Learning-Dependent Plasticity of Hippocampal CA1 Pyramidal Neuron Postburst Afterhyperpolarizations and Increased Excitability After Inhibitory Avoidance Learning Depend Upon Basolateral Amygdala Inputs

George E. Farmer and Lucien T. Thompson*

ABSTRACT: Hippocampal pyramidal neurons *in vitro* exhibit transient learning-dependent reductions in the amplitude and duration of calcium-dependent postburst afterhyperpolarizations (AHPs), accompanied by other increases in excitability (i.e., increased firing rate, or reduced spike-frequency accommodation) after trace eyeblink conditioning or spatial learning, with a time-course appropriate to support consolidation of the learned tasks. Both these tasks require multiple days of training for acquisition. The hippocampus also plays a role in acquisition of single trial inhibitory avoidance learning. The current study assessed AHP plasticity in this single-trial learning task using *in vitro* tissue slices prepared at varying intervals posttrial using intracellular current-clamp recordings. Reduced AHPs and reduced accommodation were seen in ventral CA1 pyramidal neurons within 1 h posttraining, plasticity which persisted 24 h but was extinguished >72 h posttrial. There was also a reduction in ventral CA1 AHPs and accommodation 1 h following simple exposure to the IA apparatus (a novel context) but this change was extinguished by 24 h postexposure. Reductions in AHPs and accommodation were also seen in dorsal CA1 pyramidal neurons, but were delayed until 24 h posttrial and extinguished at >72 h posttrial. Finally, transient inactivation of the basolateral complex of the amygdala (with the local anesthetics lidocaine or bupivacaine) either immediately before or immediately posttrial blocked both learning and learning-dependent changes in excitability in the hippocampus assessed 24 h posttrial. CA3 pyramidal neurons showed no reductions in AHP peak amplitude or accommodation following IA training or context exposure. © 2012 Wiley Periodicals, Inc.

KEY WORDS: postburst AHP; single trial learning; acquisition; consolidation; inactivation

INTRODUCTION

Hippocampal CA1 and CA3 pyramidal neurons show prolonged (several hundred millisecond) postburst afterhyperpolarizations (AHPs), (Schwartzkroin, 1975; Hotson and Prince, 1980; Schwartzkroin and Stafstrom, 1980; Matthews et al., 2009). These AHPs clamp the membrane potential below the threshold for firing, enhancing spike-frequency adaptation (accommodation), and reducing neuronal excitability in

response to afferent stimulation (Madison and Nicoll, 1982, 1984; Haas and Greene, 1984).

Learning-dependent AHP plasticity has been repeatedly reported in multiple species following acquisition of several different multitrial tasks. In the earliest example, decreases in peak AHP amplitude of rabbit CA1 pyramidal neurons from trained animals after delay eyeblink conditioning (EBC) were reported (Disterhoft et al., 1986). After trace EBC, a hippocampal-dependent task requiring hundreds of trials for acquisition, both CA1 (Moyer et al., 1996) and CA3 pyramidal neurons (Thompson et al., 1996) showed reductions in peak AHP amplitude, duration, and integrated area, along with reductions in accommodation. This hippocampal AHP plasticity occurred within 1 h postacquisition and persisted for up to 5 days after learning, an interval during which blockade or lesions of hippocampus ablate memory consolidation of the conditioned response (Kim et al., 1995). AHP plasticity was learning-specific, and did not occur in nonlearners.

Learning-dependent AHP plasticity occurs in other multitrial learning tasks, including learning the location of a hidden platform in a water maze (Oh et al., 2003) or acquisition of a delayed spatial win-shift task (Farmer et al., submitted for review). This plasticity was not expressed in neurons from nonlearners (Gant and Thompson, 2000; Thompson et al., 2000; Oh et al., 2003). Multitrial odor discrimination learning is dependent on both hippocampus and piriform cortex (Staubli et al., 1984). Piriform pyramidal neurons from rats with extensive discrimination training showed reduced AHPs compared to briefly trained rats, and both exhibited reduced AHPs compared to controls (Saar et al., 1998). Following odor discrimination rule learning, AHP reductions persisted for 4-day postacquisition in piriform pyramidal neurons (Saar et al., 1998) but for only 24 h in CA1 pyramidal neurons (Zelcer et al., 2006).

The amygdala, adjacent to hippocampus, is critically involved in acquisition of many learning tasks (McKernan and Shinnick-Gallagher, 1997; Hennevin et al., 1998). The basolateral nucleus (BLA) of the amygdala projects to hippocampal CA1 and to subiculum (Ottersen, 1982; Petrovich et al., 1996; Pikkarainen et al., 1999) and influences hippocampal

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function (McGaugh et al., 2002; McIntyre et al., 2003b). Amygdala activation can facilitate or attenuate acquisition of hippocampal-dependent tasks (Pare, 2003).

One single-trial task often used to assess learning and memory is inhibitory avoidance learning. Lesions of hippocampus or amygdala impair acquisition (Ammassari-Teule et al., 1991; Liang et al., 1982). While multitrial tasks have variable learning rates, single-trial tasks are well suited to determine the time course of plasticity mechanisms and their propagation between regions or neuronal phenotypes, and of the necessity for functional connectivity between the BLA and hippocampus for both behavioral plasticity (learning) and for learning-dependent AHP plasticity.

The study which follows addresses the following questions: (1) Is hippocampal AHP plasticity (i.e., reduction of postsynaptic intrinsic excitability) expressed after single-trial learning, in a task with both contextual and emotionally arousing components? (2) Is the plasticity expressed differentially in different hippocampal pyramidal neuron populations (i.e., dorsal vs. ventral CA1 or CA3)? (3) Are all later components of the AHP involved, or is plasticity specific only to mAHPs or to sAHPs? (4) What is the time course of the plasticity (i.e., is it consistent with reports of a relatively short memory consolidation period)? (5) If immediate pre- or posttrial temporary inactivation of the basolateral amygdala (BLA) blocks behavioral retention of the single-trial task, is AHP plasticity also dependent on inputs from the BLA, or independent of BLA inputs?

MATERIALS AND METHODS

Subjects

One hundred and sixty one experimentally naive 2- to 4-month old male Long Evans rats from commercial vendors (Harlan or Charles River) served as subjects for this study. Rats were housed in pairs on a 12 h light/dark cycle with *ad libitum* access to food and water in our animal facility for 1 week prior to study, and handled for 5 min daily for 2 successive days immediately prior to training in the IA task. All procedures were conducted in accordance with the Animal Care and Use Committee regulations of the University of Texas at Dallas and USDA guidelines. All training and testing groups were counterbalanced in the order in which they were run.

Temporary BLA Inactivation

A subgroup of 30 rats that remained behaviorally naive and of 31 rats that later underwent behavioral training were prepared as follows. Rats were anesthetized with isoflurane, and body temperature and respiration monitored and maintained at physiological levels. Rats were stereotaxically implanted with bilateral guide cannulae into the BLA under aseptic conditions, as follows. Two skull screw anchors were fixed to the skull, and cannulae (23 ga. stainless steel) were implanted (coordinates—from bregma P −3.0 mm, L 4.9 mm; from cortical surface

−7 mm) and secured in place with dental acrylic. Rats were given a single injection of tobramycin (1 mg kg^{-1}) and allowed 72 h to recover, with *ad libitum* access to food and water, then handled and trained as were all other subjects.

For temporary inactivation of the BLA, bilateral injection needles extending 0.3 mm beyond the tip of the guide cannulae were placed in the basolateral nucleus of the amygdala. In a holding cage, rats received infusions of 2% lidocaine or of 1% bupivacaine in 0.1 M phosphate buffered saline (PBS) or of the PBS vehicle alone either immediately prior to (i.e., within 5 min before) training trials or immediately posttrial (i.e., within 5 min after). All infusions were 0.35 μL per hemisphere (0.7 μL total) administered over a period of 1 min. Injection cannulae were left in place for an additional 1 min following the completion of the infusions to allow intracranial pressure to equilibrate. Injection cannulae were then withdrawn and capped.

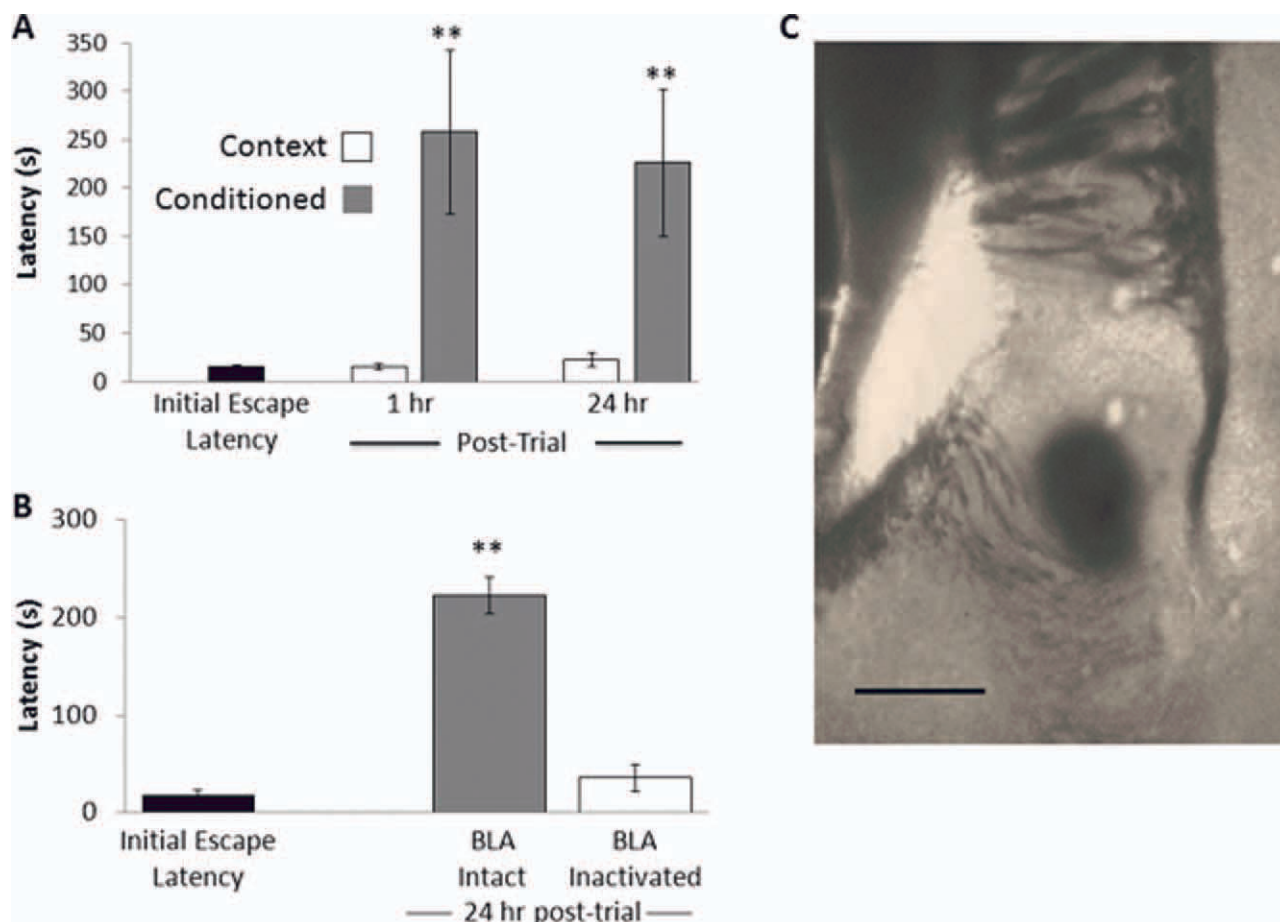## Inhibitory Avoidance Learning
Training

The apparatus used to train 61 rats consisted of a trough shaped alley 90-cm long by 15-cm high by 22-cm wide at the top by 5-cm wide at the bottom, divided into two compartments. A lamp was placed over a plastic-walled lit compartment (30-cm long) separated from a dark steel walled compartment (60-cm long) by a guillotine door. With the door open, a rat was placed in the lit compartment and its latency to escape fully into the dark compartment measured. Once the rat escaped into the dark compartment, the door was closed. After reaching the end of the compartment and turning around, the rat received a moderate foot shock (0.5 mA, 1-s duration). Moderate foot shock intensities have been shown in previous studies to produce retention latencies that can be reduced by treatments impairing amygdalar function and enhanced by treatments enhancing it (Roozendaal et al., 2009). Rats remained in the dark compartment for an additional 15 s after the shock-dark compartment pairing before removal to a transport box. Rats that underwent temporary BLA inactivation were also given behavioral retention testing 24 h following IA training.

