The basolateral amygdala (BLA) can influence distinct learning and memory formation. Hippocampal long-term potentiation (LTP), the most prominent cellular model of memory formation, can be modulated by stimulation of the BLA in its induction and early maintenance. However, it is not known how the late maintenance of LTP beyond its initial phases might be affected. Behavioral stimuli have been shown to result in a reinforcement of a transient early-LTP into a lasting potentiation. Here we show that BLA stimulation mimics the behavioral effects on early-LTP in freely moving rats when the BLA is activated within a time window of 30 min before or after tetanization of the perforant path. The reinforcement of LTP was blocked by inhibitors of muscarinic and α-adrenergic but not dopaminergic receptors and was dependent on translation. Through these heterosynaptic associative interactions, hippocampal sensory information can be stabilized by amygdaloïd influences.

**Key words:** long-term potentiation; reinforcement; heterosynaptic LTP; associative LTP; late-LTP; basolateral amygdala; hippocampus; dentate gyrus

The hippocampus is important for the formation of certain kinds of memory. Although the information presented to and sent from the hippocampal network remains uncertain, hippocampal neurons exhibit a number of intriguing biophysical properties that enable them to participate in aspects of memory formation. These include mechanisms of synaptic plasticity that can respond to incoming information by detecting associative interactions between presynaptic, postsynaptic, and heterosynaptic activity and register these conjunctions as an increase in synaptic weights (Frey and Morris, 1998a). The latter process was named long-term potentiation (LTP) (Bliss and Lomo, 1973), which has become the best-studied cellular model of memory formation. Interestingly, hippocampal LTP exhibits similar temporal stages as described for certain types of hippocampus-dependent memory. An early-LTP (with a duration of ~4–6 hr) can be dissociated from late-LTP (beyond 6 hr) by inhibition of specific protein kinases, by protein synthesis, and partially by mRNA synthesis (Krug et al., 1984; Frey et al., 1988, 1996; Frey, 1997; Frey and Morris, 1997, 1999a).

In recent studies, Seidenbecher et al. (1997) reported that early-LTP in the dentate gyrus (DG) was reinforced if an appetitive or aversive stimulation was presented within 30 min after LTP induction. This reinforcement was dependent on the activation of α-adrenergic receptors. It was speculated that the consolidation of a memory trace in the hippocampal formation, as part of a more complex memory processing system, is reinforced if a modifying, most likely extra-glutamatergic input is active within a distinct time interval. Because late-LTP in the hippocampus requires similar heterosynaptic processes (Frey, 1997; Frey and Morris, 1998a), we hypothesize that the synergistic action of different transmitter systems and therefore different brain structures are needed for the induction of cellular processes leading to the long-lasting consolidation of a memory trace. However, the brain structures involved in reinforcing LTP in the DG remain unclear.

Interestingly, stimulation of the BLA, a structure thought to be part of an emotional memory system, can influence the induction and early maintenance of DG LTP (Ikegaya et al., 1995a; Akirav and Richter-Levin, 1999) by aminergic mechanisms (Ikegaya et al., 1997), whereas lesion of the amygdala attenuates DG LTP (Ikegaya et al., 1994). These results led us to investigate whether the maintenance of DG LTP can also be modulated by BLA stimulation. Here, we have studied the effect of BLA stimulation on the early-LTP in DG. If LTP subserves cellular mechanisms during declarative learning, then a hypothetical heterosynaptic associative LTP reinforcement by BLA stimulation could be of special importance. Behavioral experiments by others (for review, see Cahill and McGaugh, 1998) have shown similar processes with respect to emotional arousal and the maintenance of declarative memory. Electrophysiological studies on the induction and early transient stages of LTP in DG (Ikegaya et al., 1995a,b, 1997; Akirav and Richter-Levin, 1999) revealed modulatory effects of the BLA on hippocampal function, but it is not known whether protein synthesis-dependent late LTP is also affected, a prerequisite for long-lasting memory traces to be formed. Interestingly, it has been shown previously that hippocampus-dependent long-term memory processes are influenced by the amygdala (Bevilaqua et al., 1997; Bianchin et al., 1999; Izquierdo et al., 1999). Here...
we report that early-LTP in the DG in vivo can be influenced in its maintenance by stimulation of the BLA.

