Long-term memory is supported not only by modulation of synaptic strength, but also by modifications in intrinsic neuronal properties. Learning-induced enhancement of neuronal excitability has been shown in the hippocampus and the piriform cortex, where it lasts for days and is involved in maintaining the learned skills. The basolateral amygdala (BLA) is suggested to encode positive and negative significance of information, thus forming a unique experimental setting to monitor bidirectional changes as a function of the valence change. In rodents, olfaction is a major modality that guides goal-directed behavior. Here, we show that intrinsic neuronal excitability in BLA pyramidal neurons is differentially modified by positive and negative olfactory learning and explore the cellular mechanisms of such bidirectional intrinsic neuronal plasticity. Learning of complex olfactory-discrimination task, in which success was rewarded with drinking water, resulted with enhanced intrinsic excitability. Such enhancement is mediated by reduction in the slow potassium current. In contrast, olfactory fear conditioning, in which the animal learned to associate the odor with an electric shock, resulted in decreased intrinsic excitability, mediated by activation of the μ-opioid-sensitive potassium current. We suggest that positive and negative changes in BLA excitability contribute to the encoding of opposite odor-value behaviors.

Keywords: basolateral amygdala, brain slices, intracellular recordings, late AHP, olfactory learning

Introduction

Long-lasting enhancement of intrinsic neuronal excitability has been hypothesized to be the mechanism subserving enhanced learning capability—a phenomenon termed “rule learning” or “learning set.” Enhanced intrinsic excitability lasts for up to several days and is widely spread throughout the local neuronal population in the relevant brain areas (Moyer et al. 1996; Saar et al. 1998; Thompson et al. 1996; Zelcer et al. 2006). Such enhanced neuronal excitability is thought to set a time window during which activity-dependent synaptic modifications are likely to occur (Saar and Barkai 2003, 2009).

Neuronal excitability is modulated by potassium currents that generate the medium and slow afterhyperpolarizations (AHPs), following repetitive firing of action potentials (Madison and Nicoll 1984; Constanti and Sim 1987; Schwindt et al. 1988; Faber et al. 2001). Indeed, the postburst AHP amplitude in hippocampal and piriform cortex neurons is reduced for days after learning (Moyer et al. 1996; Saar et al. 1998; Zelcer et al. 2006).

Activity-induced, long-lasting plasticity of intrinsic excitability resembles activity-induced modulation of synaptic strength in several central aspects: it is induced by activation of glutamatergic receptors (Melyan et al. 2002, 2004); it requires activation of second messenger systems such as PKC, PKA, and ERK (Cohen-Matsliah et al. 2007; Grabauskas et al. 2007; Oh et al. 2009); and its long-term maintenance is protein synthesis dependent (Xu et al. 2005; Cohen-Matsliah et al. 2010).

However, whereas experience-dependent synaptic plasticity is bidirectional, and commonly involves synaptic strengthening as well as synaptic weakening (Malenka and Bear 2004; Smith et al. 2009), most studies on learning-relevant modulation of intrinsic excitability suggested that enhanced excitability underlies learning, regardless of the training paradigm and its expected outcome (Moyer et al. 1996; Saar et al. 1998, 2001; Oh et al. 2003; Zelcer et al. 2006; McKay et al. 2009). Notably, one interesting study reported a learning-induced reduction in excitability in the infralimbic cortex neurons after fear conditioning (Santini et al. 2008).

The amygdala has been hypothesized to play a key role in positive reward and reinforcement, and in representing a negative value of the reward (Paton et al. 2006; Belova et al. 2007, 2008; Murray 2007). In particular, it is implicated in olfactory learning (Sullivan and Wilson 1993; Schoenbaum et al. 1998, 1999, 2003; Gottfried et al. 2003; Kilpatrick and Cahill 2003; Davis 2004). The basolateral amygdala (BLA) is thought to encode the motivational significance of olfactory cues (Schoenbaum et al. 1999) and to serve, together with the orbitofrontal cortex, to encode information used to guide goal-directed behavior during olfactory-discrimination learning (Schoenbaum et al. 1998).

The role of the BLA in encoding for reward value provides a unique model system for testing the prediction that positive and negative reward values are reflected in opposite modifications of intrinsic properties. Here, we show that contrasting motivational valence of olfactory cues, that is, anticipation of drinking water after olfactory-discrimination learning on one hand and anticipation of an electric shock after olfactory fear conditioning on the other, resulted in opposite effects on intrinsic excitability of pyramidal neurons, via 2 different potassium currents.

Materials and Methods

Behavioral Procedures

The subjects were age-matched young (2 months) adult male Sprague Dawley rats, of which those designated for the olfactory-discrimination paradigms were maintained on a 23.5-h water deprivation schedule, with food available ad libitum.

Complex Olfactory-Discrimination Learning

The olfactory-discrimination training (OD) protocol was applied daily (morning time) to each trained and pseudotrained rat, in a 4-arm
the sponge, so that the rat had to nose-poke into the hole to obtain it. Perspex holders. The water reward (0.2 mL) was placed in the hole in a 2.5-cm-diameter hole cut into the center and were placed in identical boxes constructed of opaque plastic and measuring (45 × 45 × 24) cm. (Cohen-Matsliah et al. 2009). The training apparatus was a square box (90 cm long), the rat’s body interrupted an infrared beam (I, arrow) and a drop of drinking water was released from a water hose (W) into a small drinking well. For a “trained” rat, this occurred only if the arm contained the positive-cue odor; for a “pseudotrained” rat, it occurred randomly. A trial ended when the rat interrupted a beam, or after 10 s if no beam was interrupted. A fan operated for 15 s between trials, to remove odors. Each rat underwent 20 trials per day. One trained rat and each pseudotrained or naive rat expressed as correct choices in the last 10 trials of the day. The learning curve shows a gradual improvement in performance in trained rats and no learning in pseudotrained rats, which showed no preference for any of the odors during the entire training period. Values represent mean ± SE of 15 pseudotrained and 19 trained rats. Inset: a cumulative frequency graph depicting the time required for the rats in the trained group to reach the criterion for rule learning. Note that none of the rats completed the task within 5 days after learning; a small number of rats completed rule learning after 6 days, and the majority met the criterion within 8 days. (C) Freezing levels of odor fear-conditioned rats. One day after odor fear conditioning, the rats were tested for their freezing behavior in a novel chamber. In the first minute, the rats did not exhibit any freezing behavior in response to the novelty of the chamber but exhibited very high levels of freezing when the odor to which they were conditioned was introduced into the chamber.