Context-only exposure

The same apparatus used for inhibitory avoidance learning was used for contextual exposure. 41 rats were placed in the lit compartment and escape latency to the dark compartment measured. However, these rats received no foot shock in the dark compartment, instead simply remained in the compartment for 15 s after turning around.

Naive controls

Thirty naive control rats were handled for 5 min daily for 2 days prior to use. Rats in each group were then removed to a transport box.

FIGURE 1. (A) Rats exhibited significantly enhanced escape latencies 1 h and 24 h following inhibitory avoidance learning ($P < 0.0001$). Rats that received context-only exposure did not exhibit enhanced escape latencies 1 h or 24 h posttrial. (B) Control rats exhibited significantly longer escape latencies 24 h posttrial following inhibitory avoidance learning ($P < 0.0001$), while temporary BLA inactivation (immediately pre- or posttrial with the local anesthetics lidocaine or bupivacaine) reduced escape latencies at the same interval to levels similar to those observed prior to conditioning (initial escape latency). Values reported are means ± SEM; **$P < 0.0001$. (C) Representative example of a BLA local anesthetic infusion site, stained with 0.5 μL of 0.01% fast green w/v in 0.1 M PBS. Scale bar = 500 μm. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Slice Preparation

At intervals posttrial rats were anesthetized with isoflurane and rapidly decapitated. The brains were hemisected, removed, and placed in ice cold (0–1°C) oxygenated (95% O_2–5% CO_2) sucrose artificial cerebrospinal fluid (aCSF), with equimolar concentration of sucrose to replace NaCl, containing (in mM): 3.0 KCl, 1.3 $MgSO_4$, 1.24 $NaH_2PO_4 \cdot H_2O$, 24.0 $CaCl_2 \cdot 2H_2O$, 124 sucrose, 26.0 $NaHCO_3$, and 10.0 D-glucose; pH 7.4. Sections (400 μM) of hippocampus were cut using a vibratome with one hemisphere used for coronal sections (for dorsal CA1) and the other hemisphere used for horizontal sections (for all other regions). Sections were then transferred to a holding chamber containing room temperature (∼23°C) oxygenated (95% O_2–5% CO_2) normal aCSF containing (in mM): 3.0 KCl, 1.3 $MgSO_4$, 1.24 $NaH_2PO_4 \cdot H_2O$, 24.0 $CaCl_2 \cdot 2H_2O$, 124 NaCl, 26.0 $NaHCO_3$, and 10.0 D-glucose; pH 7.4. Sections were incubated in the holding chamber for at least 1 h then transferred, one at a time, to a chamber for recording where submerged slices were perfused at a rate of 1.5 mL min^{-1} with normal aCSF at 31°C ± 1°C.

Neurophysiological Recording

Recording electrodes were pulled from thick wall (O.D. 1.5 mm, I.D. 0.89 mm) borosilicate capillary tubing (Sutter Instrument). Electrodes were filled with 3 M KCl. Only electrodes with a series resistance of 30–80 MΩ were used for intracellular recording. Voltage traces from individual CA1 or CA3 pyramidal neurons identified using an IRDC microscope (Leica Microsystems) were collected at 10 KHz using an Axoclamp 2-B amplifier (Axon Instruments) and National Instruments interface and software for analysis. A series of 400 ms current pulses ranging from −1.0 nA to 0.2 nA were injected into the cell and the subsequent voltage responses were recorded. Sag was calculated as the difference between the maximum negative membrane poten-
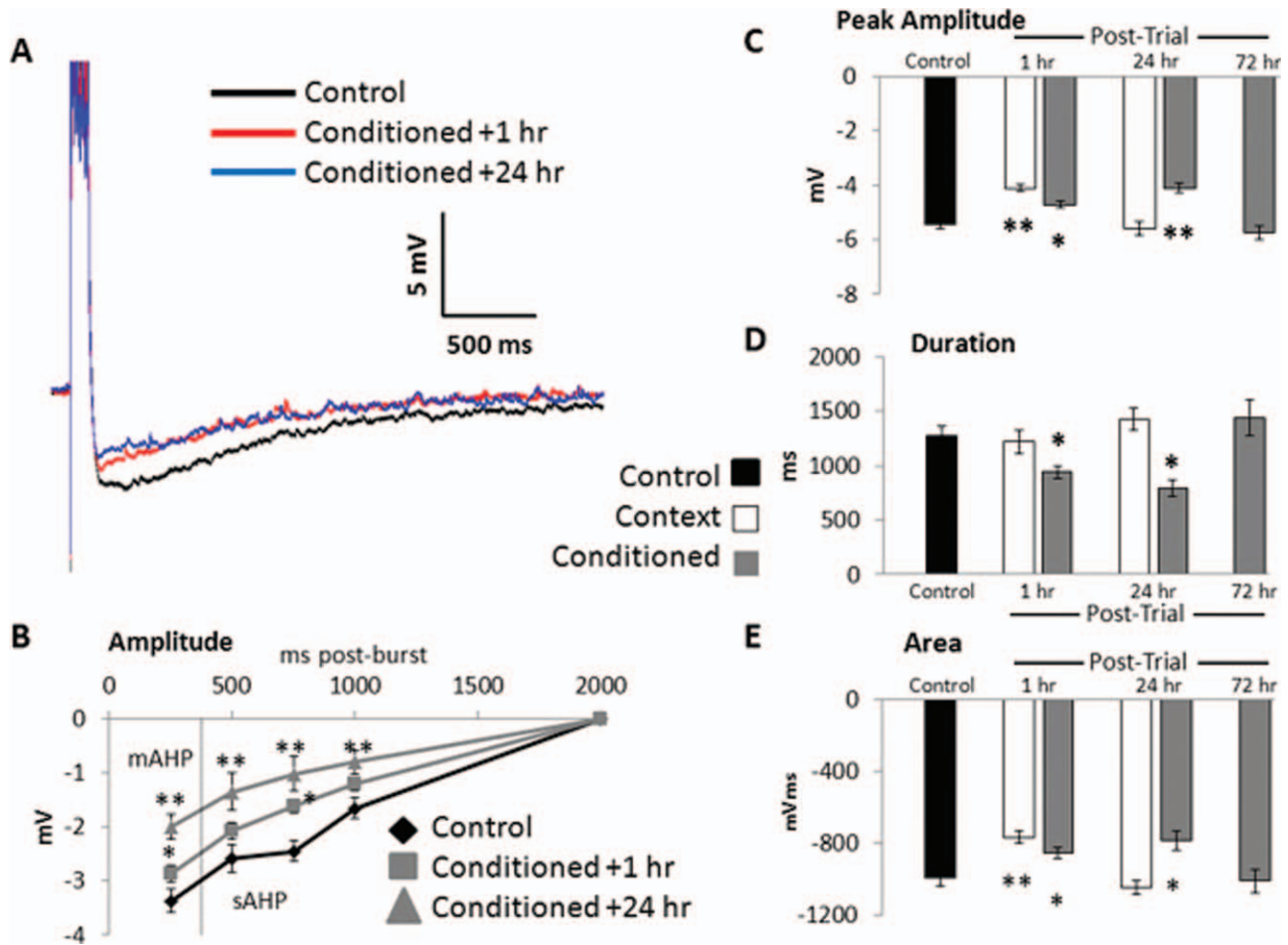
FIGURE 2.   Ventral CA1 pyramidal neurons showed learning-dependent AHP plasticity following inhibitory avoidance learning. (A) Postburst afterhyperpolarizations were significantly reduced 1 h following training, and further reduced 24 h posttraining, with significant reductions in both (B) fast (mAHP), (1 h $P <$ 0.05, 24 h $P <$ 0.01) and more persistent slow (sAHP) (24 h $P <$ 0.01) components. Significant reductions in AHP (C) peak amplitude (1 h $P <$ 0.05, 24 h $P <$ 0.01), (D) duration (1 h $P <$ 0.05, 24 h $P <$ 0.05), and (E) integrated area (1 h $P <$ 0.05, 24 h $P <$ 0.05) were observed both 1 h and 24 h posttrial but extinguished by 72 h posttrial. Context-only exposure to the IA apparatus reduced AHPs 1 h postexposure (C&E $P <$ 0.01) but this plasticity was extinguished by 24 h posttrial. Values reported are means ± SEM; *$P <$ 0.05, **$P <$ 0.01.

tial during the first 100 ms of the stimulus pulse and the average membrane potential during the last 75 ms of -1.0 nA stimulus pulses. Input resistance was calculated as the slope of the linear regression line produced from the current–voltage curve for -0.6 nA to -0.05 nA stimulus pulses. A 100 ms positive current pulse, sufficient to elicit four action potentials during the current pulse, was used to evoke postburst AHPs. The peak AHP was calculated as the difference between the resting membrane and the peak negative membrane potential after the termination of the stimulus pulse. AHP durations were calculated as the time required for AHPs to return to the resting membrane potential for at least 10 ms after the termination of stimulus pulses. AHP amplitude was also assessed at specific intervals following the stimulus pulse (250, 500, 750, 1,000, and 2,000 ms) to assess both medium (mAHP) and slow (sAHP) components of the AHP (Matthews et al., 2009). Accommodation measures were calculated as the number of spikes elicited during 800 ms

stimulus pulses of the same amplitude used to evoke AHPs. Resting membrane potential was calculated as the difference in potential before and after withdrawal of the recording electrode from the cell. Rigorous inclusion criterion were applied uniformly, so that all neurons with a resting membrane potential of -68 ± 3 mV, action potential amplitude ≥ 80 mV, and input resistance ≥ 30 MΩ were included for analysis.

