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NMDA Receptor-dependent Inhibition of Synaptic Transmission by Acute Ethanol Treatment in Rat Corticostriatal Slices

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The effects of ethanol on corticostriatal synaptic transmission were examined, using extracellular recording and analysis of population spike amplitudes in rat brain slices, to study how acute ethanol intoxication impairs striatal function. Ethanol caused a decrease in population spike amplitudes in a dose dependent manner (50–200 mM). Pretreatment with picrotoxin, a γ-amino butyric acid $(GABA)_A$ receptor antagonist, increased the population spikes but ethanol (100 mM) was still effective in decreasing the population spikes under this condition. In the presence of $_{(DL)}$-2-amino-5-phosphonovaleric acid (APV), N-methyl-D-aspartate (NMDA) receptor antagonist, the inhibitory action of ethanol on population spikes was not shown. These results suggest that ethanol inhibits the glutamatergic corticostriatal synaptic transmission through blockade of NMDA receptors.

Key Words: Striatum, Ethanol, Extracellular recording, Population spike, Glutamate receptor, Synaptic transmission

INTRODUCTION

Ethanol has a variety of actions within the central nervous system (CNS), which are thought to underlie the behavioral and cognitive consequences associated with alcohol consumption and alcoholism. Studies of the acute effects of ethanol in the CNS indicate that ethanol-induced changes in neuronal function are mediated through the modulation of various neurotransmitter-gated ion channels, such as nicotinic acetylcholine receptors, glutamate receptors, γ-aminobutyric acid $(GABA)_A$ receptors, and 5-hydroxytryptamine $(5\text{-HT})_3$ receptors (Lovinger, 1997). A considerable body of evidence suggests that the acute administration of ethanol induces changes in the electrophysiological and biochemical effects of glutamate receptor-mediated neurotransmission, such as the inhibition of *N*-methyl-D-aspartate (NMDA) receptor-mediated current (Lovinger et al, 1990; Peoples et al, 1997; Nieber et al, 1998; Wirkner et al, 2000) and non-NMDA receptor-mediated current (Wirkner et al, 2000; Moykkynen et al, 2003). These results suggest that ethanol is capable of modulating glutamatergic synaptic transmission in the CNS via its action on NMDA or non-NMDA receptors.

The neostriatum is involved in the control of movement (Graybiel et al, 1994), and it appears to be a brain region that undergoes extensive reorganization during habit learning (Jog et al, 1999) that may be related to compulsive drug seeking behavior (Gerdeman et al, 2003). The major excitatory input to the neostriatum arises from neurons in the neocortex that use glutamate as a neurotransmitter (Graybiel, 1990). Synaptic transmission at corticostriatal synapses are mediated by α-amino-3-hydroxy-5-methyl-4-isoxazolepropionate (AMPA) receptors with very little involvement of NMDA receptors (Cherubini et al, 1988).

Although studies of the acute effects of ethanol on glutamatergic synaptic transmission have been performed in various regions of the brain, the issue of how the ethanol modulates corticostriatal synaptic transmission remains unclear. Accordingly, we studied the modulatory action of ethanol on glutamatergic synaptic transmission in corticostriatal slices, using an *in vitro* extracellular recording technique.

METHODS

Brain slices were prepared from 21- to 28-day-old Sprague-Dawley rats using a previously described technique (Sung et al, 2001). Rats were anaesthetized with pentobarbital (50 mg/kg, i.p.) and killed by decapitation, in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals. The brains were removed and placed in ice-cold, modified artificial CSF (ACSF) containing (in mM) 194 sucrose, 30 NaCl, 4.5 KCl, 1 $MgCl_2$, 26

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ABBREVIATIONS: EtOH, ethanol; PS, population spike; ACSF, artificial cerebrospinal fluid; AMPA, α-amino-3-hydroxy-5-methyl-4-isoxazolepropionate; NMDA, N-methyl-D-aspartate; GABA, γ-aminobutyric acid, APV, DL-2-amino-5-phosphonovaleric acid; PTX, picrotoxin.