Figure 1. Training for odor-discrimination rule learning and fear conditioning. (A) Schematic representation of the olfactory maze. Protocols for “trained” and “pseudotrained” rats were similar: an electronic “start” command randomly opened 2 of 8 valves (V), releasing pressured airstreams with positive-cue odor (P) into one of the arms and negative-cue odor (N) into another. Eight seconds later, the 2 corresponding guillotine doors (D) were lifted to allow the rat to enter the selected arms. Upon reaching the far end of an arm (90 cm long), the rat’s body interrupted an infrared beam (I, arrow) and a drop of drinking water was released from a water hose (W) into a small drinking well. For a “trained” rat, this occurred only if the arm contained the positive-cue odor; for a “pseudotrained” rat, it occurred randomly. A trial ended when the rat interrupted a beam, or after 10 s if no beam was interrupted. A fan operated for 15 s between trials, to remove odors. Each rat underwent 20 trials per day. One trained rat and each pseudotrained or naive rat expressed as correct choices in the last 10 trials of the day. The learning curve shows a gradual improvement in performance in trained rats and no learning in pseudotrained rats, which showed no preference for any of the odors during the entire training period. Values represent mean ± SE of 15 pseudotrained and 19 trained rats. Inset: a cumulative frequency graph depicting the time required for the rats in the trained group to reach the criterion for rule learning. Note that none of the rats completed the task within 5 days after learning; a small number of rats completed rule learning after 6 days, and the majority met the criterion within 8 days. (C) Freezing levels of odor fear-conditioned rats. One day after odor fear conditioning, the rats were tested for their freezing behavior in a novel chamber. In the first minute, the rats did not exhibit any freezing behavior in response to the novelty of the chamber but exhibited very high levels of freezing when the odor to which they were conditioned was introduced into the chamber.

radial maze (Fig. 1A), with commercially available odors that are regularly used in the cosmetics and food industries. Olfactory training consisted of 20 trials per day for each rat, as in a previously described study in our laboratory (Saar et al. 1998). In short, in each trial the rat had to choose between 2 odors (positive and negative cues) presented simultaneously. Rats designated to the trained group were rewarded with drinking water upon choosing the positive cue; whereas those in the pseudotrained group were randomly rewarded with drinking water. The criterion for completion of OD learning was making at least 80% positive-cue choices in the last 10 trials of a training day (Saar et al. 1999, 2001). As we have previously reported (Saar et al. 1998, 1999), once the rats achieved good performance with the first pair of odors, their capability to learn to discriminate between new pairs of odors increased dramatically; only 1 day of training was needed to reach the criterion of 80% correct choices when a new pair of odors was presented. This enhanced learning capability, termed “rule learning” or “learning set,” suggests that in the course of completing training with the first pairs of odors, rats acquire the skill that enables them to greatly enhance their performance in the olfactory maze task (Saar et al. 1998, 1999). Every batch of rats consisted of 3 individuals: trained, pseudotrained, and naive. The pseudotrained rat was paired to the trained one and was trained through the same numbers of days and trials, thus eliminating any difference in the length of the training paradigm. Rats in the naive group were water deprived, but not exposed to the maze. Each day after the termination of the training session rats had free access to drinking water up to 30 min in their home cage. In addition to these 3 groups, we also tested naive rats that were not water deprived and were not exposed to any training. As all electrophysiological parameters that were measured in BLA neurons from this group were identical to those obtained from neurons of water-deprived naive rats, the 2 groups were unified into a single naïve group (data not shown).

Simple Olfactory Learning (3-Way Odor-Discrimination Task)

This simple olfactory task procedure was described previously (Cohen-Matsliah et al. 2009). The training apparatus was a square box constructed of opaque plastic and measuring (45 × 45 × 24) cm. Sponges measuring (6 × 7) cm horizontally and 3 cm deep had a 2.5-cm-diameter hole cut into the center and were placed in identical Perspex holders. The water reward (0.2 mL) was placed in the hole in the sponge, so that the rat had to nose-poke into the hole to obtain it. The sponges were impregnated with odors by placing 0.2 mL of a 0.5% essence solution on each corner. Odor-impregnated sponges were placed in 3 corners of the box, and the position of each odor within the box was changed for each trial. The sponges with untargeted odors had empty holes, that is, offered no reward. The odors used were cinnamon, almond, and lemon, and the rewarded odors were randomly assigned to different rats.

Habituation Sessions

Prior to the simple OD, the rats were habituated to the experimental apparatus. Water restriction, that is, 30 min access to water per day (given after training), began 1 day before training. Four habituation sessions were performed each day on 2 consecutive days. During all the habituation sessions, the rats were given free access to 0.2 mL of water placed in each of 3 corners of the box. On the first day of habituation, the water wells were not hidden by sponges; on the second day, they were placed in the holes in 3 nonimpregnated sponges. Each habituation session lasted 5 min, and they were separated by intervals of at least 5 min.

Training

Training was performed in 4 trials in a single session, with trials separated by 2-min intervals. At the beginning of the trial, the rat was positioned at the empty corner on the box, facing the wall. A 5-min maximum time was imposed for the rat to find the reward in the hole in the sponge and to consume it. The spatial arrangement of the sponges was changed between trials. Latency to nose-poke, and number of errors were taken as measures of performance. Errors were defined as nose-pokes into holes of sponges other than the targeted one, or failure to nose-poke after sniffing the sponge with the target odor. The learning criterion was 2 consecutive trials with no more than 1 error. Rats that failed to meet this criterion, or did not nose-poke within 2 min at the second and subsequent trials were eliminated from the experiment. Trained rats were rewarded when they nose-poked into the targeted sponge. Each trained rat was paired with a time-yoked pseudotrained rat, which was rewarded randomly, because the water reward was hidden in a different sponge in each trial.
Odor Fear Conditioning
Rats were trained individually and randomly assigned to one of the following experimental conditions.

Odor Fear Conditioning (Trained Group)
Prior to training to associate between the odor and the electrical shock, individual rats were placed in the fear-conditioning chamber and allowed to explore the context for 10 min on each of 2 consecutive days. On the third day, the rat was again placed in the conditioning chamber and allowed to explore for 1 min before introduction of a puff of novel odor (conditioned stimulus, CS). After 30 s the rat received an electric shock (unconditioned stimulus, US) of duration 1 s, intensity 1 mA. The CS and US were applied 3 times in total, with intervals of 2 min between applications. The rat remained in the conditioning chamber for an additional 2 min following the last shock. Thus, a conditioning session included the presentation of 3 CS–US pairs, and lasted ~8 min.