Data Analysis

All data were analyzed with the experimenter blind to the experimental conditions. Raw data collected using LabView (National Instruments) were processed using Igor (Wavemetrics), with all raw data run in a batch analysis so all traces were treated in an identical manner. Statistical analyses were run using StatView (SAS Institute). Comparisons between different conditions were made using ANOVA and Scheffe's posttests.
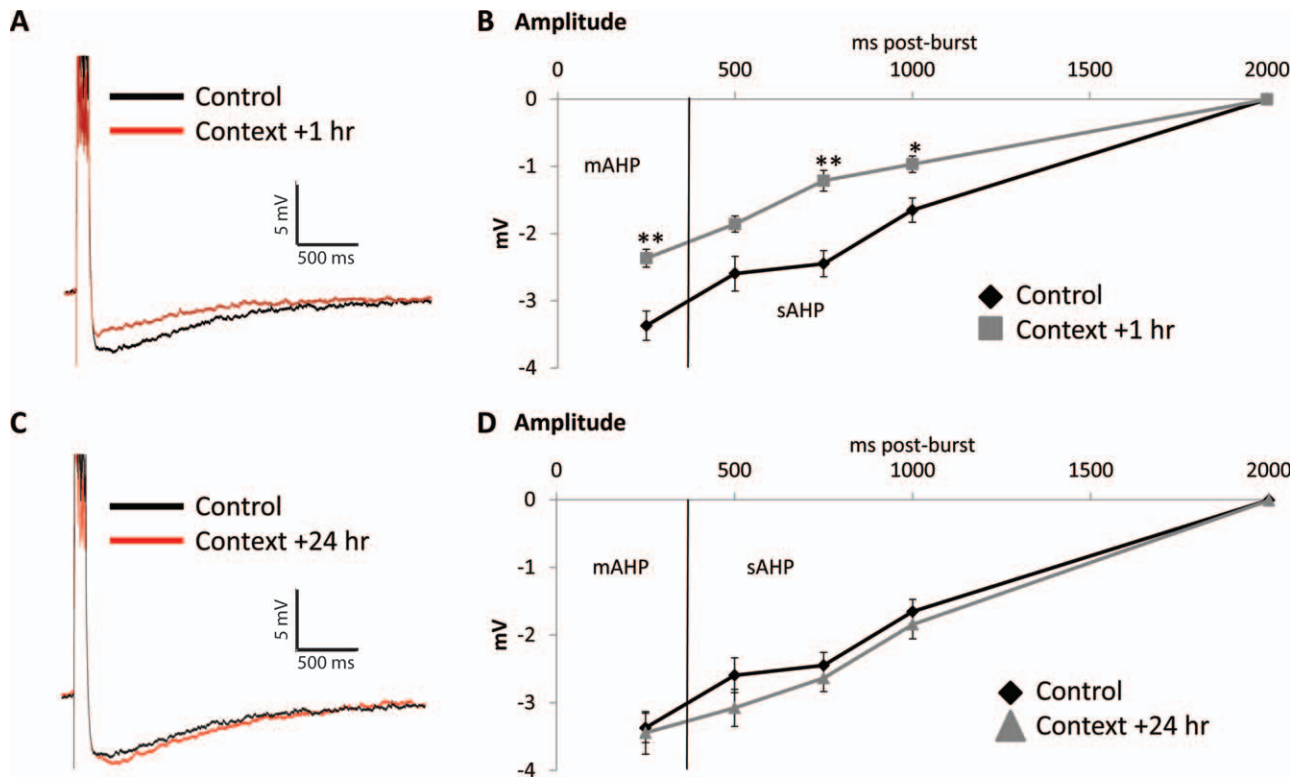
FIGURE 3. Ventral CA1 pyramidal neurons showed learning-dependent AHP plasticity following contextual exposure to the IA apparatus. (A) Postburst afterhyperpolarizations were significantly reduced 1 h following context-only exposure to the IA apparatus. (B) Both mAHP (250 ms postburst, $P < 0.01$) and sAHP (750 ms, $P < 0.01$ and 1,000 ms postburst, $P < 0.05$) components of the postburst afterhyperpolarization were significantly reduced 1 h following context-only exposure. (C) Postburst afterhyperpolarizations were indistinguishable from controls when tested 24 h after context-only exposure to the IA apparatus. (D) Both mAHP and sAHP plasticity were extinguished when tested 24 h post context-only exposure. Values reported are means ± SEM; *$P < 0.05$, **$P < 0.01$.

RESULTS

Behavioral Measures

Rats initially exposed to the lit compartment of the IA apparatus took an average of 12.9 ± 1.5 s to escape to the dark compartment, with no significant difference in escape latencies between rats that underwent inhibitory avoidance training (i.e., received a foot shock in the dark compartment) and those that were not ($P = 0.37$). All conditioned rats reacted to this moderate intensity foot shock by jumping and/or squeaking (Vazdarjanova and McGaugh, 1999; Schenberg et al., 2005). Context-only exposed rats did not show any fear-related responses while in the apparatus (i.e., no freezing, defecating/urinating, vocalizations, etc.). A separate group of rats ($n = 6$) tested with this moderate intensity shock prolonged escape latency (see Fig. 1A) when retested 1 h or 24 h later, while those exposed to the context-only ($n = 8$) without foot shock pairing did not (ANOVA, $F(4, 130) = 70.5$, $P < 0.0001$). Rats that received pretraining infusions of lidocaine ($n = 10$) or posttraining infusions of bupivacaine ($n = 10$) exhibited statistically similar retention latencies when retested 24 h later and where condensed into one group (BLA inactivated). Temporary pre- or posttrial BLA inactivation blocked the enhancement of escape latency observed in rats with intact BLA 24 h following training (see Fig. 1B).

Ventral CA1 Plasticity

Intracellular current clamp recordings from 116 pyramidal neurons in the ventral CA1 were used to assess plasticity after inhibitory avoidance learning. CA1v pyramidal neurons exhibited postburst AHPs similar to those reported in earlier studies (Gustafsson and Wigstrom, 1981; Dutar and Nicoll, 1989; Moyer et al., 1996). As seen in Figure 2A, AHPs from trained animals were reduced 1 h and 24 h posttraining compared to naive controls. An analysis of AHP amplitude at various postburst intervals (250, 500, 750, 1,000, and 2,000 ms) revealed reductions in both fast (mAHP; measured at 250 ms postburst) and slow (sAHP; measured from 500 to 1,000 ms postburst) components (see Fig. 2B). mAHP would effect peak AHP amplitude while sAHP would effect duration and either could affect integrated area of the AHP. As predicted from this analysis, conditioned rats exhibited reductions in peak AHP amplitude (see Fig. 2C), duration (see Fig. 2D), and area (see Fig. 2E) 1 h and 24 h posttrain-
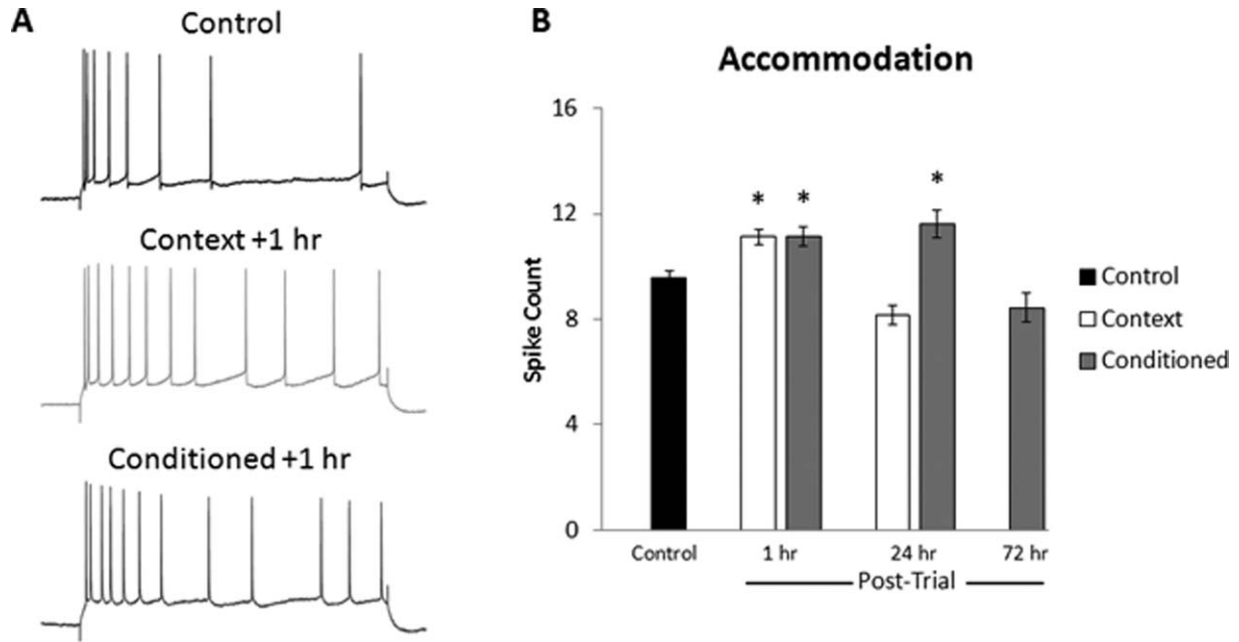
FIGURE 4. Training in the IA task transiently also reduced spike-frequency accommodation in ventral CA1 pyramidal neurons. (A) Ventral CA1 pyramidal neurons fired more action potentials in response to a prolonged depolarizing pulse following training. (B) Transient reductions in accommodation were apparent 1 h ($P < 0.05$) and 24 h ($P < 0.05$) posttrial but extinguished by 72 h following training. Similar to the AHP plasticity seen in Figure 1, context-only exposure reduced accommodation 1 h postexposure ($P < 0.05$), an effect that was extinguished by 24 h posttrial. Values reported are means $\pm$ SEM; *$P < 0.05$.

TABLE 1.

Membrane Properties of Ventral CA1, Dorsal CA1, and CA3 Pyramidal Neurons From Controls and After Contextual Fear Conditioning or Context-Only Exposure to the IA Apparatus

	Rats (n)	Cells (n)	Input resistance (MΩ)	Sag (mV)	Resting potential (mV)	Spike width (mV)	AP amplitude (mV)
CA1v							
Control	19	29	35.5 ± 1.9	6.2 ± 0.4	−66.8 ± 0.9	1.3 ± 0.02	86.0 ± 1.2
Context 1 h	18	25	37.5 ± 2.1	5.6 ± 0.5	−66.9 ± 1.3	1.3 ± 0.02	85.2 ± 0.8
Context 24 h	4	11	31.6 ± 2.3	6.4 ± 0.7	−66.9 ± 1.3	1.4 ± 0.01	88.1 ± 0.6
Trained 1 h	22	32	41.0 ± 1.9	6.2 ± 0.4	−65.4 ± 0.9	1.3 ± 0.02	84.5 ± 0.8
Trained 24 h	5	14	41.8 ± 1.6	5.7 ± 0.6	−66.7 ± 1.2	1.4 ± 0.02	84.4 ± .08
Trained > 72 h	2	5	44.3 ± 3.4	5.7 ± 1.2	−65.6 ± 3.5	1.3 ± 0.06	84.8 ± 1.4
CA1d							
Control	8	12	40.9 ± 1.5	8.3 ± 0.5	−65.6 ± 1.6	1.2 ± 0.02	83.0 ± 2.5
Context 1 h	8	19	35.3 ± 1.9	7.3 ± 0.4	−67.0 ± 0.6	1.2 ± 0.02	83.6 ± 0.7
Context 24 h	4	9	41.8 ± 2.4	9.0 ± 0.6	−68.5 ± 1.3	1.2 ± 0.01	88.0 ± 1.0
Trained 1 h	9	15	37.5 ± 2.2	8.3 ± 0.6	−65.9 ± 1.2	1.3 ± 0.02	86.0 ± 1.0
Trained 24 h	6	14	36.7 ± 2.8	9.4 ± 0.7	−66.7 ± 1.0	1.3 ± 0.01	88.2 ± 0.8
Trained > 72 h	3	6	41.2 ± 3.1	9.8 ± 0.8	−65.5 ± 2.6	1.3 ± 0.02	87.3 ± 1.0
CA3							
Control	15	21	46.6 ± 2.5	4.9 ± 0.5	−67.0 ± 0.8	1.2 ± 0.02	81.7 ± 1.1
Context 1 h	18	20	47.5 ± 2.9	3.4 ± 0.5	−68.8 ± 1.1	1.2 ± 0.02	85.8 ± 0.5
Context 24 h	7	9	66.0 ± 5.8	2.5 ± 1.2	−67.1 ± 1.8	1.3 ± 0.03	87.7 ± 0.8
Trained 1 h	17	24	53.5 ± 2.4	4.4 ± 0.5	−68.1 ± 1.4	1.1 ± 0.03	82.2 ± 1.6
Trained 24 h	12	19	43.9 ± 4.3	5.7 ± 0.9	−68.5 ± 1.3	1.3 ± 0.01	85.1 ± 0.9