MATERIALS AND METHODS

Subjects and surgery. Experiments were performed on 8-week-old Wistar rats (200–250 gm). All experiments were performed in compliance with the relevant laws and institutional guidelines and have been approved by the Land Sachsen-Anhalt.

For chronic implantation of electrodes, the animals were anesthetized with pentobarbital [40 mg/kg, i.e., 40 mg was dissolved in 10 ml saline and 1 ml/100 gm was injected intraperitoneally as an initial dose, supplemented by (0.1 mg)–0.5 ml (2 mm) intraperitoneal injections if necessary] and placed in a stereotactic frame (David Kopf Instruments, Tujunga, CA). The scalp was incised and retracted, and head position was adjusted to place bregma 1 mm higher than lambda. Small holes were drilled in the skull for the placement of stimulating and recording electrodes. The electrodes consisted of insulated stainless steel wires 125 μm in diameter. A monopolar recording electrode was placed in the DG–granular cell layer [coordinates ~2.8 mm posterior to bregma (AP), 1.8 mm lateral to midline (L), 3.2–3.5 mm ventral from dura (V); coordinates from the atlas of Paxinos and Watson (1998); a bipolar stimulating electrode was implanted in the medial perforant pathway (AP ~6.9 mm, L 4.1 mm, V 2.4–2.7 mm)]. For stimulating the amygdala, a monopolar electrode was placed into the basolateral amygdala (AP 10.5–12.0 mm, L 5.0–6.0 mm) with an indifferent electrode consisting of silver bar wire lowered on dura anterior to the stimulating electrode. The electrodes were adjusted to optimize the population spike (PS) amplitude in the perforant path–DG system. All rats were allowed 8–10 d recovery after surgery before the electrophysiological experiments in freely moving animals. The positioning of electrodes was checked in each animal histologically after the end of the experiment, and only those animals with a correct positioning of the electrodes were included in further analyses [interestingly, no effects of DG LTP were detected in experiments in which the histological confirmation of electrode positioning afterward revealed a placement of the amygdala-stimulating electrode in the central instead of the basolateral nucleus (data not shown)].

Recording. All electrophysiological recordings were performed in special experimental boxes, where animals were connected by a flexible cable to a 10-channel swivel that allowed them to move freely with ad libitum access to water and food (Frey et al., 1996; Seidenbecher et al., 1997). Biphasic current pulses (0.1 msec per cycle, 150–250 μA) were applied to the perforant path to evoke extracellular field potentials in the DG of ~40% of the maximal PS. PS recording and analysis were favored against the slope of field EPSPs because the latter is relatively unstable in the hilar region of the dentate gyrus in freely moving animals, especially if taken into consideration that the stimulation intensity was adjusted to obtain a population spike that influenced strongly the dipole of the field EPSP in the hilus. The spike, however, is required to induce LTP. A few experiments showed a reasonable, larger field EPSP, which could be used for calculations, and we provide representative examples of the time course of field EPSP changes in the text. Analysis of the time course below revealed similar results as PS measurements, suggesting that the recorded and analyzed PS is not just a measure of changes in excitability but also represents adequate synaptic function. This is supported by the fact that, to our knowledge, LTP has never been reported to be associated with changes of excitability. The basolateral amygdala was stimulated by impulses with an intensity of standardized 300 μA independent of the stimulation protocol (biphasic constant current pulses, 0.2 msec duration per polarity). This stimulation intensity evoked an average BLA DG potential as shown in Figure 1a.

After a stable baseline was recorded for at least 30 min (recordings every 5 min), an “unsaturated” LTP was induced by three bursts of 15 impulses, 200 Hz, 0.2 msec pulse width each stimulus, interburst interval 10 sec, resulting in a potentiation that decayed within 4–7 hr to pretetanus value. In the series with late-LTP, tetanization consisted of 20 bursts of 15 impulses, 200 Hz, 0.2 msec pulse width each stimulus, interburst interval 10 sec (“strong tetanus”). This stimulation paradigm resulted in late-LTP with a duration of 8 hr, the longest time point we have investigated. Averaged responses were recorded every 15 min for up to 8 hr after tetanization.

For estimation of the time window for “reinforcement” of the unsaturated DG LTP by stimulation of the basolateral amygdala, the following stimulating protocols were used. At various time points (5, 15, and 30 min) before or after tetanization of the perforant path, the basolateral amygdala was stimulated by high frequency [three bursts of 15 impulses, 200 Hz, 0.2 msec pulse width each stimulus, interburst interval 10 sec (weak tetanus) at 300 μA] or low frequency (45 impulses at 0.1 Hz, 0.2 msec pulse width, each stimulus at 300 μA).