Odor Exposure (Pseudo Group)
Individual rats were trained under the same odor fear-conditioning protocol, without receiving the electric shocks on Day 3. Thus, their odor exposure session included the presentation of the CS only, and lasted ~8 min.

Contextual Conditioning (Context Group)
Individual rats in the context group were trained under the same odor fear-conditioning protocol, but with 2 main differences: they were not habituated to the context before the fear-conditioning session, and no odor was presented during conditioning. Thus, these animals were exposed to the (novel) context and received 3 electrical shocks. The session lasted ~8 min as previously described (Motanis and Maroun 2010).

Behavior in the chamber was video recorded and was subsequently analyzed for freezing, which was defined as absence of all movement except for respiration (Kim et al. 1992). The average freezing level of each group was calculated from the percentage of time the rats spent in a frozen state during the behavioral test.

To examine the success of the fear learning, 2 animals were trained, of which one was behaviorally tested to assess the success of rule learning; and 2) 3 days after rule learning. Coronal brain slices, of which one was behaviorally tested to assess the success of

Brain Slice Preparation and Recordings
The OD trained rats were sacrificed at 1 of 3 time points: 1) before rule learning, 5 days after the beginning of training with the first pair of odors; 2) 1 day after acquiring the rule, that is, after learning to discriminate between 2 pairs of odors; and 3) 3 days after rule learning (Fig. 1B).

Rats that were trained in the simple olfactory maze and in the fear-conditioning paradigms were sacrificed at 1 of 2 time points: 1) 1 day after learning; and 2) 3 days after learning. Coronal brain slices, 400 μm, that included the BLA area were cut (Thompson et al. 2008) and kept in oxygenated (95% O2 + 5% CO2) Ringer’s solution, which comprised (in mM): NaCl, 124; KCl, 3; MgSO4, 2; NaH2PO4, 1.25; NaHCO3, 26; CaCl2, 2; and glucose, 10.

Intracellular recordings were performed at 34.5 °C, with 4 M K-acetate filled sharp glass microelectrodes with an axoclamp 2 A amplifier and analyzed using pCLAMP software. The identity of rats (paradigm and day of training) from which the neurons were taken and recorded was not known to the person conducting the experiments and measurements.

Cell input resistance (Rm) was determined by calculating the best linear regression fit to a voltage–current curve constructed from voltage responses to 100-ms current pulses ranging between +0.5 and −0.5 nA. Spike width was measured at the spike threshold.

The μ-opioid-receptor agonist N-NalMe-Phe4-Glyol5-enkephalin (DAMGO) (0.5 μM) was applied via the perfusion solution.

Neuronal Adaptation Measurements
At the neuron resting potential, 1-s pulses of depolarizing current were injected into the cell body via the recording electrode, in order to determine the threshold current intensity needed to generate a single action potential (Ith). Adaptation was calculated from the response to a standard 1-s current step of intensity Ith × 2 (Fig. 2A, B). Firing frequency was calculated for each interspike interval (ISI).

Postburst AHP Measurements
To standardize AHP recordings (Saar and Barkai 2003, 2009), the neuron membrane potential was depolarized to ~60 mV by direct current (DC) application via the recording electrode, and the AHP amplitude was measured after application of an additional 100-ms depolarizing current step that generated 6 action potentials (Fig. 3A), after which the DC depolarization was maintained. The AHP amplitude was determined from an average of 8 consecutive responses to stimuli applied once every 10 s. Under these conditions, a postburst AHP that lasted up to several seconds appeared in all BLA pyramidal neurons.

Synaptic Stimulation
Synaptic stimulation was delivered via a bipolar tungsten electrode positioned at the cortical afferents and stimulus intensity was adjusted to elicit a single action potential in the BLA pyramidal cell—which was held at resting potential—each time the synaptic stimulus was applied. Subsequently, a train of 20 synaptic stimuli at frequency of 20 Hz was applied to the cell (see Fig. 5A). Five such trains were applied at 10-s intervals. The number of spikes elicited by each stimulus was calculated as the average number of spikes elicited by these 5 trains.

Statistical Analysis
Differences were determined by means of mixed ANOVA. All the ANOVA tests were followed by 1-way ANOVA and Student’s t-tests, and by using a Bonferroni correction, when appropriate, to maintain alpha at 0.05. All tests were 2-tailed and a P value of <0.05 was considered statistically significant. All tests were performed with SPSS software, version 13.0 (SPSS, Chicago, IL, USA). All post hoc comparisons were made by means of least significant difference multiple comparison tests. Values are presented as mean ± SE.

Results
Three hundred sixty-eight cells, identified as pyramidal neurons on the basis of their passive and active electrophysiological characteristics (Washburn and Moises 1992a, 1992b), were recorded from 166 rats. All these neurons fired a single action potential in response to intracellularly applied threshold intensity stimulation. In response to prolonged depolarizing pulses with stimulus intensities higher than the threshold intensity, the neurons generated repetitive spike firing, with varied degrees of neuronal adaptation.

OD-Learning-Induced Enhancement of Intrinsic Excitability of BLA Neurons
We first examined whether OD learning in the 4-armed maze (complex OD learning) induced modifications in the intrinsic neuronal excitability of BLA pyramidal neurons, and assessed the kinetics of these modifications. In light of our previous findings that in the piriform cortex-enhanced neuronal excitability is apparent 1–3 days after OD learning (Saar et al. 1998) and in the hippocampus from the fifth day during learning to the first day after learning (Zelcer et al. 2006), cells were recorded at 3 time points after the beginning of training: 1) on the fifth day of training, prior to acquisition of rule learning; 2) 1 day after rule learning; and 3) 3 days after rule learning (Fig. 1B). Intrinsic neuronal excitability was
measured for each neuron in terms of the number of spikes elicited by a 1-s depolarizing pulse, of stimulus intensity twice the threshold current (see Experimental procedures). As shown in Figure 2A–C, 2-factor ANOVA (2 [Group, testing day] × 1 [spikes]) showed significant effects of the Group ($F_{2, 137} = 3.56; P = 0.03$) and testing day ($F_{2, 137} = 3.22; P = 0.04$), but no significant interaction between the Group and the testing day ($F_{2, 137} = 2.084; P = 0.089$).

Post hoc Student’s t-test showed that the trained group differed significantly from the pseudo and naïve groups ($P < 0.005$ for both). In contrast, there was no significant difference between the naïve and the pseudo groups ($P > 0.05$). The trained group showed significantly more spikes (12.14 ± 0.89) than the naïve and pseudo groups, which showed 9.6 ± 0.89 and 8.9 ± 1.06 spikes, respectively.