No differences in membrane properties of ventral CA1, dorsal CA1, and CA3 pyramidal neurons were observed between controls and after inhibitory avoidance learning or context-only exposure to the IA apparatus. Input resistance, sag, resting potential, spike width, and action potential amplitude values represent means ± SEM.
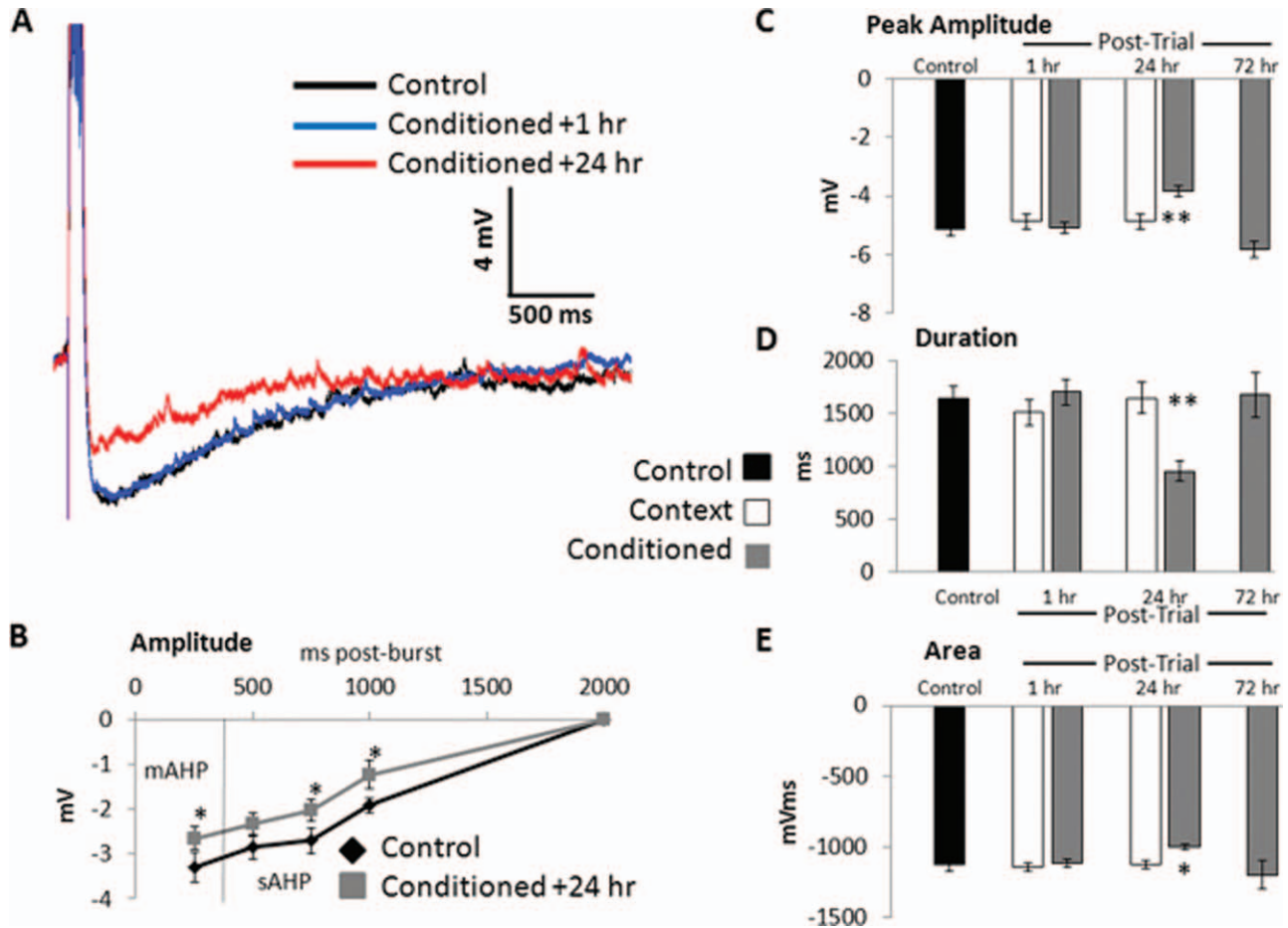
FIGURE 5. Dorsal CA1 pyramidal neurons exhibited transient learning-dependent AHP plasticity that developed more slowly but extinguished at the same rate seen in ventral CA1 following inhibitory avoidance learning, i.e., AHP reductions were not observed 1 h posttrial but were significant 24 h posttrial and extinguished by 72 h posttrial. (A) Postburst afterhyperpolarizations were significantly reduced 24 h following training with significant reductions in both (B) mAHP ($P < 0.05$) and sAHP ($P < 0.05$) components. Significant reductions in AHP (C) peak amplitude ($P < 0.01$), (D) duration ($P < 0.01$), and (E) integrated area ($P < 0.05$) were observed 24 h posttrial but extinguished by 72 h posttrial. Unlike in ventral CA1, context-only exposure to the IA apparatus did not result AHP reductions in dorsal CA1 neurons at any interval tested. Values reported are means ± SEM; *$P < 0.05$, **$P < 0.01$.

ing. This learning-dependent AHP plasticity was transient and extinguished by 72 h posttraining. Context-only exposure also reduced fast and slow components of AHPs at 1 h (see Figs. 3A,B) compared to controls. This contextual effect had extinguished by 24 h later (see Figs. 3C,D).

Analyses of variance indicated a significant effect of training on the AHP amplitude of CA1v pyramidal neurons at 250 ms ($F(5,115) = 12.7$, $P < 0.0001$), 500 ms ($F(5,115) = 11.2$, $P < 0.0001$), 750 ms ($F(5,115) = 10.2$, $P < 0.0001$), and 1,000 ms ($F(5,115) = 7.7$, $P < 0.0001$) postburst. Similarly, significant learning-dependent reductions in peak AHP amplitude were observed 1 h and 24 h posttrial but for only 1 h following context-only exposure ($F(5,115) = 13.37$, $P < 0.0001$). Significant reductions in AHP duration were also observed 1 h and 24 h posttrial ($F(5,115) = 5.37$, $P < 0.0001$). Significant reductions in AHP area were also observed 1 h and 24 h posttrial but for only 1 h following context-only exposure ($F(5,115) = 5.22$, $P < 0.001$).

Figure 4 shows another learning-dependent increase in excitability, a reduction in accommodation. Neurons from trained and context-only exposed animals fired more action potentials in response to a sustained depolarizing pulse (see Fig. 4A), but with different time courses for extinction of this plasticity. Conditioned and context-only exposed rats exhibited reductions in accommodation (see Fig. 4B) compared to controls. Significant reductions in accommodation were observed 1 h and 24 h posttrial but for only 1 h following context-only exposure ($F(5,115) = 9.11$, $P < 0.0001$). Inhibitory avoidance learning did not alter other membrane properties measured (see Table 1).

Because learning-dependent plasticity was observed in CA1v pyramidal neurons with a transient time course that persisted for only 24 h posttrial in this single-trial aversive learning task, the next experiment investigated similarities and differences in AHP plasticity in dorsal CA1 pyramidal neurons from control, conditioned, or context-only exposed rats.
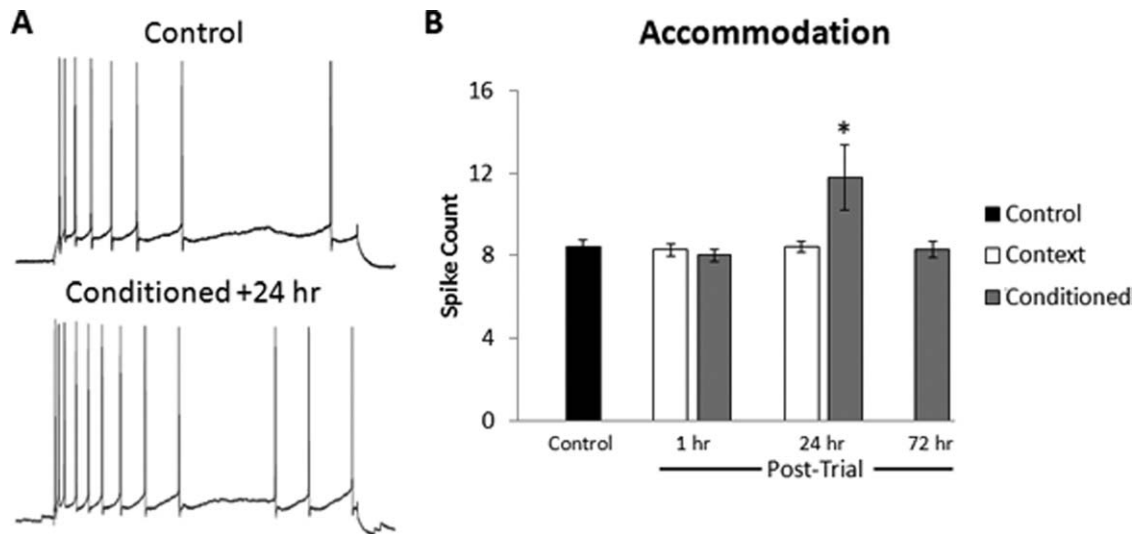
FIGURE 6. Training in the IA task transiently reduced spike-frequency accommodation in dorsal CA1 pyramidal neurons, an effect that again developed more slowly but extinguished at the same rate as in ventral CA1. (A) Dorsal CA1 pyramidal neurons fired more action potentials in response to a prolonged depolarizing pulse 24 h following training. (B) Transient reductions in accommodation were observed 24 h ($P < 0.05$) posttrial but extinguished by 72 h following training. Also different from ventral CA1, context-only exposure to the IA apparatus did not reduce accommodation in dorsal CA1 neurons at any interval tested. Values reported are means ± SEM; *$P < 0.05$.

Dorsal CA1 Plasticity

Intracellular current clamp recordings from 75 pyramidal neurons in the dorsal CA1 (CA1d) were used to assess plasticity after inhibitory avoidance learning. CA1d pyramidal neurons exhibited postburst AHPs similar to those reported in earlier studies (Oh et al., 2003). However, while AHPs from conditioned animals were reduced in CA1d neurons 24 h posttrial compared to naive controls (Fig. 5A), this effect was not seen 1 h posttrial unlike in CA1v neurons. An analysis of AHP amplitudes at various postburst intervals (from 250 to 1,000 ms) 24 h posttrial revealed reductions in both mAHP and sAHP components in neurons from conditioned rats compared to controls (see Fig. 5B). Conditioned rats exhibited reductions in peak AHP amplitude (see Fig. 5C), duration (see Fig. 5D), and area (see Fig. 5E) 24 h posttrial but not 1 h posttrial in neurons from conditioned rats. Figures 5C–E also shows that neurons from context-only exposed rats exhibited no AHP plasticity. The learning-dependent AHP plasticity in CA1d was transient, beginning later than in CA1v, but similarly extinguished by 72 h following conditioning.

Analyses of variance showed a significant effect of conditioning on fast and slow components of the AHP in CA1d pyramidal neurons at 250 ms ($F(5,74) = 6.5$, $P < 0.0001$), 500 ms ($F(5,74) = 9.4$, $P < 0.01$), 750 ms ($F(5,74) = 11.6$, $P < 0.0001$), and 1,000 ms ($F(5,74) = 5.9$, $P < 0.0001$) postburst when assessed 24 h posttrial. Similarly, significant reductions were observed 24 h posttrial, in conditioned but not context-only exposed rats in peak AHP amplitude ($F(5,74) = 5.60$, $P < 0.0001$), in AHP duration ($F(5,74) = 4.72$, $P < 0.001$), and in AHP area ($F(5,74) = 1.81$, $P < 0.01$).