Pharmacology. Substances were applied intravenicularly through chronically implanted cannulae [anterior horn of the right lateral ventricle, for detail, see Seidenbecher et al. (1997)] 1 hr before PP tetanization (control experiments without substance). Application of the drugs 5 min (propranolol, SCH 23390, atropine) or 10 min (AP-5, 100 nmol, from RBL) after perforant path (PP) tetanization (control experiments without out-stimulation of the BLA) did not influence the time course of early LTP [for propranolol, see Seidenbecher et al. (1997); other data not shown]. All of the above substances had no effect on baseline evoked potentials nor on early-LTP, with the exception of AP-5, which blocked early-LTP when applied before PP tetanization (Fig. 4a). The latter result confirms earlier results with similar biophysical properties that can diffuse within 5 min to their place of action, i.e., from the ventricle to the dentate gyrus. Anisomycin (0.905 mol; ICN Biochemicals, Costa Mesa, CA) was injected 2 hr before the PP was tetanized. To avoid possible nonspecific side effects of the presence of the reversible protein synthesis inhibitor anisomycin after intracerebroventricular injection, we recorded control experiments in which anisomycin was first determined at which anisomycin was still effective in inhibiting protein synthesis when applied sufficiently before induction of LTP. This was achieved by measuring the incorporation of radioactive-labeled amino acids into hippocampal proteins. It was found that anisomycin inhibited the incorporation of amino acids into hippocampal proteins by ~90% for at least 2 hr after its application (data not shown), the time at which LTP was induced. In the series with anisomycin and LTP induction, only those experiments with normal post-tetanic potentiation were used for statistical evaluation. In all cases the injection was performed at 1 μl/min to a total volume of 5 μl.

Statistics. Data analyzed here are from non-Gaussian populations but show near identical shapes of distributions. Therefore, nonparametric tests were performed. Within-group comparisons were made using the Wilcoxon test for paired samples. For comparisons between groups the Mann–Whitney U test was used after performing the Kruskal–Wallis test for the different groups. Differences were considered statistically significant only when p < 0.05 in Kruskal–Wallis and the post test. For clarity when comparing data, the mean of percentage change of the PS amplitude measured in millivolts ± SEM is shown.

RESULTS

Our studies revealed that low-frequency control stimulation of the perforant path or the BLA did not dramatically influence DG potentials (Fig. 1). Weak tetanization of the perforant path resulted only in early-LTP decaying to baseline values within 8 hr (Fig. 1b, ●). Strong tetanization, in contrast, revealed late-LTP with a duration of at least 8 hr, the latest time point we have investigated (Fig. 1b, ○).

BLA stimulation before and after tetanization of DG

We then investigated whether stimulation of the BLA before, simultaneously with, or after tetanization of the perforant pathway influences early-LTP in the DG. As shown in Figure 2a (●), the duration of LTP in the DG, induced by a tetanization protocol that normally would lead only to early-LTP, can be influenced by a subsequent high-frequency stimulation of the BLA applied 15 min after the tetanization of the perforant path. Although short-term potentiation (STP) (<1 hr) was not influenced, the maintenance of LTP was changed significantly. The transient time course of LTP induced by weak tetanization of the perforant path was transformed (or reinforced) to a long-lasting potentiation with a duration of at least 8 hr. As mentioned earlier, for technical reasons the DG LTP reinforcement by BLA stimulation...
Figure 1. Reinforcement of hippocampal early-LTP by stimulation of the basolateral nucleus of the amygdala in freely moving rats. a, Schematic illustration of electrode localization. For clarity, in this section the DG stimulation electrode is shown activating the perforant pathway (broken line). Originally, this electrode was positioned in the angular bundle (see Materials and Methods). Insets show analog examples of recordings obtained before (dotted line) and after (filled line) LTP induction of the perforant path (top left) and after stimulation of the BLA (top right). b, Control recordings: induction of early-LTP (●, n = 18) or late-LTP (○, n = 5) by a weak or strong tetanus of the perforant path, respectively, or tetanization of the BLA (□, n = 11), or after application of 45 impulses at an LFS in the BLA (△, n = 11), and finally after LFS of the perforant path alone (◇, n = 6). Low-frequency stimulation of the perforant path did not severely influence baseline potentials for the investigated 8 hr (Fig. 1b, ◇). A statistically significant difference was detected only at 6 hr after low-frequency stimulation when compared with prestimulation values (Wilcoxon test, p < 0.05). High-frequency (Fig. 1b, □) or low-frequency stimulation (Fig. 1b, ○) of the BLA resulted in a slowly developing long-term depression at the DG synapses. At 2 hr a statistically significant depression of the initial baseline potentials was observed 82.9 ± 4.18% (millivolts; percentage change ± SEM) in the group with a high-frequency train to the amygdala and 71.6 ± 10.24% in the group with a low-frequency train, respectively. That remained at this level until 7 hr after LTP induction; the 30 min interval (n = 3) was 116.7 ± 1.33% at 1 hr and 113.5 ± 3.47% at 8 hr after LTP induction; the 30 min interval (n = 3) results were 125.9 ± 4.09% at 1 hr versus 94.5 ± 9.47% at 8 hr after LTP induction. We do not know whether an increase in the time interval between BLA and perforant path tetanization beyond 30 min results in a reinforced long-lasting potentiation. Future experiments should be conducted to investigate this time window more thoroughly.