Post hoc analysis also showed significant differences between the training days. The average value from cells recorded 1 day after training was significantly different from that obtained from cells recorded 3 days after training ($P < 0.005$), but not from that obtained from cells recorded on the fifth day during training. One day after rule learning, the trained group showed significantly greater excitability, as expressed in the greater numbers of spikes, than the other groups: trained, 15.07 ± 1.1; pseudo, 11.9 ± 1.9; naïve, 8.34 ± 1.5. Thus, OD rule learning was accompanied by significant enhancement in the number of spikes only during 1 day following rule learning.

Notably, the averaged values of the currents required to elicit a single action potential ($I_{th}$) did not differ between groups ($0.55 ± 0.33$ nA for naïve, $0.53 ± 0.43$ for trained...
during training, $0.63 \pm 0.27$ for trained 1 day after learning, $0.46 \pm 0.25$ for trained 3 days after learning, $0.47 \pm 0.31$ for pseudo during training $0.49 \pm 0.23$ for pseudotrained 1 day after training and $0.58 \pm 0.23$ for pseudotrained 3 days after training). Thus, differences in numbers in spikes evoked by the intracellular pulses with the intensity of $I_{2\text{h}} \times 2$ (see Materials and Methods section) are not the result of differences between the currents intensities applied to neurons from the different groups. As shown below, other basic membrane properties were also not modified by training.

In accordance with the increase in the average number of spikes, neuronal adaptation in neurons from trained rats was reduced 1 day after learning. This reduction became apparent during the fourth ISI, and it was maintained throughout the response (Fig. 2D). Furthermore, the difference between neurons from trained and those from pseudotrained rats increased with the duration of the response. The ratio between the levels of neuronal adaptation in neurons from trained and from pseudotrained rats increased as long as repetitive spike firing persisted (Fig. 2E), indicating that the differences in neuronal excitability increased with increasing levels of neuron activity.

**Postburst AHP is Reduced in Neurons from Complex OD-Trained Rats**

We next examined the relations between learning-induced enhancement in neuronal excitability and changes in the postburst AHP at the same time points, during and after learning. The average amplitude of the postburst AHP elicited by a 100-ms pulse of sufficient intensity to elicit 6 action potentials while the neuron membrane potential was held at $-60 \text{ mV}$ was measured in trained ($n = 49$), pseudo ($n = 31$), and naïve ($n = 31$) animals (see Fig. 3A).

As shown in Figure 3B, 2-factor ANOVA ($2 \times [\text{Group}, \text{Day}] \times 1$ [AHP]) showed a significant effect of Group ($F_{2, 102} = 3.99, P = 0.02$) without significant effects of training day ($F_{2, 102} = 0.07; \text{ns}$) or of interaction ($F_{4, 102} = 1.59; \text{ns}$).

Post hoc analysis showed that the trained group differed significantly from the naïve group, and showed decreased amplitudes of AHP ($7.4 \pm 0.26$ and $8.1 \pm 0.31 \text{ mV}$, respectively; $P > 0.05$). Similarly, no significant difference was observed between the pseudo and naïve groups ($8.1 \pm 0.31$ and $8.6 \pm 0.32 \text{ mV}$, respectively; $P > 0.05$).

**OD-Learning-Induced Enhanced Firing and AHP Reduction Were Not Due to Changes in Basic Membrane Properties**

Postburst AHP potentially could be reduced not only as a result of direct modifications in its underlying currents, but also as a consequence of modifications in the passive and active properties of neuron membranes. Such modifications in basic membrane properties may also affect repetitive spike firing. However, the basic passive membrane properties, such as resting potential and input resistance, and active membrane properties, such as spike amplitude and width, were not modified in BLA neurons after OD rule learning (Table 1). These data indicate that learning-induced changes in neuronal excitability and AHP amplitude were not the result of a general change in neuronal properties that affected both parameters.

**Relations Between Enhanced Spike-Firing Frequency and AHP Reduction**

OD-learning-induced enhancement of neuronal excitability was apparent in most recorded BLA neurons. This can be seen in the cumulative frequency distributions that compare these values between trained and control neurons (naïve- and pseudotrained) (Fig. 4A). Although the changes in AHP amplitude were also found 1 day following OD rule learning, no direct correlation was found between the AHP and the number of spikes generated by each neuron in response to the prolonged 1-s depolarizing pulse (Fig. 4B). We further examined whether such a relation existed for any specific phase of the response. We therefore divided the response of the neurons to 3 periods, corresponding to the first, second, and third groups of 4 action potentials. Whereas no correlation was found between the AHP amplitude and the average firing frequency of the first and second groups of 4 spikes, a strong correlation was found between the AHP amplitude in each neuron and the average firing frequency of spikes #9–12.
Membrane properties of BLA neurons are not modified by OD learning

<table>
<thead>
<tr>
<th>Groups</th>
<th>Time point</th>
<th>Passive properties</th>
<th>Action potential</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$V_m$ (mV)</td>
<td>$R_{in}$ (MΩ)</td>
</tr>
<tr>
<td>Naïve</td>
<td>−75.6 ± 8.2</td>
<td>43.3 ± 15.6</td>
<td>89.0 ± 13.3</td>
</tr>
<tr>
<td></td>
<td>n = 37 (15)</td>
<td>n = 29 (15)</td>
<td>n = 37 (15)</td>
</tr>
<tr>
<td>Pseudotrained</td>
<td>During learning</td>
<td>−74.8 ± 4.6</td>
<td>49.2 ± 22.8</td>
</tr>
<tr>
<td></td>
<td>n = 16 (7)</td>
<td>n = 17 (7)</td>
<td>n = 16 (7)</td>
</tr>
<tr>
<td></td>
<td>1 day after learning</td>
<td>−77.7 ± 6.0</td>
<td>46.4 ± 18.1</td>
</tr>
<tr>
<td></td>
<td>n = 12 (8)</td>
<td>n = 13 (6)</td>
<td>n = 12 (6)</td>
</tr>
<tr>
<td></td>
<td>3 days after learning</td>
<td>−73.0 ± 6.2</td>
<td>31.3 ± 12.1</td>
</tr>
<tr>
<td></td>
<td>n = 13 (9)</td>
<td>n = 14 (9)</td>
<td>n = 12 (9)</td>
</tr>
<tr>
<td>Trained</td>
<td>During learning</td>
<td>−73.5 ± 7.5</td>
<td>42.7 ± 15.6</td>
</tr>
<tr>
<td></td>
<td>n = 22 (10)</td>
<td>n = 21 (10)</td>
<td>n = 22 (10)</td>
</tr>
<tr>
<td></td>
<td>1 day after learning</td>
<td>−76.8 ± 8.0</td>
<td>36.5 ± 16.1</td>
</tr>
<tr>
<td></td>
<td>n = 29 (10)</td>
<td>n = 28 (10)</td>
<td>n = 28 (10)</td>
</tr>
<tr>
<td></td>
<td>3 days after learning</td>
<td>−77.3 ± 12.2</td>
<td>48.9 ± 18.0</td>
</tr>
<tr>
<td></td>
<td>n = 19 (9)</td>
<td>n = 15 (9)</td>
<td>n = 19 (9)</td>
</tr>
</tbody>
</table>