Figure 6 shows learning-dependent plasticity in accommodation was observed in conditioned but not in context-only exposed rats. Significant reductions in accommodation were observed 24 h posttrial, in conditioned but not context-only exposed rats ($F(5,74) = 4.31$, $P < 0.001$). Inhibitory avoidance learning did not alter other membrane properties measured (see Table 1).

Because learning-dependent AHP and accommodation plasticity was observed in ventral and dorsal CA1 pyramidal neurons, the next experiment investigated similarities and differences in learning-dependent plasticity in CA3 pyramidal neurons.

CA3 Plasticity

Intracellular current clamp recordings from 93 pyramidal neurons in ventral CA3 were used to assess plasticity after inhibitory avoidance learning. CA3 pyramidal neurons exhibited postburst AHPs similar to those reported in earlier studies (Schwartzkroin and Stafstrom, 1980; Aicardi and Schwartzkroin, 1990; Thompson et al., 1996). Similar to CA1d pyramidal neurons (Fig. 7A), AHPs in CA3 neurons from conditioned rats were reduced 24 h posttrial compared to naive controls. An analysis of AHP amplitude at various postburst intervals (250, 500, 750, 1,000, 2,000, 3,000, and 4,000 ms) revealed reductions in sAHP (from 500 to 1,000 ms postburst) but not in mAHP components (see Fig. 7B). This analysis revealed learning-dependent AHP plasticity, while more traditional analyses of peak AHP amplitude (Fig. 7C), duration (Fig. 7D), and area (Fig. 7E) did not. None of the analyses showed any AHP plasticity related to context-only exposure.

Analyses of variance indicated a significant effect of conditioning but not context-only exposure on the AHP amplitude
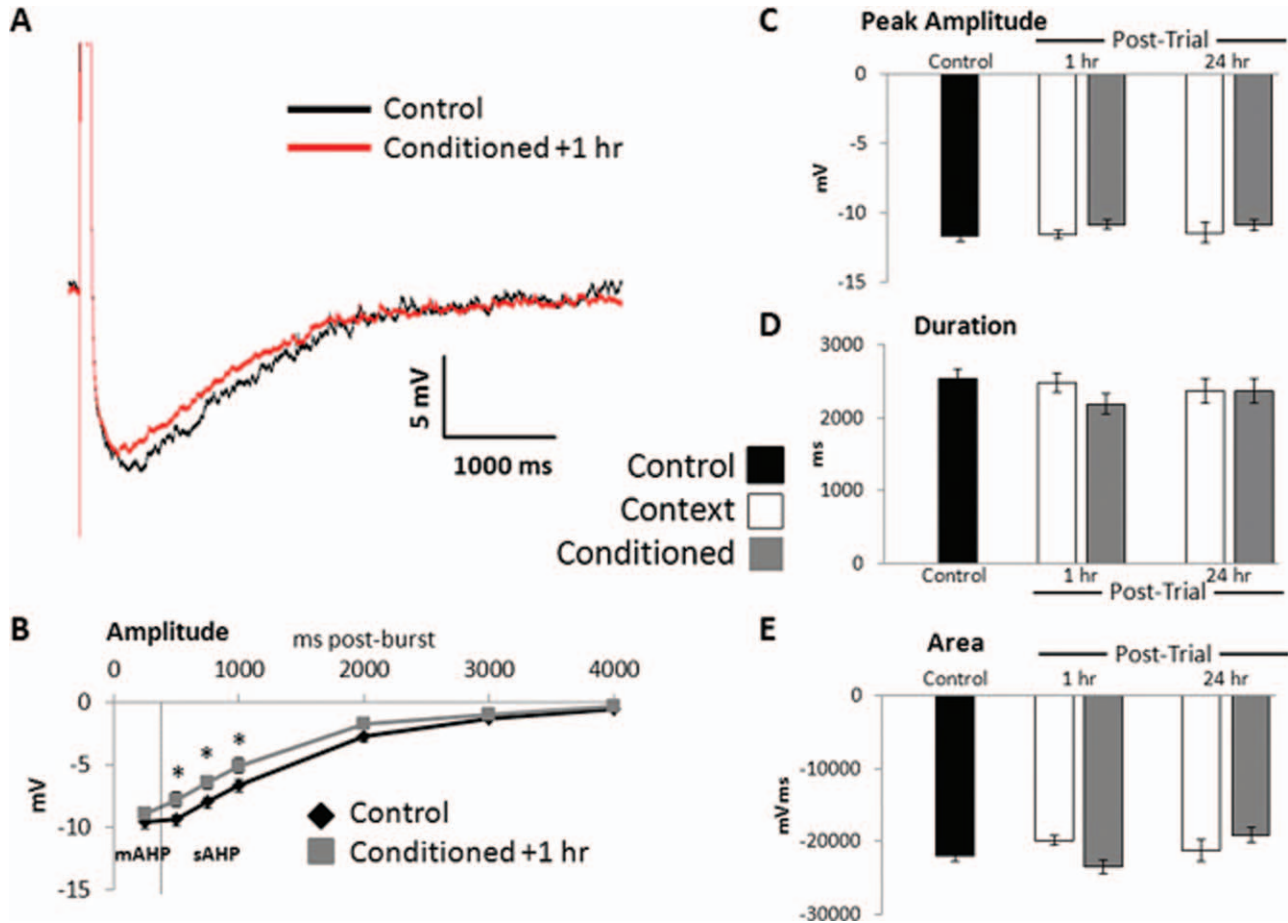
FIGURE 7. AHP plasticity in CA3 pyramidal neurons was different from that seen in CA1, i.e., peak AHP amplitudes were unaffected, so reductions were restricted to the sAHP. (A) While CA3 pyramidal neurons exhibited reductions concentrated in the late (sAHP) components of the postburst afterhyperpolarization, these effects developed sooner after training than the AHP reductions seen in CA1 pyramidal neurons. Reductions were observed 1 h posttrial (B) with significant reductions only in the sAHP ($P < 0.05$); these effects extinguished within 24 h posttrial. No reductions in AHP (C) peak amplitude, (D) duration or (E) integrated area were observed following IA training or context-only exposure. Values reported are means ± SEM; *$P < 0.05$.

of CA3 pyramidal neurons at 500 ms ($F(4,92) = 6.2$, $P < 0.05$), 750 ms ($F(4,92) = 8.9$, $P < 0.01$), and 1,000 ms ($F(4,92) = 5.8$, $P < 0.05$) postburst when assessed 24 h posttrial. However, no significant reductions were observed posttrial in conditioned or context-only exposed rats in measures of peak AHP amplitude ($F(4,92) = 1.23$, $P = 0.3$), AHP duration ($F(4,92) = 0.92$, $P = 0.45$), or AHP area ($F(4,92) = 0.10$, $P = 0.98$).

Figure 8 shows that no learning-dependent plasticity in accommodation was observed posttrial in CA3 neurons from conditioned or context-only exposed rats ($F(4,92) = 0.43$, $P = 0.78$). Inhibitory avoidance learning also did not alter other membrane properties measured in CA3 pyramidal neurons (see Table 1).

Because learning-dependent AHP plasticity was observed in ventral and dorsal CA1 pyramidal neurons in this single-trial aversive learning task, the next experiments investigated the necessity of BLA inputs for learning-dependent plasticity in both dorsal and ventral CA1 pyramidal neurons.

BLA Inactivation

Block of ventral CA1 plasticity

Intracellular current clamp recordings from 135 pyramidal neurons in ventral CA1 were used to assess effects of BLA inactivation on hippocampal plasticity after inhibitory avoidance learning.

While the literature suggests that immediate posttrial BLA treatments would be most disruptive of consolidation (Vazdarjanova and McGaugh, 1999; Miranda et al., 2003; Hui et al., 2004), both immediate pretrial and immediate posttrial BLA inactivation produced the same behavioral and neurophysiological effects in the current study. Rats without cannula implants (intact) and vehicle-treated rats both exhibited AHP and
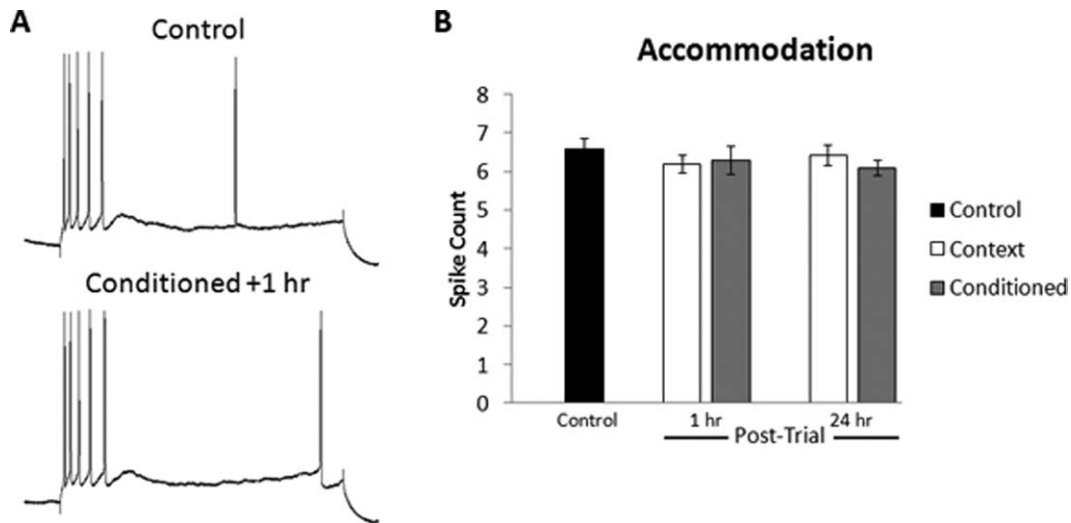
FIGURE 8. Training in the IA task or context-only exposure did not reduce spike-frequency accommodation in CA3 pyramidal neurons. (A) CA3 pyramidal neurons fired similar numbers of action potentials as controls following IA training in response to a prolonged depolarizing pulse. (B) No reductions in accommodation were observed 1 h or 24 h following IA training or after context-only exposure. Values reported are means ± SEM.

accommodation measures when assessed 1 h and 24 h posttrial that were statistically identical between groups and comparable to that reported above in Figures 2–4. Because intact and vehicle-treated groups exhibited no significant differences between groups (using unpaired t tests) in peak AHP amplitude (1 h, $P = 0.9$; 24 h, $P = 0.9$), duration (1 h, $P = 0.9$; 24 h, $P = 0.9$), area (1 h, $P = 0.3$; 24 h, $P = 0.9$), or accommodation (1 h, $P = 0.2$; 24 h, $P = 0.9$) data from these groups were condensed for graphic purposes (Figs. 9 and 10) and are referred to as BLA intact. In a similar manner, rats that received immediate pretrial lidocaine or immediate posttrial bupivacaine infusions into the BLA had AHP and accommodation measures when assessed 1 h and 24 h posttrial that were statistically identical between these treatment groups. Because pre- and posttrial BLA inactivation exhibited no significant differences (using unpaired t tests) between groups in measures of peak AHP amplitude (1 h, $P = 0.7$; 24 h, $P = 0.7$), duration (1 h, $P = 0.9$; 24 h, $P = 0.8$), area (1 h, $P = 0.9$; 24 h, $P = 0.3$), or accommodation (1 h, $P = 0.9$; 24 h, $P = 0.9$) data from these groups were also condensed for graphic purposes and are referred to as BLA inactivated.