Involved transmitter systems

The next series of experiments was conducted to elaborate which transmitter systems are involved in the reinforcing effect of amygdala stimulation on early LTP in the DG. A number of transmitters, including dopamine, norepinephrine, acetylcholine, and opioids, are known to modulate LTP (Dunwiddie et al., 1982; Bliss et al., 1983; Krug et al., 1983; Stanton and Sarvey, 1985). We showed earlier (for review, see Frey, 1997; Frey and Morris, 1998a) that late-LTP requires the heterosynaptic activation of nonglutamatergic receptors during tetanization. In a control experiment low-frequency stimulation, respectively) that remained at this level until the end of the experiment (Wilcoxon test, p < 0.05). However, statistical comparison of the BLA-stimulated control series revealed no significant difference (Mann–Whitney U test) with the exception at 7 hr (low-frequency perforant path control vs low-frequency BLA stimulation). The arrow indicates the time point of weak or strong tetanization or LFS, respectively.
The muscarinergic antagonist atropine, but not the dopaminergic receptor antagonist AP-5 was therefore applied intracerebroventricularly 5 min before tetanization (Fig. 4c), as shown in Figure 4b, the NMDA receptor antagonist did not influence the time course of reinforced LTP.

Figure 5 illustrates the action of the other tested receptor blockers on the reinforced potentiation. As shown in Figure 5, a and c, only the β-adrenergic receptor antagonist propranolol and the muscarinergic antagonist atropine, but not the dopaminergic D1 receptor antagonist SCH 23390 (Fig. 5b), were effective in blocking the reinforced potentiation. Similar time courses were obtained in experiments with measurable field EPSPs [e.g., propranolol (single experiment): 117.1% at 1 hr vs 90.7% at 8 hr after LTP induction; and atropine (n = 2): 116.5 ± 4.40% vs 91.1 ± 5.55%]. When one of the two blockers was delivered into the ventricle after LTP induction in the DG, but 10 min before tetanization of the BLA, only early-LTP was seen, as was the case in the control experiments with weak tetanization of the perforant path alone.

Protein synthesis dependence of reinforcement

A last series of experiments investigated whether the reinforcement of early-LTP was accompanied by protein synthesis (Fig. 6). The protein synthesis inhibitor anisomycin was applied 2 hr before tetanization to avoid possible effects on LTP induction (Fig. 6a). Under these conditions, early-LTP by weak tetanization of the perforant path could be induced, although the duration was shorter when compared with control early-LTP in nontreated groups (indicating a distinct requirement of protein synthesis during early-LTP). The reinforcing effect on early-LTP by subsequent BLA stimulation was prevented by anisomycin, suggesting a requirement of protein synthesis for the transformation from early- to late-LTP.

