSC2), indicating that these connections displayed a paired-pulse depression in our recording conditions (Fig. 4B1; top light traces). The mean paired-pulse ratio (EPSC2 amplitude/EPSC1 amplitude) was 0.7 ± 0.18. After the paired-pulse characteristics of the unitary connections were established, we determined whether the unitary input was depressed by a preceding extracellular stimulation (Fig. 4B1; bottom dark traces). The extracellular input was therefore stimulated 50 ms before testing the unitary input (Fig. 4B1; bottom dark traces). The independence of both inputs was assumed when there was <10% difference between the unitary EPSC1 obtained with or without a preceding extracellular stimulation (Fig. 4B1, inset).

Once the independence of the two inputs was established, we switched to the current-clamp mode to compare the predicted sum corresponding to the algebraic summation of the two EPSPs elicited alternately to the experimental sum obtained by stimulating the two inputs simultaneously (Fig. 4, A and B, right). As shown in the examples of Fig. 4, the EPSPs of the predicted and experimental sums were well superimposed, suggesting a linear summation of the two synaptic responses (Fig. 4, A4 and B3).

For 11 recorded FS interneurons, the amplitude and width at half-amplitude of the predicted and experimental sums obtained at different membrane potentials were not significantly different and were correlated with linear coefficients of regression of 0.99 and 0.93, respectively (Fig. 5, A1 and A2; $P > 0.05$, Wilcoxon $t$-test). These data indicate that, in FS cells, the integration of the responses elicited by independent inputs was linear and that the kinetics of EPSPs did not change during the summation of different responses.

To determine whether the linearity of the experimental sum of the EPSPs was dependent on the membrane potential, we plotted the ratio experimental/predicted sum amplitudes as a function of the potential (from $-85$ to $-57$ mV; Fig. 5B1). We did not observed any significant correlation between this ratio and either the holding potential (○) or the potential at the peak
of the response (■; coefficients of regression of $-0.01$ and $-0.02$, respectively). The ratio experimental/predicted EPSP amplitude was also independent of the amplitude of the unitary EPSP (Fig. 5B2; coefficient of regression of $-0.22$) and of the extracellular EPSP (data not shown; coefficient of regression of 0.2) and had a mean value of $103 \pm 6\%$ ($n = 11$). These results show that the responses elicited by two independent inputs were integrated linearly by FS cells even near the action potential threshold.

**DISCUSSION**

Paired recordings in neocortical slices showed that both calcium-permeable AMPA and NMDA receptors mediate the synaptic responses at pyramidal-FS connections. The contribution of NMDA receptors was, however, almost negligible at subthreshold potentials. By combining paired recordings with extracellular stimulations, we also demonstrated that the sum of synaptic responses elicited simultaneously by two independent excitatory inputs in FS cells is algebraic at subthreshold potentials.

**Glutamate synaptic receptors at pyramidal-FS connections**

It has been shown previously that neocortical FS interneurons express a relatively low proportion of the AMPA receptor subunit GluR2 (Lambolez et al. 1996). It is now clearly established from studies on recombinant and native receptors, that AMPA receptors lacking this subunit have a large single-channel conductance, an inwardly rectifying $I-V$ curve, and a high calcium permeability (see Jonas and Burnashev 1995, for review). Our present data demonstrate that, as established for extrasynaptic receptors of FS cells (Angulo et al. 1997), AMPA receptors contributing to synaptic transmission at pyramidal-FS connections displays an inward rectification. The good correlation between the rectification index and the calcium permeability of native AMPA receptors (Lino et al. 1994; Itazawa et al. 1997) allows us to estimate the permeability ratio of Ca$^{2+}$ over monovalent cation of AMPA receptors at pyramidal-FS synapses to be close to 1, i.e., almost 10 times higher than that of nonrectifying receptors. The activation of pyramidal-FS synapses is thus always associated with a Ca$^{2+}$ influx in the postsynaptic FS cell, through AMPA receptors at hyperpolarized membrane potentials and through NMDA receptors at depolarized potentials (see Fig. 2).