Learning-dependent AHP plasticity occurred only in CA1v neurons from BLA-intact (Fig. 9A) but not BLA-inactivated rats (Fig. 9C). An analysis of AHP amplitude at various postburst intervals (from 250 to 1,000 ms) revealed reductions in both mAHP and sAHP components in neurons from the BLA-intact (Fig. 9B) but not the BLA-inactivated rats (Fig. 9D). Analyses of variance indicated a significant effect of BLA inactivation on the AHP amplitude of CA1v pyramidal neurons at 250 ms ($F(4,125) = 13.0$, $P < 0.0001$), 500 ms ($F(4,125) = 10.5$, $P < 0.0001$), 750 ms ($F(4,125) = 11.4$, $P < 0.0001$), and 1,000 ms ($F(4,125) = 8.3$, $P < 0.0001$) postburst in BLA-intact but not BLA-inactivated rats.

Similarly, increases in excitability were seen in CA1v neurons from BLA-intact but not BLA-inactivated rats, with plasticity in peak AHP amplitude, duration, area, and in accommodation 1 h and 24 h posttraining (Figs. 10A–D). Significant reductions were observed 1 h and 24 h posttrial in BLA-intact but not BLA-inactivated rats in peak AHP amplitude ($F(4,125) = 18.6$, $P < 0.0001$), duration ($F(4,125) = 15.5$, $P < 0.0001$), area ($F(4,125) = 6.9$, $P < 0.0001$), and in accommodation ($F(4,125) = 12.9$, $P < 0.0001$). Inhibitory avoidance learning did not alter other membrane properties measured in BLA-intact or BLA-inactivated ventral CA1 pyramidal neurons (see Table 2).

BLA inactivation also blocked the context-dependent transient AHP plasticity seen in ventral CA1 neurons 1 h following exposure to the IA apparatus. An analysis of AHP amplitudes at various postburst intervals (from 250 to 1,000 ms) revealed transient reductions in both mAHP and sAHP components in neurons from BLA-intact but not from BLA-inactivated rats that underwent context-only exposure to the IA apparatus (Figs. 9E,F). Significant differences in AHP amplitude were detected at 250 ms ($F(2,62) = 23.9$, $P < 0.0001$), 500 ms ($F(2,62) = 14.2$, $P < 0.0001$), 750 ms ($F(2,62) = 25.0$, $P < 0.0001$), and 1,000 ms ($F(2,62) = 20.5$, $P < 0.0001$) postburst. BLA-inactivated rats exhibited AHP and accommodation measures indistinguishable from controls (peak AHP amplitude, -5.5 ± 0.3 mV; duration, $1,443 \pm 158$ ms; area, $-1,008 \pm 44$ mVms; and accommodation, 9.8 ± 0.5 spikes). AHPs were significantly reduced 1 h following context-exposure in BLA-intact but not BLA-inactivated rats, with effects on peak AHP amplitude ($F(2,62) = 13.3$, $P < 0.0001$), area ($F(2,62) = 11.9$, $P < 0.0001$), and accommodation ($F(2,62) = 15.9$, $P < 0.0001$), but not duration ($F(2,62) = 2.1$, $P = 0.12$) when compared to naive controls. Context-only exposure did not
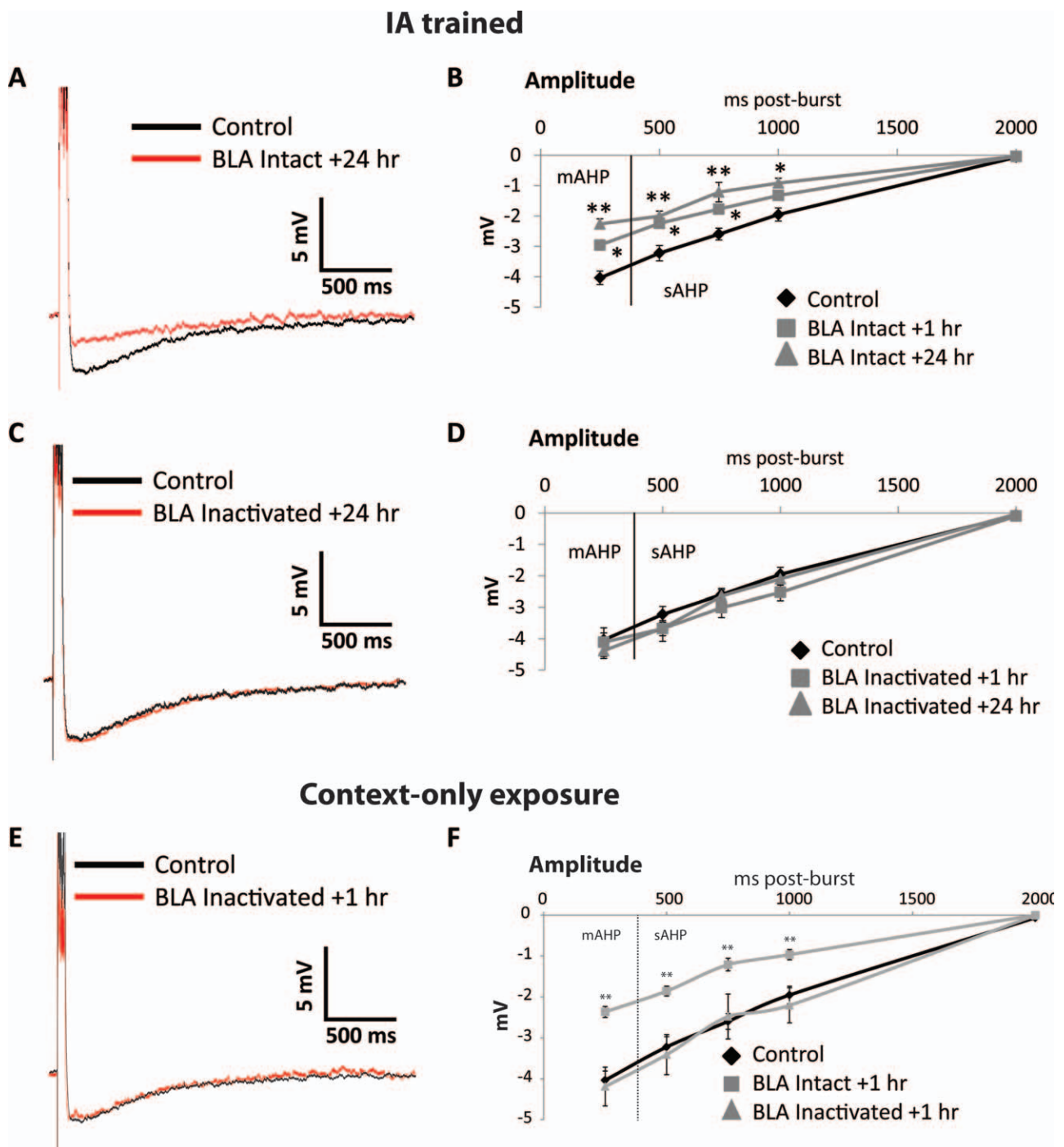
FIGURE 9. Ventral CA1 pyramidal neurons showed learning-dependent AHP plasticity in (A) BLA-intact but not (C) BLA-inactivated rats following inhibitory avoidance learning. (E) BLA inactivation also blocked the context-dependent AHP plasticity seen 1 h postcontext-only exposure that is shown in Figure 3A. Learning-dependent reductions in mAHP and sAHP components of the postburst afterhyperpolarization of ventral CA1 pyramidal neurons were blocked by temporary BLA inactivation following inhibitory avoidance learning. (B) BLA-intact rats exhibited significant learning-dependent reductions in both mAHP (1 h $P < 0.05$, 24 h $P < 0.01$) and sAHP (1 h $P < 0.05$, 24 h $P < 0.01$) components of the postburst afterhyperpolarization. (D) Temporary BLA inactivation blocked the learning-dependent reductions in the mAHP and sAHP both 1 h and 24 h following IA training. (E) Temporary BLA inactivation blocked the context-dependent reductions in the mAHP and sAHP 1 h following exposure to the IA apparatus. Values reported are means ± SEM; $^*P < 0.05$, $^{**}P < 0.01$.
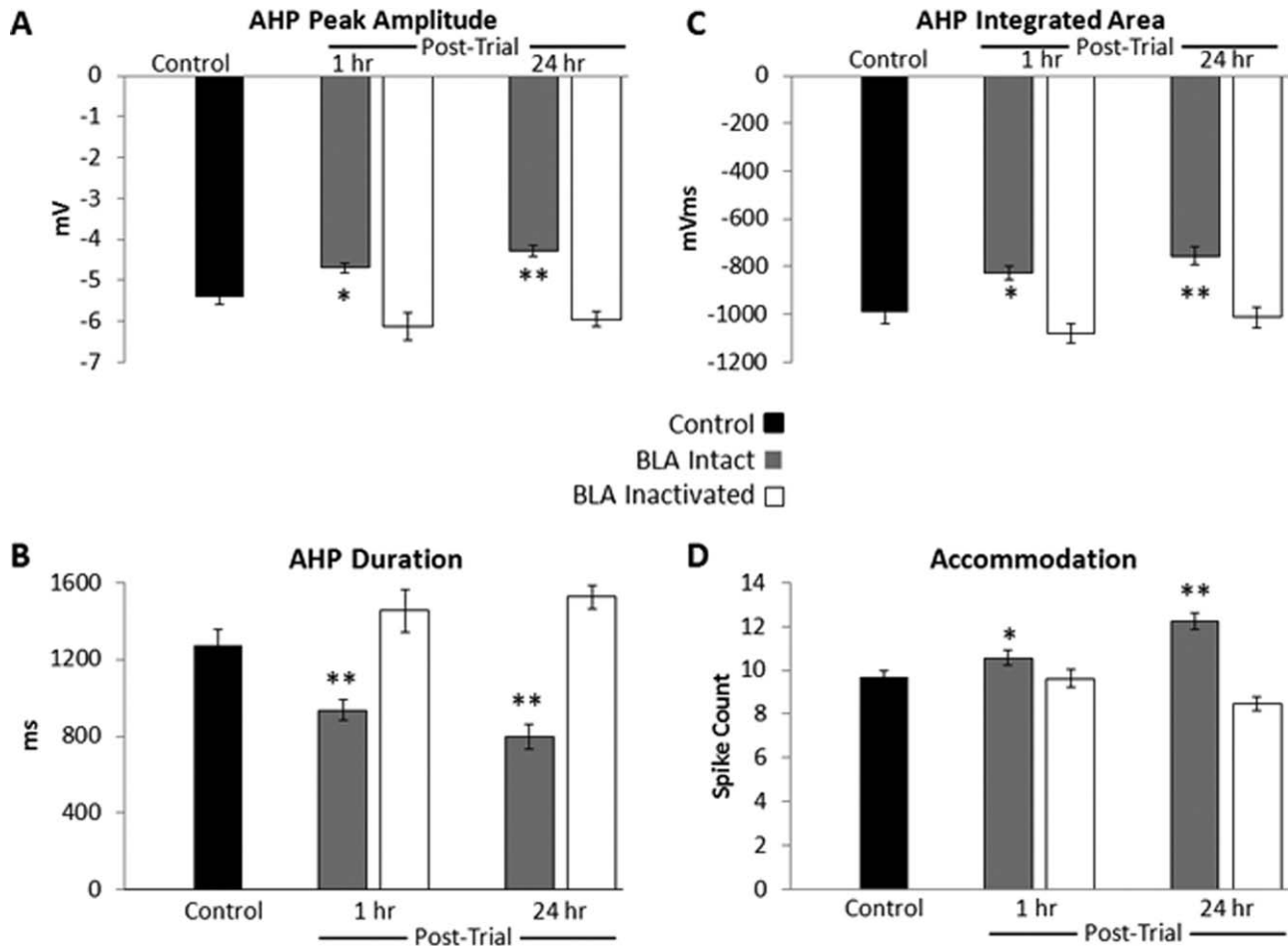
FIGURE 10. Learning-dependent changes in ventral CA1 pyramidal neuron excitability observed following inhibitory avoidance learning was blocked by temporary BLA inactivation with the local anesthetics lidocaine or bupivacaine. BLA inactivation blocked the reductions in AHP (A) peak amplitude, (B) duration, (C) integrated area and (D) accommodation observed in BLA intact treated rats both 1 h and 24 h following IA training. Values reported are means ± SEM; *$P < 0.05$, **$P < 0.01$.

alter other membrane properties measured in BLA-inactivated ventral CA1 pyramidal neurons (see Table 2).