Note: Membrane resting potential ($V_m$) was determined from the voltage change accompanying electrode withdrawal from the cell at the end of the recording. Input resistance ($R_{in}$) was determined by calculating the best linear regression fit to a voltage–current curve, constructed from voltage responses to 100-ms current pulses ranging between +0.5 and −0.5 nA. Action potential amplitude was measured from the resting potential to the peak. Basic membrane properties in cells from naïve, pseudotrained, and trained rats were similar to each other when recorded in normal conditions. Values represent mean ± SD. n, number of cells. The number of rats is noted in brackets.

Figure 4. Only persistent firing frequency is related to the AHP amplitude. (A) Cumulative frequency distributions of the numbers of spikes in neurons from controls (pseudotrained + naïve) and from trained neurons, respectively, 1 day after rule learning. Each point represents the number of spikes in 1 cell. Numbers of spikes in neurons from trained rats form a curve that is smoothly shifted to the right along the x-axis relative to that derived from controls, indicating that most recorded neurons from the trained group enhanced their firing rate 1 day after rule learning. (B) In both control and trained neurons, no direct relation was detected between the postburst AHP amplitude and the number of spikes generated in response to the prolonged intracellular stimulation. Dotted line: linear fit for control neurons ($R = 0.144$, $P = 0.25$). Solid line: linear fit for trained neurons ($R = −0.02$, $P = 0.92123$). (C) The average firing frequency of the first 4 spikes in each neuron, elicited by the standard prolonged pulse, was independent of the amplitude of the postburst AHP in the corresponding neuron taken from controls (empty circles) or from trained rats 1 day after rule learning (filled circles). (D) Similar independence is apparent for the average firing frequency of the second group of 4 spikes, that is, spikes # 5–8, of the response. (E) The average firing frequency of the third group of 4 spikes, that is, spikes # 9–12, of the response shows a highly significant correlation to the postburst AHP amplitude for each particular neuron. Linear fits are presented for all the values in each graph, $R$ and $P$ values for the average frequency of each group are noted in boxes.

Valence is reflected in intrinsic plasticity  Motanis et al.
(Fig. 4C–E). Thus, it appears that the slow potassium currents that mediate the postburst AHP (Madison and Nicoll 1984; Constanti and Sim 1987; Schwindt et al. 1988; Saar et al. 2001; Brosh et al. 2006) are particularly efficient in controlling the delayed firing rate of the neurons.

**Learning-Induced Enhanced Excitability in Response to Repetitive Synaptic Stimulation**

Neurons do not respond to somatic currents in vivo, and therefore, we next examined whether BLA pyramidal neurons also showed enhanced excitability in response to repetitive synaptic activation. The cortical afferents to each recorded neuron were stimulated 20 times at intervals of 50 ms, at an intensity adjusted such that the first stimulus elicited 1 spike. An EPSP with amplitude of about 15 mV had to be evoked in order to evoke an action potential. This was similar for neurons from trained rats and controls. Such similarity is expected since basic membrane properties, such as resting potential, membrane input resistance, and the threshold current required to elicit a single action potential, were not modified after learning. We hypothesized that neurons from trained animals would respond to a given stimulation with more action potentials than those from naïve animals. Indeed, Figure 5 shows that 1 day following OD learning resulted in a pronounced increase in the ability of neurons to follow repetitive afferent stimulation with reliable repetitive spike generation (Fig. 5A, B).

Application of repeated-measures ANOVA to the 19 responses elicited by the 2nd to 20th synaptic stimulations showed significant difference between the 2 groups ($F_{1, 20} = 12.6; P = 0.002$), a significant effect of the pulse number ($F_{18, 360} = 4.1, P = 0.004$), but without significant interaction (ns).

Thus, the probability of action potential generation following 19 synaptic pulses in the trained group was significantly higher than that in the naïve group (trained [$n = 11$]: $0.73 \pm 0.08$; naïve [$n = 11$] $0.29 \pm 0.08$). Moreover, as shown for the responses to intracellularly applied currents (Fig. 2D), the difference between neurons from trained and naïve rats became more pronounced as the number of synaptic stimulations increased. The ratio of average neuronal spike generation between neurons from trained and naïve rats, respectively, increased as repetitive spike firing persisted (Fig. 5C).

**Simple Olfactory-Discrimination Learning is Not Associated with Changes in Neuronal Excitability**

Is OD-learning-induced enhancement of neuronal excitability the result of the reward valence or of the complexity of the task? Due to the fact that acquisition of the OD rule learning was gradual and slow and occurred over several days of training, we examined the effect of learning in a simple water-rewarded olfactory-discrimination task in which animals learned to associate between a specific odor and the water reward in a few trials (see Experimental procedures and also Cohen-Matsliah et al. 2009).

As shown in Figure 6A, intrinsic neuronal excitability was recorded at 2 time points: 1 and 3 days after learning. Two-factor ANOVA (2 [Group] × 1 [Spikes]) did not show significant differences related to Group ($F_{2, 68} = 1.35$, ns), testing day ($F_{1, 68} = 0.32$, ns) or their interaction ($F_{2, 68} = 0.73$, ns). The average postburst AHP values also did not differ among neurons from the 3 groups ($F_{2, 53} = 2.2$, ns) (Fig. 6B).

Furthermore, there was no significant effect of learning day ($F_{1, 53} = 0.01$, ns) or of the interaction between Group and learning day ($F_{2, 53} = 0.96$, ns).

These data suggest that whereas complex olfactory learning resulted in enhancement of the intrinsic excitability of BLA neurons and reduction in AHP amplitude, simple olfactory learning was not accompanied by a similar effect, although a tendency toward an increase in the number of spikes can be observed (Fig. 6A, B).

