Stimulation of the Lateral Hypothalamus Provokes the Initiation of Robust Long-Term Potentiation of the Thalamo-Cortical Input to the Barrel Field of the Adult, Freely Moving Rat

V. L. Ezrokhi, V. A. Korshunov, V. A. Markevich, L. L. Voronin, E. Welker, and M. I. Zajchenko


Long-term potentiation in the thalamo-cortical input to the somatosensory cortex barrel field has been reported to be inducible in vitro only during a narrow critical period of the first postnatal week. Here we explored whether this is due to inability of adult synapses to express LTP or lack of appropriate conditions for LTP induction in slice preparations. We recorded thalamo-cortical field potentials (FPs) from the barrel field of chronically prepared adult rats. In the first series, several parameters of conditioning tetanization of thalamus (T) have been tried. Statistically significant LTP of 135–150% relative to the baseline was observed only in rare cases (3/18) so that the mean changes were not statistically significant. In the second series, five trains of 100 Hz stimulation of T were paired with a “reinforcing” stimulation of the lateral hypothalamus (LH). In most cases (9/13), thalamo-cortical FPs were potentiated. The mean post-tetanic amplitude was 238 ± 42% (±SEM) relative to the baseline (n = 13). The potentiation persisted for >1 h and typically even further increased when tested 24–48 h later. LTP magnitude strongly correlated with the initial paired-pulse ratio (PPR, coefficient of correlation r = 0.98) so that the LTP magnitude was larger (333 ± 107, n = 6) in cases with PPR > 1.3. The mean PPR tended to decrease after LTP (from 2.05 to 1.65). Altogether the results suggest that LTP is inducible in the thalamo-cortical input to the barrel field of normal adult rats. The dependence of the LTP magnitude upon the initial PPR suggests that inputs with low initial release probability undergo larger LTP. Together with the tendency to a decrease in the PPR this suggests an involvement of presynaptic mechanisms in the maintenance of neocortical LTP.

KEY WORDS: freely moving rats, thalamo-cortical barrel field potentials, hypothalamus, long-term potentiation.
showed that LTP in this connection can be induced only during a narrow critical period of the first postnatal week [11, 15, 22, 35]; however, the experimental conditions used in these studies could influence LTP reproducibility. The experiments were done in vitro. Moreover, the protocol of LTP induction used pairings of afferent pulses with a steady postsynaptic depolarization that was different from more conventional procedures of high frequency afferent tetanus. Relatively high testing frequency (0.1 to 1 Hz) was applied that could induce “synaptic habituation” and concomitant decreases in release probability, making the respective synapses “presynaptically silent” [20]. In contrast, several studies on acute in vivo preparations demonstrated the presence of long-term plasticities in the thalamocortical pathway in adult animals [1, 8, 13, 16]. However, these in vivo studies used procedures distinct from that used for induction of LTP in the hippocampus and with rare exceptions [1] have been performed on anesthetized animals [8, 13, 16]. Interestingly, other neocortical areas showed higher resistance to LTP in nonanesthetized animals as compared to anesthetized ones. LTP induction in the non-anesthetized animals demanded multiple sessions over many days [39] comparable to a one-month period necessary to induce a potentiation of short-latency thalamo-cortical responses with whisker pairings [1]. Altogether, the possibility of induction of LTP at thalamo-cortical synapses similar to that in the monosynaptic hippocampal pathways remains to be conclusively demonstrated.

Here we attempted to induce LTP during a single session in experiments on non-anesthetized rats using either thalamic conditioning trains with various parameters or pairings of a thalamic train with additional “reinforcing” stimulation of the lateral hypothalamus ( LH ). Earlier studies have shown that such additional reinforcement enables one to produce fast behavioral conditioning [44] and potentiation of monosynaptic responses evoked by direct stimulation of the motor cortex [47]. We found a potentiation that could be especially robust following thalamic high frequency trains delivered together with “reinforcing” stimulation of LH. The potentiation was not decrementing during the recording session (up to >1 h) and could persist over several days. The magnitude of the thalamo-cortical LTP was stronger for cases with high initial paired-pulse facilitation (PF) ratio, and the PF ratio decreased after LTP. These observations indicate involvement of presynaptic mechanisms in the maintenance of LTP in the thalamo-cortical synapses.

MATERIALS AND METHODS

Animal Preparation. Adult Wistar rats weighing 350–450 g were used. The surgery has been done under ketamine anesthesia (150 mg/kg) with additional local novocaine injections at the surgery places. To stimulate the thalamus, isolated tungsten wire (0.1 mm diameter) bipolar electrodes were implanted according to the stereotaxic atlas of J. Koenig and R. Klippel [25] at coordinates AP 2.2; L 3.0; H 4.4–5.0. Recording electrodes were placed at the cortex at AP 2.2; L 5.5 and H about 1.0–2.0. The final position of the electrodes before their fixation was adjusted according to the maximum amplitude and shortest latency of the thalamo-cortical field potential (FP). The electrodes for LH stimulation were placed at the coordinates AP 3.5, L 1.5 and H 8.5 according to the stereotaxic atlas of G. Paxinos and C. Watson [31]. The stimulating and recording electrodes were soldered to individual gold-plated male pins. Both the electrodes and pins were fixed to the skull with dental cement.

The rat was allowed a minimum of 48 h to recover from surgery and was placed in an experimental cage of about 30 × 30 × 40 cm. A flexible cable, allowing the animal to move about freely in the experimental chamber was connected to the electrode pins. By means of the cable, the stimulating and recording electrodes were connected respectively to constant current stimulation units (with stimulus isolation) and to an amplifier (MG440, Medicor, Hungary), via a field effect transistor preamplifier placed near the rat’s head.

The experiments were controlled by an IBM personal computer connected to the stimulation units and to an amplifier via an interface including digital-to-analog and analog-to-digital converters. The computer system controlled the stimulation units and collected each evoked potential waveform. Recorded signals were amplified, filtered (0.5 Hz–10 kHz band pass), digitized (sampling rate 50 µsec), and stored on computer disk at 12-bit resolution.

In the first series with the thalamic (T) conditioning tetanization, the strength of the test pulses (0.05–0.1 msec, 0.065–0.3 mA) was selected to induce FP of about 30–40% of the maximum amplitude. Typically, single testing stimuli were applied as groups of 10 pulses, typically with intervals of 25 to 35 sec within the group and with various intervals (5 to 30 min) between the groups. Both the interval between the pulses within the group and the intervals between the groups were varied randomly to prevent response habituation and time conditioning. In most experiments, the testing continued for at least 1 h to produce a stable baseline response. Parameters of the thalamic tetanization were broadly varied in these pilot experiments in the attempt to find the best conditions for LTP induction. In most experiments, the tetanus consisted of 70 trains (each of 4 pulses at 100 Hz) repeated with 14 msec intervals. The stimulus strength and duration were the same as those of the testing pulses. In the second series, paired thalamic and lateral hypothalamus tetanization (T + LH) was used as a conditioning procedure. Paired (50 msec interval) thalamic stimuli were used as baseline testing stimuli. The stimulus strength of the testing pulse was varied so that the amplitude of the first response (FP1) was from 0.1 to 0.5 mV in