$NaHCO_3$, 1.2 NaH_2PO_4, 10 D-glucose adjusted to pH 7.4 by bubbling 95% O_2/5% CO_2 through the solution. The brain which contains the cerebral cortex and striatum was sectioned coronally (400 μm thick) with a manual vibratome (Campden Instruments, Loughborough, UK). The brain slices were then transferred to ACSF containing (in mM) 124 NaCl, 4.5 KCl, 2 $CaCl_2$, 1 $MgCl_2$, 26 $NaHCO_3$, 1.2 NaH_2PO_4, 10 D-glucose adjusted to pH 7.4 by bubbling with 95% O_2/5% CO_2. The slices were allowed to recover for at least 1 hour in ACSF at room temperature. One hemislice, containing the cortex and striatum, was submerged in a recording chamber and constantly superfused with ACSF bubbled with 95% O_2/5% CO_2. The flow rate was maintained for 2~3 ml/min using a peristaltic pump (Miniplus 2, Gilson, France). The temperature of the bath solution was maintained at 31±1°C.

All recordings were performed in the dorsolateral striatum to record population spikes evoked by the stimulation of excitatory afferents from the cerebral cortex. Electrical stimuli were delivered through a bipolar, Teflon®-coated tungsten electrode placed in the white matter dorsal to the striatum. Synaptically driven population spikes were recorded with a glass micropipette (<1 MΩ tip resistance) filled with 0.9% saline, placed at a site <2 mm ventral to the stimulating electrode. The position of the recording electrode was optimized by recording responses to low frequency stimulation (0.1~0.2 ms, 0.5~1.5 mA at 0.1 Hz), and the electrode was set at a depth that permitted the maximal PS amplitude to be observed. The stimulus intensity was then adjusted to evoke a population spike with amplitude approximately half of the maximum using a stimulus isolator (A360, World Precision Instrument, Sarasota, USA). Once the population spikes of the half-maximal amplitude triggered by 0.05 Hz stimuli had been stably maintained for 10~15 min, drugs were started to deliver. Population spikes were amplified 1000 - fold using a differential AC amplifier (Model 1700, A-M systems, Seattle, USA), and low-pass filtered at 5 kHz. The resulting amplified signals were digitized at 10 kHz using a CIO-DAS08/JR-AO interface (Measurement Computing Corporation, Middleboro, USA) and stored on a computer using the LTD230d software program (Anderson & Collingridge, 2001). All chemicals used in this experiment were ACS grade and were purchased from Sigma (St. Louis, MO). Drugs were diluted with ACSF immediately before use from stock solutions prepared according to the manufacturer's instructions and were delivered to the recording chamber with a peristaltic pump.

All averaged data are presented as the means±SE. The amplitudes of the first 30 population spikes before application of the drug were averaged and defined as the baseline response, and subsequent drug responses were compared to this value. When antagonists were pretreated before ethanol application, we analyzed the effect of ethanol by comparing its maximum effect with the average of the highest phase before ethanol treatment. All PSs data were normalized to the baseline response. The statistical significance of changes in synaptic responses relative to the amplitude of the baseline response amplitude was determined using a Student's paired t-test. The statistical criterion for significance was $p<0.05$.

RESULTS

The application of ethanol into the bath reversibly decreased the amplitude of the population spikes in a dose dependent manner (Fig. 1). At a concentration of 50 mM, the average amplitude of the population spikes was decreased by 6.4±4.8% (n=6, p=0.2427) of the baseline, and at 100 mM ethanol, the average amplitude of the population spikes was decreased by 22.7±6.3% (n=7, $p<0.05$) of the baseline. The average amplitude of the population spikes was decreased by 35.4±6.6% (n=7, $p<0.05$) and 46.1±6.0% (n=8, $p<0.05$) of the baseline for the treatment with 150 mM and 200 mM ethanol, respectively. Within the range of concentrations tested, ethanol inhibited corticostriatal population spikes in a concentration-dependent manner with an IC_{50} of 189.0±0.5 mM. Thus, we used 100 mM ethanol as a test concentration for following experiments.