**Fear Conditioning-Induced Reduction of Intrinsic Excitability of BLA Neurons**

The above results show that acquisition of the positive-reward complex OD rule learning was associated with enhanced neuronal excitability and reduced postburst AHP in the BLA. In light of the predominant role of the BLA in encoding the

**Figure 5.** Learning-induced enhancement in excitability elicited by synaptic activation. (A) Examples of firing patterns of action potentials in BLA pyramidal neurons from a naïve and a trained rat. In response to the application of repetitive stimulation applied at 20 Hz, the cells responded with action potentials, with a highest probability at the onset of the pulse. In these conditions, the neuron from the naïve rat fails to respond with repetitive spike generation. (B) A quantitative description of learning-induced enhancement of repetitive spike firing. With a synaptic stimulus intensity adjusted to always elicit an action potential in response to the first stimulus, the probability of firing an action potential at each interspike interval (ISI) along the train was calculated by averaging the responses for 5 trains of stimuli for each cell, and then calculating the average for all neurons in each group. Starting from the third interval, a clear difference appears between the trained and the naïve groups. Values represent means ± SE. Data were taken for 3 trained rats, and 3 naïve rats. The n indicated in the figure is the number of cells. (C) The ratio between the probabilities of firing action potentials in neurons of the trained and naïve rats increased linearly as the interspike interval increased. Thus, as demonstrated by the examples in panel A and the averages in panel B, the difference in synchronically elicited excitability between neurons from trained and control rats, respectively, increased with prolongation of the stimulus.
negative emotional value of odors (Vernet-Maury 1980; Blanchard et al. 1990; Fendt et al. 2005; Masini et al. 2005; Takahashi et al. 2005; Sevelinges et al. 2009; Shionoya and Datiche 2009; Butler et al. 2010; Staples and McGregor 2006), we next examined whether aversive olfactory learning, in which acquisition of the association was robust and rapid, would differentially affect the intrinsic properties in the BLA. First, we tested whether odor-conditioned rats learned the association between the CS, that is, odor, and US, that is, electric shock. We measured the freezing levels of a separate group of rats 1 day after odor fear conditioning; that is, freezing behavior when introduced to the context (chamber), the chamber itself; and 2) the CS (the same odor used to condition the rats).

Figure 1C shows that whereas the rats did not exhibit any freezing behavior when introduced to the context (chamber), they showed very high freezing levels when introduced to the CS (odor), indicating that they learned the CS–US association and did not generalize the CS.

Intrinsic neuronal excitability was recorded in neurons from 3 groups of animals; the odor-conditioning-trained group (n = 37), the odor-exposure pseudotrained group (n = 37) and the naïve group (n = 23) at 2 time points after learning: 1 and 3 days after learning. As shown in Figure 7A–C, 2-factor ANOVA (2 [Group and Day] × 1 [spikes]) showed a significant difference between the groups (F2, 86 = 13.08; P = 0.001). However, there was no significant effect of Day (F1, 91 = 0.25, ns) or of the interaction between Group and Day (F1, 91 < 1, ns).

Post hoc analysis showed that the odor-conditioning-trained animals were significantly different from the naïve group (P < 0.005) and from the pseudotrained group (P < 0.001), and that the pseudo-trained group was significantly different from the naïve group (P < 0.05). Specifically, on average, the neurons from the odor-conditioning-trained rats elicited fewer spikes in response to the 1-s depolarizing pulse, of stimulus intensity twice the threshold current (5.32 ± 0.7) than those from naïve (11.56 ± 0.95) or pseudotrained ones (7.8 ± 0.80).

These results show that odor fear conditioning resulted in reduction in the amount of spiking in the BLA. To examine whether odor FC learning-induced modulation of repetitive spike firing was specific to the odor-context association we compared odor conditioning-trained animals (odor conditioning; n = 14) with animals that underwent contextual conditioning without presentation of the odor (contextual conditioning; n = 14). Independent t-test showed that the 2 groups differed significantly in the numbers of spikes (odor conditioning: 5.07 ± 0.53; contextual conditioning: 8.5 ± 0.9; t(26) = 3.06; P < 0.05). These results confirm that the observed change was specific to the odor fear-conditioning learning.

Reduced Neuronal Excitability after Negative Reward Learning is not Accompanied by Modulation of the Postburst AHP

We next examined the relations between odor fear-learning-induced reduction in neuronal excitability and the postburst AHP. Neurons were recorded at either 1 or 3 days after training, from 3 groups of animals: the odor-conditioning-trained group (trained; n = 27), the odor exposure pseudotrained group (pseudo: n = 31), and the naïve group (naïve: n = 16). There was no significant effect of group (F2, 68 = 1.0; ns), testing day (F1, 68 = 0.01, ns), or their interaction (F2,68 = 0.1; ns). The average values of AHP in the odor-conditioning-trained group were (8.1 ± 0.42) compared with (7.6 ± 0.4) and (8.50 ± 0.54) in the pseudotrained and naïve animals, respectively.

Thus, in contrast to OD learning, odor fear-conditioning-induced reduction of neuronal excitability was not accompanied by postburst AHP modulation (Fig. 7D,E). This lack of a relationship between reduction in neuronal excitability and AHP modulation is not surprising; the postburst AHP amplitude was correlated with repetitive firing frequency only in the later part of the response (Fig. 4).

Notably, the input resistance of neurons from the odor fear-conditioning group was significantly smaller than that of...
Figure 7. Neuronal excitability, but not AHP amplitude, is reduced after fear conditioning learning. (A and B) Examples of neuronal firing patterns in BLA pyramidal neurons from the 3 groups, 1 and 3 days after learning. Traces are shown for neurons from: naïve rats (left trace); pseudotrained rats, exposed to the odor only (middle trace); and trained rats, odor fear conditioned (right trace). Note that the neurons taken from trained rats become almost completely silent after the initial part of the response. (C) The average numbers of spikes recorded from each experimental group, 1 and 3 days after learning. The average number of spikes in neurons from the odor fear-conditioned rats was significantly smaller than those in neurons from the naive and pseudotrained groups (P < 0.05), 1 and 3 days after learning. A significant reduction (P < 0.05) in the average number of action potentials was observed also for the pseudotrained group (P < 0.05), compared with the naive group at both time points. Numbers in columns represent the numbers of recorded neurons. The following numbers of rats were used on the various days: 4 naïve rats 1 day after learning; 4 naïve rats 3 day after learning; 11 odor-exposed pseudotrained 1 day after learning; 6 odor-exposed pseudotrained 3 days after learning; 10 odor-conditioned trained 1 day after learning; and 9 odor-conditioned trained 3 days after learning. (D) Postburst AHP measurements in BLA pyramidal neurons. Neurons were held at a membrane potential of −60 mV, and an AHP was generated by a 100-ms depolarizing current step of intensity sufficient to generate a train of 6 action potentials, injected via the recording electrode. Examples from typical naïve and trained neurons are superimposed. (E) Averaged amplitudes of AHPs did not differ between the 3 groups 1 and 3 days after learning. The same number of rats was used for repetitive spiking and AHP measurements. Presented are the average values for each day ± SE. Numbers in columns represent the numbers of recorded neurons.