Block of dorsal CA1 plasticity

Intracellular current clamp recordings from 107 pyramidal neurons in dorsal CA1 were used to assess effects of BLA inactivation on hippocampal plasticity after inhibitory avoidance learning.

Dorsal CA1 neurons from intact and vehicle-treated rats had AHP and accommodation measures when assessed 1 h and 24 h posttrial that were statistically identical between these groups and comparable to that reported above in Figures 5 and 6. Because intact and vehicle-treated groups exhibited no significant differences between groups (using unpaired t tests) in peak AHP amplitude (1 h, $P = 0.8$; 24 h, $P = 0.9$), duration (1 h, $P = 0.9$; 24 h, $P = 0.9$), area (1 h, $P = 0.9$; 24 h, $P = 0.9$), or in accommodation (1 h, $P = 0.5$; 24 h, $P = 0.1$) data from these groups were condensed for graphical purposes (Figs. 11 and 12) and are referred to as BLA intact. Similar to observations in CA1v, CA1d neurons from rats that received lido-

caine or bupivacaine infusions into the BLA also had AHP and accommodation measures when assessed 1 h and 24 h posttrial that were statistically identical between these treatment groups. Because pre- and posttrial BLA inactivation exhibited no significant differences (using unpaired t tests) between groups in measures of peak AHP amplitude (1 h, $P = 0.4$; 24 h, $P = 0.4$), duration (1 h, $P = 0.9$; 24 h, $P = 0.9$), area (1 h, $P = 0.9$; 24 h, $P = 0.9$), or accommodation (1 h, $P = 0.6$; 24 h, $P = 0.5$) data from these groups were condensed and are referred to as BLA inactivated.

Learning-dependent AHP plasticity occurred only in CA1d neurons from BLA-intact (Fig. 11A) but not BLA-inactivated rats (Fig. 11B). An analysis of AHP amplitude at various postburst intervals (from 250 to 1,000 ms) revealed reductions in both mAHP and sAHP components in neurons from the BLA-intact (Fig. 11C) but not the BLA-inactivated rats (Fig. 11D). Analyses of variance indicated a significant effect of BLA inactivation on the AHP amplitude of CA1d pyramidal neurons at 250 ms ($F_{(4,106)} = 7.6$, $P < 0.0001$), 500 ms ($F_{(4,106)} = 15.7$, $P < 0.001$), and 1,000 ms ($F_{(4, 106)} = 6.3$, $P < 0.0001$) postburst 24 h posttrial in the BLA-intact animals.

TABLE 2.

Membrane Properties of Ventral CA1 and Dorsal CA1 Pyramidal Neurons From Controls and After BLA Inactivation Following Contextual Fear Conditioning

	Rats (n)	Cells (n)	Input resistance (MΩ)	Sag (mV)	Resting potential (mV)	Spike width (mV)	AP amplitude (mV)
CA1v							
Control	19	29	35.5 ± 1.9	6.2 ± 0.4	−66.8 ± 0.9	1.3 ± 0.02	86.0 ± 1.2
Trained 1 h	22	37	41.0 ± 1.9	6.2 ± 0.4	−65.4 ± 0.9	1.3 ± 0.02	84.5 ± 0.8
Saline 1 h	2	6	53.4 ± 4.0	8.0 ± 1.4	−69.6 ± 1.2	1.4 ± 0.04	89.3 ± 0.8
Lidocaine 1 h	2	5	38.9 ± 4.7	8.5 ± 0.2	−67.2 ± 3.5	1.3 ± 0.03	86.7 ± 1.5
Bupivacaine 1 h	1	3	46.6 ± 13.4	8.2 ± 1.9	−69.6 ± 1.9	1.3 ± 0.03	88.1 ± 1.0
Context Inactivation 1 h	2	9	42.3 ± 2.6	7.9 ± 0.7	−68.1 ± 0.3	1.3 ± 0.02	87.2 ± 0.9
Trained 24 h	5	14	41.8 ± 1.6	5.7 ± 0.6	−66.7 ± 1.2	1.4 ± 0.02	84.4 ± .08
Saline 24 h	3	8	52.5 ± 2.5	9.5 ± 0.4	−67.8 ± 1.3	1.5 ± 0.05	83.5 ± 0.9
Lidocaine 24 h	4	7	41.8 ± 2.4	9.0 ± 0.6	−67.4 ± 3.5	1.2 ± 0.01	86.5 ± 0.7
Bupivacaine 24 h	7	17	40.4 ± 2.7	9.0 ± 0.4	−67.5 ± 1.3	1.3 ± 0.02	88.0 ± 0.8
CA1d							
Control	8	12	40.9 ± 1.5	8.3 ± 0.5	−65.6 ± 1.6	1.2 ± 0.02	83.0 ± 2.5
Trained 1 h	9	15	37.5 ± 2.2	8.3 ± 0.6	−65.9 ± 1.2	1.3 ± 0.02	86.0 ± 1.0
Saline 1 h	3	6	42.6 ± 0.0	8.0 ± 0.7	−67.7 ± 0.7	1.3 ± 0.03	87.3 ± 1.3
Lidocaine 1 h	2	6	36.3 ± 5.1	6.4 ± 0.7	−67.6 ± 3.1	1.3 ± 0.02	86.7 ± 1.5
Bupivacaine 1 h	1	3	42.4 ± 0.0	6.6 ± 0.6	−67.4 ± 2.9	1.3 ± 0.01	85.1 ± 1.3
Trained 24 h	6	14	36.7 ± 2.8	9.4 ± 0.7	−66.7 ± 1.0	1.3 ± 0.01	88.2 ± 0.8
Saline 24 h	5	15	42.3 ± 2.7	7.9 ± 0.7	−68.9 ± 1.0	1.3 ± 0.01	85.3 ± 0.8
Lidocaine 24 h	5	18	43.5 ± 3.8	7.1 ± 0.4	−64.2 ± 2.5	1.4 ± 0.02	88.6 ± 0.6
Bupivacaine 24 h	7	18	39.1 ± 2.9	8.2 ± 0.4	−69.2 ± 1.6	1.2 ± 0.02	87.6 ± 0.5

No differences in membrane properties of ventral CA1 and dorsal CA1 pyramidal neurons were observed between controls and after BLA inactivation following inhibitory avoidance learning. Input resistance, sag, resting potential, spike width, and action potential amplitude values represent means ± SEM.

Increases in excitability were seen in CA1d neurons from BLA-intact but not BLA-inactivated rats, with plasticity in peak AHP amplitude, duration, area, and in accommodation 24 h posttrial (Fig. 12A–D). Significant reductions were observed 24 h posttrial in BLA-intact but not BLA-inactivated rats in peak AHP amplitude ($F(4,106) = 18.2$, $P < 0.0001$), duration ($F(4,106) = 11.3$, $P < 0.0001$), area ($F(4,106) = 6.9$, $P < 0.001$), and in accommodation ($F(4,106) = 4.4$, $P < 0.01$). Inhibitory avoidance learning did not alter other membrane properties measured in BLA-intact or BLA-inactivated dorsal CA1 pyramidal neurons (see Table 2).

DISCUSSION

Hippocampal pyramidal neurons in ventral and dorsal CA1 exhibited enhanced excitability following single-trial inhibitory avoidance learning, exhibiting learning-dependent plasticity in both AHP and accommodation measures. Reductions in both mAHP and sAHP components were accompanied by reductions in peak AHP amplitude, duration, and area. These learning-dependent reductions in AHPs were associated with another increase in excitability, i.e., a reduction in accommodation, firing more action potentials during a prolonged depolarizing

pulse than neurons from naive animals. The AHP and accommodation plasticity observed in CA1v neurons following conditioning were transient (i.e., seen 1 h and 24 h posttrial) and extinguished within 72 h posttrial. In addition to learning-specific plasticity, context-dependent plasticity was observed in CA1v neurons 1 h after a single exposure to the IA apparatus. This very transient context-dependent plasticity was unique to CA1v neurons and extinguished by 24 h posttrial. Learning-dependent plasticity observed in CA1d neurons followed a time course different from that observed in CA1v neurons. Learning-dependent increases in excitability were slower to develop in CA1d neurons (i.e., observed 24 h posttrial) than in CA1v neurons, but still extinguished 72 h posttrial as in CA1v. Learning-dependent reductions in the sAHP from CA3 pyramidal neurons were also observed 24 h posttrial and extinguished by 72 h, but this plasticity was not associated with learning-dependent changes in more traditional measures of AHP plasticity and was also insufficient to affect accommodation.