DISCUSSION

In summary, it was shown that only a weak transient form of LTP is affected by BLA stimulation in the intact animal. Induction of late-LTP by a strong tetanus in the DG is not influenced in either its induction or its maintenance, at least during the 8 hr after tetanization that we have investigated (Fig. 2c). Heterosynaptic, late associative effects on early-LTP occur when the amygdala is stimulated within a distinct time interval, before or after induction of LTP in the DG. Our pharmacological experiments using the NMDA receptor inhibitor AP-5 revealed that BLA stimulation does not interfere with the reinforcing effects in DG via a direct glutamatergic innervation, as would be expected during saturation experiments in which the same glutamatergic inputs are tetanized subsequently until an asymptotic level of potentiation is achieved (Barnes et al., 1994; Moser et al., 1998). However, direct activation of AMPA receptors in the DG by BLA stimulation cannot be excluded. The subsequent depolarization of granular cells and activation of voltage-dependent calcium channels therefore could be involved in the processes, resulting in a reinforced potentiation. However, the absence of morphological data describing a direct innervation of the DG by BLA makes this assumption unlikely (Pikkarainen et al., 1999).

We have proposed recently that consolidation of hippocampal LTP requires the synergistic activation of both glutamatergic inputs and an additional modulating transmitter system during the induction of LTP, during which coactivation of the latter is necessary to trigger the synthesis of plasticity-related proteins (for review, see Frey and Morris, 1998a). This is a prerequisite for the formation of late-LTP, i.e., its consolidation. Artificial
Electrical field stimulation in the brain may lead to late LTP if the stimulus is strong enough to reach sufficient heterosynaptic inputs, as could be the case for the series with strong tetanization that is shown here. More subtle stimulation may involve homosynaptic inputs that initiate early-LTP if not preceded or followed by activation of an additional input of another transmitter system. However, the latter protocol seems to be the more physiological way of neuronal functioning.

Early-LTP in the DG in the intact animal can be transformed into protein synthesis-dependent late-LTP by heterosynaptic and associative mechanisms when both the perforant pathway and the basolateral nucleus of the amygdala are stimulated within a time window of \(~30\) min. The order of “paired” stimulation is not important, i.e., whether tetanization of the DG or electrical stimulation of the BLA occurred first, and it is not important whether a high-frequency train or a low-frequency stimulation was delivered to the BLA. With respect to the order of stimulation, our data seem to be in contrast to earlier findings in which DG LTP was reinforced by behavioral stimuli only if the latter was presented after tetanization (Seidenbecher et al., 1997). A possible explanation could be that the behavioral and aversive stimuli used in these experiments involve the serial and parallel interaction of more complex structures at different times than the artificial direct stimulation of the BLA at a given time. However, regarding the order of stimulation, our results are in accordance with the properties of “synaptic tagging” (Frey and Morris, 1998b) (see below).

BLA action on DG LTP is neither direct (Pikkarainen et al., 1999) nor mediated by NMDA receptor stimulation but triggered through brain structures carrying norpinephrine or acetylcholine, or both, but not dopamine. However, because the receptor blockers were applied intraventricularly, a direct action of noradrenergic or muscarinic processes, or both, in the BLA cannot be excluded. Therefore, the reinforcement of DG LTP by BLA stimulation can also involve additional mechanisms such as the action of “modulated” BLA stimulation on different receptor systems and the BLA-dependent regulation of stress hormones required for normal hippocampal function (Brinton and McEwen, 1989; Cahill and McGaugh, 1998; Ferry et al., 1999). This would resemble findings in which hippocampus-associated learning is strongly influenced by BLA modulation (Packard et al., 1994; Cahill et al., 1995; Cahill and McGaugh, 1998).

Questions remain such as why simultaneous tetanization of the DG and BLA does not influence the maintenance of early-LTP (data not shown). It can be speculated that the effect of BLA stimulation on DG LTP is triggered by synergistic actions of glutamatergic and nonglutamatergic mechanisms that require a sequence of processes to be activated. It is not important which of the systems was activated first, but a simultaneous activation prevents the induction of events leading to the reinforcement of LTP. Heterosynaptic, nonglutamatergic receptor activation during tetanization may negatively influence the required level of depolarization for late-LTP to occur [e.g., BLA-stimulated norpinephrine release activates hippocampal interneurons (Bergles et al., 1996)]. Another possibility might be that simultaneous heterosynaptic, i.e., glutamatergic and \(\beta\)-adrenergic, receptor activation in the dentate gyrus cannot sufficiently shift processes such as intracellular calcium transients (Stanton and Heinemann, 1986; Gray and Johnston, 1987) required for late-LTP. The different regulation of calcium may then influence the balance between activated kinases and phosphatases in favor of short-lasting plastic events (Coussens and Teyler, 1996).