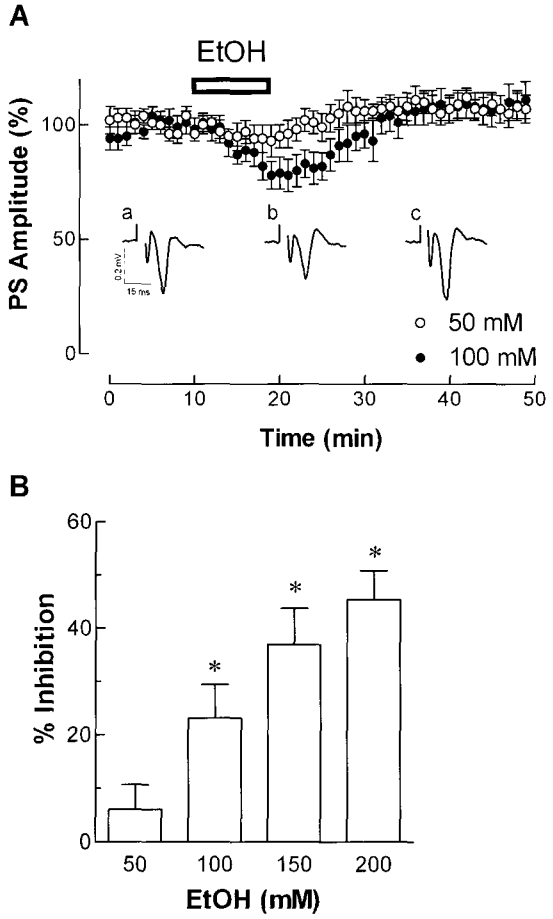

Fig. 1. Ethanol (EtOH) inhibits the corticostriatal synaptic transmission in a dose-dependent manner. (A) Plot of average population spikes (PSs) data shows that ethanol inhibits corticostriatal PS amplitudes (50 and 100 mM). The PSs were normalized to the baseline mean amplitude. The bar above plotted graph indicates the period of ethanol application. The representative traces of PSs before (a), during (b), and washing (c) after ethanol (100 mM) treatments. (B) The bar graph shows the dose-dependent inhibition of PSs by ethanol (50, 100, 150 and 200 mM). *$p<0.05$ when compared to baseline PSs.

It is well known that ethanol enhances $GABA_A$ receptor-mediated transmission in various regions of the brain (Lovinger, 1997) and the most striatal projection neurons

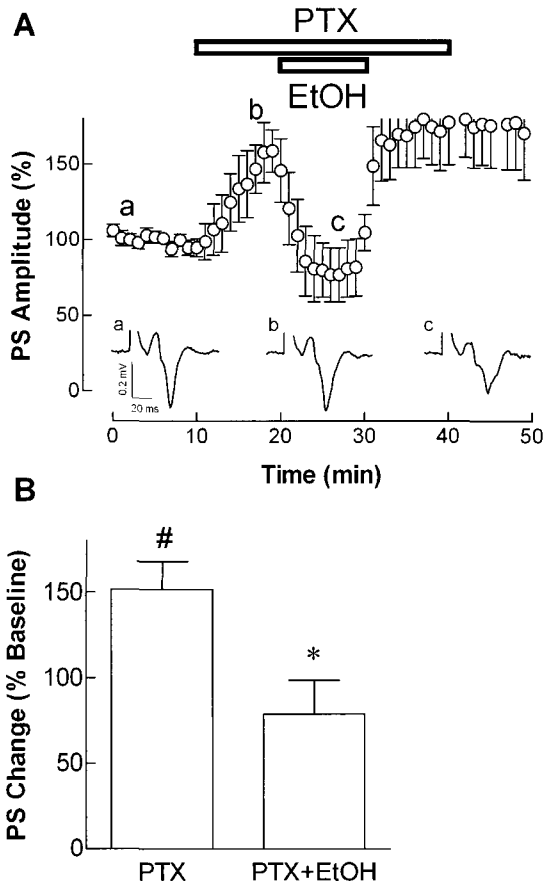

Fig. 2. Ethanol (EtOH, 100 mM) inhibits the corticostriatal synaptic transmission even after the blockade of $GABA_A$ receptor. (A) Plot of the data showing that PSs are decreased by 100 mM ethanol with 50 μM of picrotoxcin (PTX), a GABAA receptor antagonist. The PS amplitudes were increased by pretreatment of PTX, however pretreatment of PTX cannot prevent the inhibitory effect of ethanol on the corticostriatal synaptic transmission. The PSs were normalized to the baseline mean amplitude. The representative traces of PSs shows ACSF (a), PTX treatment (b), and ethanol treatments (c). (B) The bar graph shows the average changes of PSs during treatment of PTX only and PTX with ethanol. #$p<0.05$ when PSs amplitudes changes by PTX treatment compared to the normal ACSF, *$p<0.05$ when PSs amplitudes changes by coapplication of PTX with ethanol to PTX only.