The calcium-dependent potassium currents underlying mAHPs and sAHPs are mediated largely by apamin-sensitive SK and apamin-insensitive sI_{AHP} channels, respectively. Although calcium-dependence of the mAHP via SK channel activation is a dominant viewpoint in the literature, there is evidence that the mAHP may also be generated by voltage-dependent K^+ channels (Storm, 1989; Gu et al., 2005). Both
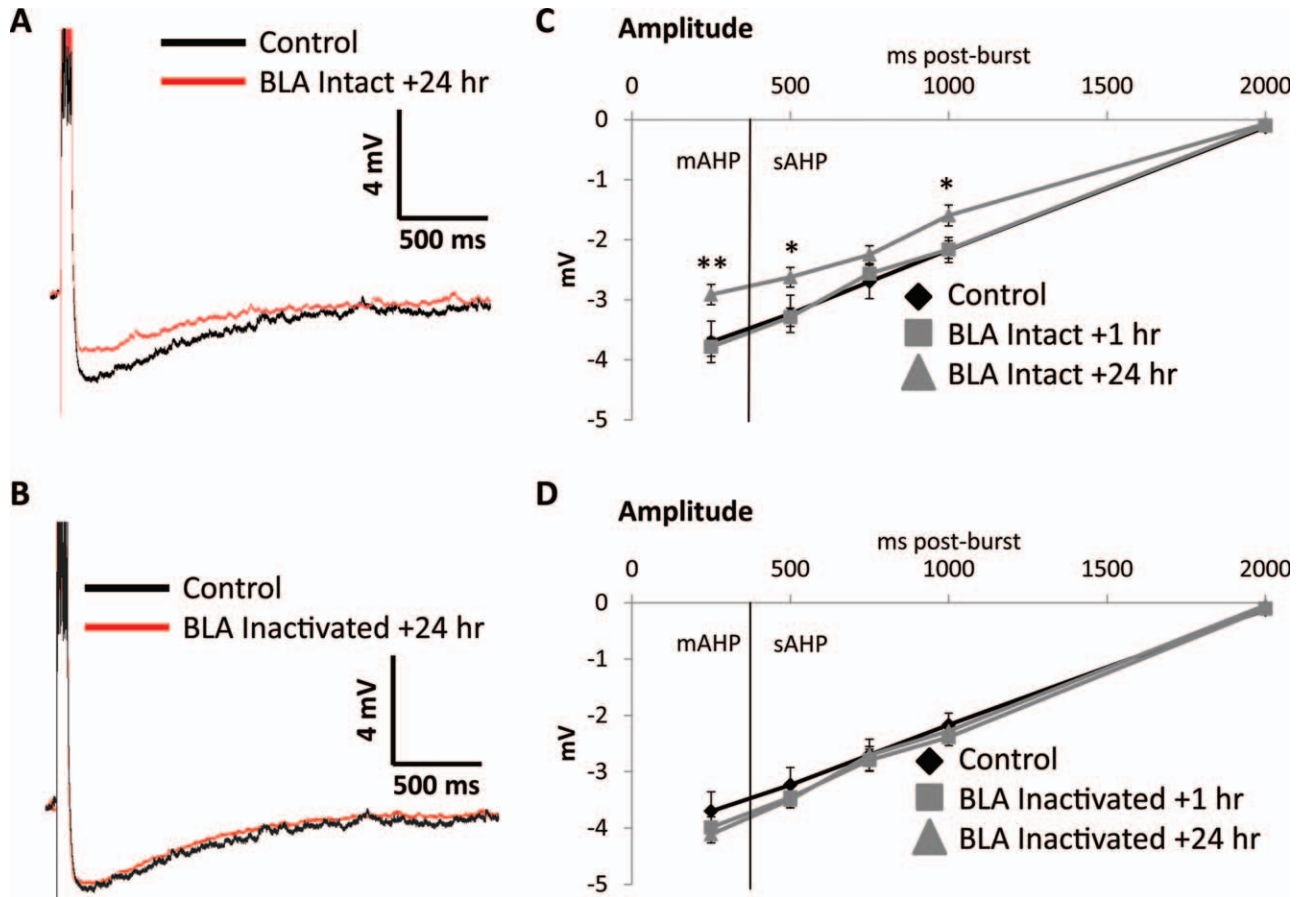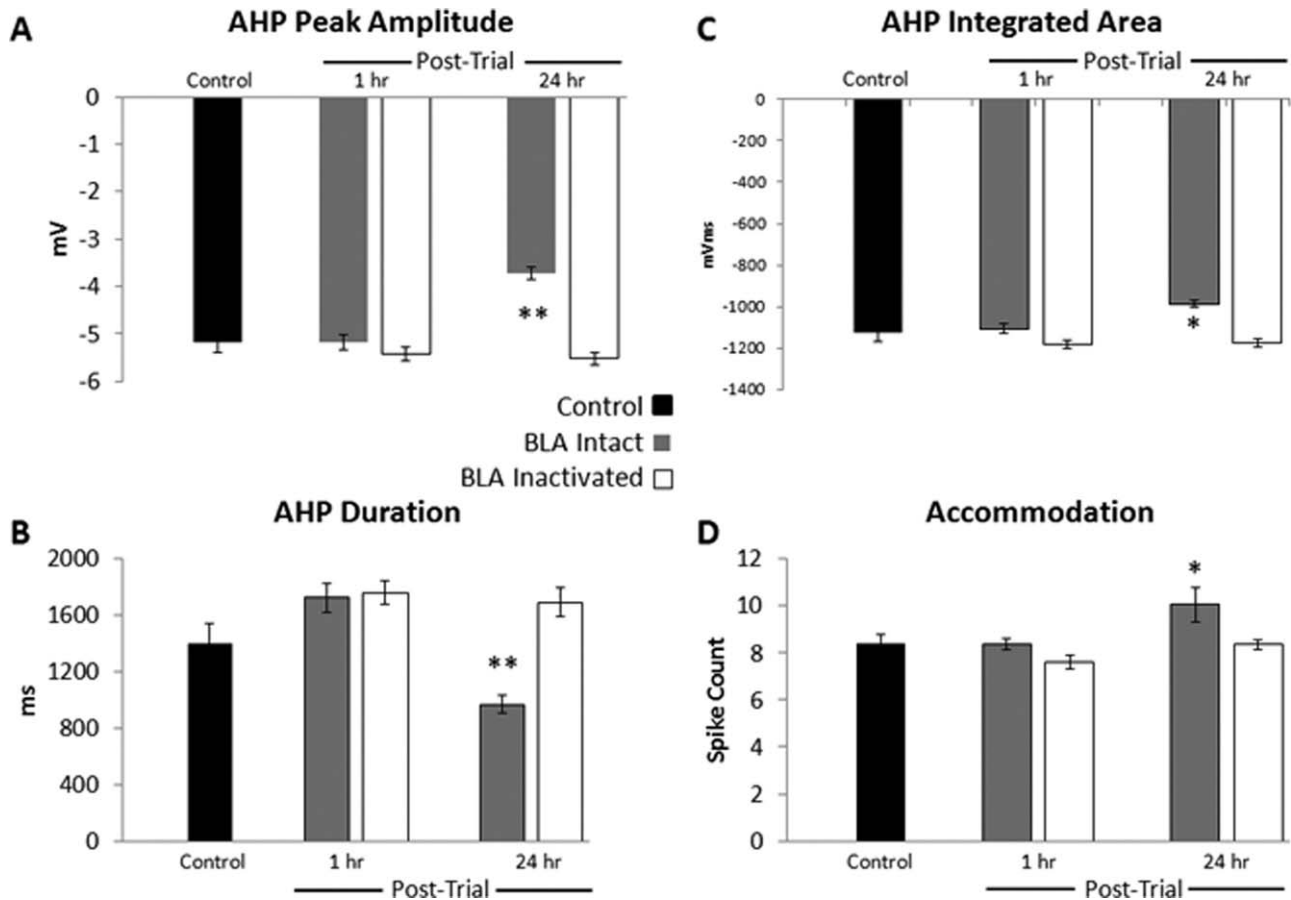
FIGURE 11. Dorsal CA1 pyramidal neurons showed learning-dependent AHP plasticity 24 h posttrial in (A) BLA-intact but not (B) BLA-inactivated rats following inhibitory avoidance learning. (C) BLA-intact rats exhibit significant learning-dependent reductions in both mAHP (250 ms $P < 0.01$) and sAHP (500 ms $P < 0.05$, 1,000 ms $P < 0.05$) components of the postburst afterhyper-polarization 24 h following IA training. (D) Temporary BLA inactivation blocks the learning-dependent reductions in the mAHP and sAHP observed 24 h following IA training. Values reported are means ± SEM; *$P < 0.05$, **$P < 0.01$.

currents clamp the membrane potential below the threshold for action potential generation. Plasticity in SK-mediated currents can effect peak AHP amplitude whereas sI_{AHP} currents mediate duration, and both can effect accommodation. Learning-dependent reductions in mAHP and sAHP have been reported in hippocampus following acquisition of trace eyeblink conditioning (Matthews et al., 2009). In addition, NE has been shown to reduce both currents via PKA-dependent phosphorylation (Pedarzani and Storm, 1995; Lancaster et al., 2006; Oh et al., 2009). Learning-dependent AHP plasticity in multitrial tasks has been shown to be PKA- but not PKC-dependent (Oh et al., 2009).

Learning-dependent AHP plasticity occurred with different time courses in dorsal and ventral CA1. Other studies have suggested differential roles for dorsal and ventral hippocampus, although the specific mechanism for these differences is not known. As an example, dorsal but not ventral hippocampal lesions impair spatial learning (Bannerman et al., 1999, 2002; Pothuizen et al., 2004), while ventral but not dorsal hippocampal lesions reduce anxiety (Bannerman et al., 2002; Kjelstrup et al., 2002).

Our findings are consistent with reports of NE release following both inhibitory avoidance learning and novel context exposure. Following inhibitory avoidance learning, NE levels in the BLA transiently increase within 15 min, returning to baseline levels by 30 min posttrial (McIntyre et al., 2003a). The magnitude of NE release was directly related to foot shock intensity, with more intense emotionally arousing stimuli producing the greatest NE release. Novel context exposure, on the other hand, is associated with smaller increases in plasma NE (De Boer et al., 1990). Phosphorylation-dependent sAHP reductions have been consistently reported after β-receptor activation (Madison and Nicoll, 1982; Madison and Nicoll, 1986; Pedarzani and Storm, 1993). The relatively brief increase in NE release reported is not fully consistent with the longer, but still transient and time limited, time course of the AHP reductions observed here, which suggests changes in gene transcription protein translation, or posttranslational modification, etc. also may have occurred and should be addressed experimentally in future studies. The AHP plasticity observed in CA1v is similar to that seen in basolateral amygdala (BLA) immediately

FIGURE 12.   Learning-dependent changes in dorsal CA1 pyramidal neuron excitability observed 24 h following inhibitory avoidance learning was blocked by temporary BLA inactivation with local anesthetics lidocaine or bupivacaine. BLA inactivation blocked the reduction in AHP (A) peak amplitude, (B) duration, (C) integrated area and (D) accommodation observed in BLA intact treated rats 24 h following IA training. Values reported are means ± SEM; *$P < 0.05$, **$P < 0.01$.

after conditioning but persisted longer and was also briefly expressed after novel context exposure (Farmer et al., submitted for review). In contrast, plasticity in CA1d neurons was slower to develop, well after AHP plasticity in BLA had extinguished. Future studies may need to examine regional specific time courses of NE release simultaneously in BLA and CA1v and CA1d after training or contextual exposure.

Our data are consistent with the hypothesis that information processing in hippocampus and amygdala are related. The AHP plasticity observed in ventral and dorsal CA1 pyramidal neurons was dependent on an intact basolateral amygdala. Temporary inactivation of the BLA *in vivo* blocked the learning-dependent plasticity seen in CA1v and CA1d *in vitro* following inhibitory avoidance learning. The basolateral complex, which includes the lateral (LA) and basolateral (BLA) nuclei, is involved in consolidation of inhibitory avoidance learning (Parent and McGaugh, 1994; Silva and Tomaz, 1995; Quirarte et al., 1997). Beta-agonists injected into the basolateral complex induce plasticity (i.e., increase expression of the immediate early gene product Arc) in the hippocampus (McIntyre et al., 2005). Activity in the amygdala can modulate excitability in the hippocampus and facili-

tate consolidation of new memories. Because BLA pyramidal neurons do not exhibit context-dependent AHP plasticity following a single exposure to the novel IA apparatus (Farmer et al., submitted for review), other plasticity mechanisms may modulate the very transient contextual plasticity seen in CA1v neurons here.

Inhibitory avoidance learning is a declarative memory task involving the hippocampus. Damage or inactivation of the hippocampus impairs task acquisition (Izquierdo and Medina, 1993; Chen et al., 1996). Other learning tasks which evoke AHP plasticity, including spatial learning, trace eyeblink conditioning, and olfactory discrimination, take multiple trials for acquisition. Learning-dependent plasticity observed in hippocampus (Moyer et al., 2000) or piriform cortex (Barkai and Saar, 2001) following multitrial learning does not occur after the first training trial, but instead late in the learning process. Both regions exhibit learning-dependent plasticity that persists for several days returning to basal levels after 3–5 days. This interval has been identified as that during which consolidation of learning occurs. In inhibitory avoidance learning with a moderate foot shock, learning occurred after only a single trial (see Fig. 1) and was retained both 1 h and 24 h posttrial.

Learning-dependent plasticity was observed 1 h (CA1v) and 24 h (both CA1v and CA1d) following this single trial, and extinguished within 72 h in both regions. This is consistent with other findings that the consolidation period for this single-trial task is much shorter than that for multitrial tasks (Hui et al., 2004). The single-trial learning-dependent plasticity in CA1 pyramidal neurons not only showed a more rapid development but was also more transient than that observed in multitrial learning paradigms. Taken together, the transient nature of the excitability changes reported here suggest that persistence of learning-dependent plasticity in CA1 and in other brain regions may be related to the time required for acquisition and consolidation of a task.

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