A 5 min delay of subsequent stimulation of the two brain structures, however, revealed reinforced LTP. This could have been achieved by heterosynaptic stimulation of the cAMP/PKA cascade, a prerequisite for late-LTP to occur (Frey et al., 1993), or by hormone-dependent regulation of plasticity-relevant proteins in the hippocampus through cAMP/PKA-dependent processes initiated either in the hippocampus (Bevilaqua et al., 1997) or indirectly in the BLA (Frey and Morris, 1998a). In addition, it cannot be ruled out that other brain structures directly interact with the granular cells in the DG because the BLA does not directly innervate the DG granular cells (Pikkarainen et al., 1999). BLA activation requires the additional stimulation of as yet unidentified structures directly connected with the DG by adrenergic or muscarinergic fiber systems or influences the level of potentiation 15 min after induction of DG LTP (a) and maintenance (b). Only the series of simultaneous stimulation of the BLA and DG and the series during which the BLA was stimulated 15 min before perforant path tetanization showed a statistically significant enhanced STP measured 15 min after LTP induction (a). The potentiation at 8 hr (b) returned to pretetanization levels when the perforant pathway was tetanized alone or simultaneously with BLA, but not when the BLA was stimulated within 15 min before or after LTP induction in DG. In the series during which LTP was induced in the DG after BLA stimulation with a 30 min interval, a remaining statistically significant potentiation was still observed, which is probably attributable to the initial effect on STP by BLA stimulation.

Figure 3. Time window of LTP reinforcement of DG LTP by BLA stimulation. Level of potentiation 15 min (a) and 8 hr (b) after induction of early-LTP in DG to illustrate the effect of BLA stimulation on the induction of DG LTP (a) and maintenance (b). Only the series of simultaneous stimulation of the BLA and DG and the series during which the BLA was stimulated 15 min before perforant path tetanization showed a statistically significant enhanced STP measured 15 min after LTP induction (a). The potentiation at 8 hr (b) returned to pretetanization levels when the perforant pathway was tetanized alone or simultaneously with BLA, but not when the BLA was stimulated within 15 min before or after LTP induction in DG. In the series during which LTP was induced in the DG after BLA stimulation with a 30 min interval, a remaining statistically significant potentiation was still observed, which is probably attributable to the initial effect on STP by BLA stimulation.
of stress hormones, which may then finally modulate neuronal plasticity in the DG.

Interestingly, our studies revealed a model to study early and late associative components of long-lasting plastic changes with an interaction of heterosynaptic components within the minute or even hour range, respectively. Further studies will determine the key players and the locus of action of BLA-dependent reinforcement of DG LTP.

The described time window, the protein synthesis dependence of the reinforcement, and the heterosynaptic associative components of these processes lead us to speculate that the described effects might be related to a phenomenon that we have recently described as synaptic tagging (Frey and Morris, 1997, 1998a).

Synaptic tagging characterizes a late associative property of LTP, which requires the transient setting of a synaptic tag with the function of capturing and processing plasticity-related proteins, thus facilitating consolidation, from a short-term into a long-lasting synaptic plastic change. Interestingly, it has been shown that under distinct circumstances the setting of the tag is sufficient to result in late-LTP at that input, if a heterosynaptic input was stimulated within a specific time window.

Considering the proposed role of LTP in information processing and the described interaction of the hippocampus and amygdala during distinct learning tasks (LeDoux, 1993; Packard et al., 1994; Cahill et al., 1995; Izquierdo and Medina, 1997; Cahill and McGaugh, 1998; Roozendaal et al., 1999), the data presented...
here may provide a hint for more detailed investigation of interstructural, associative interactions at the cellular level. We have shown that BLA stimulation can modulate hippocampus-specific long-lasting plasticity beyond its induction and early maintenance. However, future studies will show whether cellular consolidation under these conditions exceeds the investigated 8 hr. Our data support the hypothesis that describes the amygdala as a structure involved in the formation/modulation of declarative memory in other brain structures that might be related to emotionally arousing events (for review, see Cahill and McGaugh, 1998). The investigation and description of structures and processes that are functionally correlated may illuminate interneuronal mechanisms required for long-lasting plastic changes and the formation of declarative memory.

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