**Integration of pyramidal cell inputs in FS interneurons**

Unitary EPSPs at pyramidal-FS connections described in the present work like those reported previously for most of adult neocortical pyramidal-interneuron connections (Buhl et al. 1997; Deuchars and Thomson 1995; Thomson 1997; Thomson et al. 1993, 1995) had a shorter duration than EPSPs at adult pyramidal-pyramidal pairs (Deuchars et al. 1994; Thomson 1997). Several parameters such as the substantial contribution of NMDA receptors (Jones and Baughman 1988; Thomson et al. 1988), the slow decay of AMPA receptor–mediated EPSCs (Hestrin 1993), and the presence of subthreshold voltage-activated inward currents (Deisz et al. 1991; Markram and Sakmann 1994; Schwindt and Crill 1995) and cable properties (Stafstrom et al. 1984) explain the relatively long duration of EPSPs recorded in pyramidal cells. These characteristics facilitate the temporal integration of the unitary excitatory inputs in pyramidal neurons. In contrast, the faster decay of AMPA receptor–mediated EPSCs associated with an almost negligible activation of NMDA receptors at subthreshold potentials contribute to the short duration of the EPSPs recorded in FS interneurons and therefore limit the temporal integration in these cells.

Synaptic responses elicited by two independent inputs were integrated linearly by FS cells at the resting membrane potential.
tial and near the action potential threshold. This linearity was maintained even when the amplitude of extracellular stimulus elicited EPSPs were substantially larger than unitary EPSPs (Fig. 4). This indicates that neither steady-state nor transient depolarizations modify the integration of synaptic inputs in FS cells. In the CNS, linear summation of excitatory inputs has been also reported for spinal chord motoneurons (Skydsgaard and Hounsgaard 1994), and neocortical (Cash and Yuste 1998) and CA1 hippocampal pyramidal cells (Langmoen and Andersen 1983). Recently, Urban and Barrionuevo (1998) described sublinear summations of synaptic responses elicited on the same apical dendrite of hippocampal CA3 pyramidal cells. The activation of dendritic A-type potassium channels would explain the reduction of excitatory synaptic responses of large amplitude (Cash and Yuste 1998; Hoffman et al. 1997; Urban and Barrionuevo 1998). Transient A-type currents are also present in neocortical FS interneurons (Massengill et al. 1997) and could in principle affect synaptic integration in these cells. However, even when synaptic responses of large amplitude were evoked with extracellular stimulation, we observed linear summation. Our results thus favor a passive integration of excitatory inputs, independent of their amplitude, in FS interneurons. However, we do not know the locations of the tested synaptic inputs on the FS cell dendrites. Therefore we cannot exclude that we did not sample in our experiments inputs converging onto the same dendritic compartment and interacting more actively.

The linear summation of the synaptic responses allowed us to estimate the number of pyramidal cells needed to be activated simultaneously to drive FS interneurons from −72 mV (near resting membrane potential) to the action potential threshold (−55 mV). We divided the membrane potential change necessary to reach the threshold (+17 mV) by the average EPSP amplitude including failures (2.1 ± 1.3 mV). Given the present recording conditions and assuming that all connections studied remained intact in a 300-μm-thick slice, the average number of pyramidal cells necessary to reach the threshold was 8 ± 5 cells (n = 18). This number is in the range of that estimated at granule cell to basket cell excitatory connections in the dentate gyrus (Geiger et al. 1997). It is worth noting, however, that at other excitatory connections onto inhibitory GABAergic interneurons, a single presynaptic neuron could be sufficient to make the postsynaptic cell fire (Ali and Thomson 1998; Barbour 1993; Debanne et al. 1995; Markram et al. 1998; Miles 1990).

The low level of temporal summation and the linear summation of excitatory inputs in FS cells suggest that the synchronous activation of an average of eight pyramidal cells is necessary to elicit a discharge in these interneurons. It is difficult to extrapolate this estimate from our in vitro recordings to in vivo conditions where the FS interneurons are exposed to a variety of modulators and where the background synaptic activity of the cortical network strikingly differs from that observed in slices (Paré et al. 1998). Higher synaptic activity, however, will decrease the input resistance of postsynaptic cells (Paré et al. 1998), leading to even less temporal integration and favoring the likelihood that FS interneurons play the role of coincidence detectors.

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