Table 2

<table>
<thead>
<tr>
<th>Group</th>
<th>Passive properties</th>
<th>Action potential</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>V&lt;sub&gt;rest&lt;/sub&gt; (mV)</td>
<td>R&lt;sub&gt;in&lt;/sub&gt; (MΩ)</td>
</tr>
<tr>
<td>Naive</td>
<td>−77.0 ± 7.6</td>
<td>44.6 ± 26.5</td>
</tr>
<tr>
<td>Trained: odor fear</td>
<td>−72.2 ± 7.7</td>
<td>31.35 ± 17.6</td>
</tr>
<tr>
<td>conditioning</td>
<td>n = 18 (10)</td>
<td>n = 17 (10)</td>
</tr>
<tr>
<td>Pseudo: odor exposure</td>
<td>−69.9 ± 3.4</td>
<td>34.09 ± 15.2</td>
</tr>
<tr>
<td></td>
<td>n = 25 (11)</td>
<td>n = 22 (11)</td>
</tr>
</tbody>
</table>

Note: Membrane resting potential (V<sub>rest</sub>) was determined from the voltage change accompanying electrode withdrawal from the cell at the end of the recording. Input resistance (R<sub>in</sub>) was determined by calculating the best linear regression fit to a voltage–current curve constructed from voltage responses to 100-ms current pulses ranging between ±0.5 and −0.5 nA. Action potential amplitude was measured from the resting potential to the peak. Values represent mean ± SD, n, number of cells. The number of rats is noted in brackets.

µ-Opioid-Receptor-Dependent Reduction in Neuronal Excitability is Ocluded by Learning

A particularly interesting mechanism of reducing intrinsic excitability in lateral amygdala pyramidal neurons involves enhancement of a dendritic voltage-dependent potassium current by activation of µ-opioid receptors (Faber and Sah 2004). We therefore examined the possibility that odor fear conditioning might induce a long-lasting reduction of excitability as a result of persistent modulation of µ-opioid receptors.

Slices were prepared from odor-conditioning-trained (trained: n = 13) and naïve (naïve: n = 13) animals, and the number of spikes elicited before and after application of the µ-opioid-receptor agonist, DAMGO, was recorded. Application of repeated-measures ANOVA before and after DAMGO/αCSF application showed only a significant interaction (F<sub>1, 24</sub> = 5.3; P = 0.03), with no significant effect of group (F<sub>1, 12</sub> < 1) or of recording time (F<sub>1, 12</sub> < 1). Follow-up t-tests showed that DAMGO significantly affected the naïve group only: the number of spikes in this group was reduced following DAMGO application (pre: 9.2 ± 1.1; post: 6.0 ± 0.91; P = 0.045), and this effect was not observed in the trained animals (ns). This effect became apparent shortly, although not immediately, after the onset of the pulse (Fig. 8A,B).

DAMGO did not affect repetitive action potential firing in neurons from odor-conditioning-trained rats (Fig. 8A,B); the average number of action potential after conditioning and before DAMGO (5.4 ± 1.2, n = 13) was not modified by the drug (7.7 ± 1.0).

The effect of DAMGO on repetitive spike firing was not mediated by modulation of the postburst AHP. Application of...
repeated-measures ANOVA did not reveal a significant effect on AHP; the groups (trained: \( n = 10 \) and naïve: \( n = 10 \)) did not differ (\( F_{1, 18} = 0.31; \) ns). However, there was a significant effect of time of measurement, that is, before or after drug application (\( F_{1, 18} = 16.3; \) \( P = 0.001 \)) but no interaction (ns) between time and group. Here too, the averaged values of currents required to elicit a single action potential (\( I_{th} \)) did not differ between groups (0.71 ± 0.46 nA 1 day after fear conditioning, 0.69 ± 0.25 3 days after fear conditioning, 0.60 ± 0.29 1 day after exposure only, 0.73 ± 0.34 3 days after exposure only).

These results suggest that DAMGO effects on AHP did not differ between the trained and the naïve groups, but that there was a difference between pre- and post-drug application, showing that both groups changed in the same direction following application of the drug (Fig. 8C).

**Valence Outcome is Reflected in the Direction of Intrinsic Plasticity**

The strong relation between the valence of the outcome and the direction of intrinsic neuronal plasticity in BLA pyramidal neurons is summarized in Figure 9. For each learning paradigm, the average number of spikes in neurons from trained rats was normalized to the average number of action potentials elicited in neurons from naïve and pseudotrained rats 1 day after learning. Complex OD learning resulted in a positive change and simple OD resulted in a tendency toward the same direction (although the difference falls short of statistical significance), whereas odor FC resulted in a negative change.

These data suggest that both forms of positive-reward OD learning modified these neurons to fire more action potentials, whereas odor fear conditioning modified BLA neurons in the opposite direction and resulted in reduced intrinsic excitability.

**Discussion**

OD-learning-induced modulation of intrinsic neuronal excitability was previously shown in 2 brain areas: the piriform cortex (Saar et al. 1998) and the hippocampus (Zelcer et al. 2006). In the present study, we show that such modifications occurred also in BLA pyramidal neurons when complex-OD rule learning was completed. However, BLA neurons showed unique bidirectional plasticity of intrinsic excitability that reflected the value of the odor. The direction of such plasticity is strongly correlated with the valence of the reward, rather than with the difficulty of the task.

**Relevance of the Amygdala to Olfactory Learning**

The amygdala has been suggested to play a key role in positive reward and reinforcement, as well as in representing negative value of the reward (Paton et al. 2006; Belova et al. 2007, 2008; Murray 2007). In particular, several studies showed that the amygdala is involved in olfactory learning (Sullivan and Wilson 1993; Schoenbaum et al. 1998, 1999,
Odor Fear-Conditioning-Induced Modulation of Intrinsic Excitability

Olfactory fear conditioning also affected intrinsic neuronal excitability in BLA pyramidal neurons, but in the direction opposite to that induced by positive OD learning. Such bidirectional plasticity significantly increases the ability to modulate the output of the BLA. Notably, reduced spike firing persisted up to the third day after learning—a prolonged effect compared with that of neuronal excitability enhancement related to the positive reward.

An interesting study showed that whereas bath application of muscarine suppressed the AHP in BLA neurons, focal application to the soma and proximal dendrites could result in enhanced AHP reduction of repetitive spike firing (Power and Sah 2008).

It is notable that a previous study aimed to examine fear-conditioning-induced modulation of intrinsic neuronal excitability in lateral amygdala (LA) neurons suggested that such learning was related to enhanced neuronal excitability and reduced AHP in a subset of neurons that are crucial for learning (Rosenkranz and Grace 2002; Zhou et al. 2009). In particular, LA amygdale neurons become more excitable due to an increase in the membrane input resistance, an effect in which dopamine has a key role. It would therefore be interesting to further examine the possibility that learning can be expressed in 2 different ways in the LA and the BLA, respectively: enhancing neuronal excitability in 1 region (LA), and reducing it in the other (BLA). Another possibility would be that training in olfactory fear conditioning, as in the present study, and auditory fear conditioning, as used by Zhou et al. (2009) induce differing effects on intrinsic neuronal properties. This interpretation is supported by our present finding that contextual fear conditioning was not associated with similar changes to those associated with odor conditioning, which tends to support the uniqueness of odor conditioning in exerting these effects.

The Mechanism Underlying Odor Fear-Conditioning-Induced Modulation of Intrinsic Excitability

Application of DAMGO, a µ-opioid agonist, reduced firing frequency in BLA pyramidal neurons, as previously shown for lateral amygdala neurons (Faber and Sah 2004). However, such reduction was occluded by previous learning. Thus, the present data support the notion that olfactory fear-conditioning-induced reduction in neuronal excitability results from long-term µ-opioid-activated modulation of intrinsic properties, presumably by activation of a voltage-dependent potassium channel containing Kv1.2 subunits (Faber and Sah 2004). Accordingly, the strong reduction in intrinsic excitability that followed fear learning was not accompanied by a parallel modulation in the postburst AHP. This lack of correlation was to be expected, because fear conditioning affected the earlier part of the intracellular response, by reducing the average number of spikes from about 10 to <5, whereas the postburst AHP affected only later-occurring action potentials. Surprisingly, DAMGO application also reduced the postburst AHP in neurons from fear-conditioned rats. These findings show that the conductance underlying the postburst AHP was reduced by fear-conditioning learning, but that such reduction was masked by µ-opioid-sensitive currents.

Relations Between the AHP Reduction and Repetitive Firing After OD Learning

Although enhanced firing frequency and reduced postburst AHP were observed in most neurons after OD learning, no direct correlation was found between these 2 parameters over the full length of the intrinsically elicited response for each particular neuron. However, such correlation existed for the later part of the response, that is, with regard to the average firing frequency for spikes #9-12 in each response. Spikes occurring at this late phase were more likely to be affected by the slow, calcium-dependent potassium current—the $s_{AHP}$ (Sah and Faber 2002). Recording from lateral amygdala pyramidal neurons showed that the $s_{AHP}$ indeed played a prominent role in controlling prolonged firing (Faber and Sah 2002). Notably, in neurons of the BLA, the $s_{AHP}$ was generated in the dendrites and thus also affected postsynaptic potentials amplitude and summation in the soma (Power et al. 2011). Learning-induced reduction in the $s_{AHP}$ was also shown in the hippocampus after water maze learning (Oh et al. 2003) and in the piriform cortex after training in the complex OD-learning paradigm (Brosh et al. 2006).

OD-rule learning was expressed in enhanced excitability also in response to repetitive synaptic stimulation. Whereas it seemed that differences in responses between trained and control rats became more apparent as the number of stimuli increased (Fig. 5C), when the slow AHP was activated, neurons from trained rats showed enhanced excitability starting from the third response to trains of 50-Hz stimuli (Fig. 5C,D). These results suggest that learning-induced enhancement to synaptic stimulation is probably mediated not only by modulation of the slow AHP, but also by other synaptic or intrinsic modifications that are activated at earlier stage(s) of the response.
Relation to OD-Learning-Induced Modulation of Neuronal Excitability in Other Brain Regions

OD-learning-induced modifications in intrinsic neuronal properties, manifested in enhanced neuronal excitability and reduced postburst AHP, appear to be a common feature detected in several relevant brain areas: the piriform cortex (Saar and Barkai 2005), the hippocampus (Zelcer et al. 2006), and the BLA. However, such modifications follow differing time courses. They appeared in the hippocampus 1 day before OD rule learning was achieved and disappeared 1 day after learning, even if training was continued with other pairs of odors (Zelcer et al. 2006). In contrast, intrinsic modifications occurred in piriform cortex neurons only after rule learning but were maintained for 3–4 days after the last training session (Saar et al. 1998). BLA neurons showed such intrinsic plasticity only for 1 day after rule learning. Such a wide spread phenomenon; OD-learning-induced modulation intrinsic neuronal occurs in several brain areas, likely reflects the difficulty of the olfactory-discrimination task, which requires joint activation of several central brain areas.

One major consequence of enhancing the prolonged firing frequency of most excitatory neurons in a network is increased sustained output of the network (Barkai et al. 1994). Thus, these various brain regions seem to increase their activity during differing phases of acquisition and maintenance of the OD rule, in a manner related to their roles. For example, in light of these time courses, it can be speculated that the hippocampus is more involved in the formation of the rule (Zelcer et al. 2006), whereas the piriform cortex is more instrumental in maintaining the skill (Saar et al. 1998). As BLA neurons showed enhanced firing rate for only 1 day after rule learning, these data support the notion that the role of the BLA is to encode the motivational significance of the input, as previously suggested by Schoenbaum et al. (1999), whereas the long-term memory related to the significance of the input is stored in other brain area(s). It is worthwhile noting that odor fear-learning-induced modulation of firing properties outlasted the opposite effects induced by positive OD learning.

In conclusion, our present findings show that complex OD rule learning and olfactory fear-conditioning learning are accompanied by opposite, transient, modifications in intrinsic neuronal properties of BLA neurons, mediated by 2 different cellular mechanisms. Such opposing modifications may mediate the amygdala’s role in identifying the value of correct performance in the olfactory tasks.

Supplementary Material
Supplementary material can be found at: http://www.cercor.oxfordjournals.org/.

Notes
Conflict of Interest: None declared.

References


1086 Valence is reflected in intrinsic plasticity · Motanis et al.