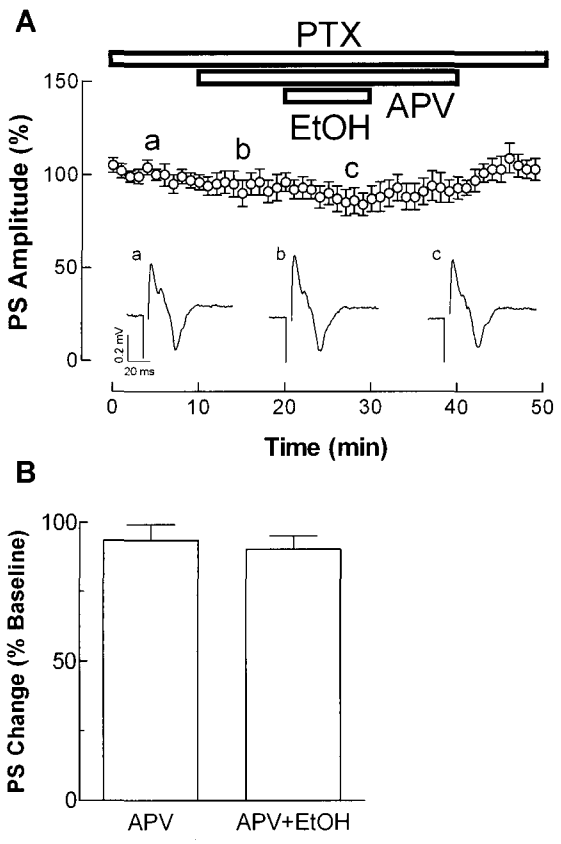

Fig. 3. The inhibitory action of ethanol (EtOH, 100 mM) on corticostriatal synaptic transmission is mediated by the NMDA receptors. (A) Plot of the data shows that ethanol does not change the PSs under the pretreatment of picrotoxin (PTX, 50 μM) and (DL)-2-amino-5-phosphonopentanoic acid (APV, 100 μM). The PSs were normalized to the baseline mean amplitude. The representative traces of PSs shows PTX (a), PTX plus APV treatment (b), and ethanol treatments (c). (B) The bar graph shows the average changes of PSs during treatment of APV only and APV with ethanol. In this experiment, brain slices were incubated in ACSF containing PTX over 1~2 hours and PTX were continuously treated during the recording period to exclude the role of the $GABA_A$ receptor in ethanol action.

utilize GABA, as a neurotransmitter (Graybiel, 1990). Therefore, we determined whether ethanol (100 mM) inhibits the population spikes in the presence of picrotoxin (50 μM), a $GABA_A$ receptor antagonist. The amplitude of the population spikes after picrotoxin treatment were increased significantly (Fig. 2; 51.6±16.5%, n=5, $p<0.05$), and ethanol still caused a decrease in the amplitude of the population spikes (Fig. 2A, 47.7±10.1%, $p<0.05$). The results indicate that ethanol inhibits corticostriatal synaptic transmission, independent of a GABAergic mechanism.

It has been demonstrated that corticostriatal excitatory postsynaptic potentials evoked by intrastriatal or cortical stimulation are composed of non-NMDA and NMDA components, although the non-NMDA component predominates under normal experimental conditions (Cherubini et al, 1988; Jiang & North, 1991; Calabresi et al, 1992; Lovinger, 1993). To examine whether NMDA glutamate receptors are involved in the inhibitory action of 100 mM ethanol, (DL)-2-amino-5-phosphonovaleric acid (APV, 100 μM), an NMDA receptor antagonist, was applied for 10 min prior to the ethanol treatment (Fig. 3A). In this experiment, brain slices were incubated in ACSF containing picrotoxin (50 μM) for 1~2 hours and picrotoxin was continuously present during the recording period to exclude the role of the $GABA_A$ receptor in ethanol action. By APV alone, the amplitude of population spikes was not changed significantly (2.9± 2.2%, Fig. 3; n=7, p=0.23). In the presence of APV, ethanol did not inhibit the population spikes amplitude significantly (6.4±5.7%, p=0.30).

DISCUSSION

Many studies have implicated a role of ligand-gated ion

channels in the acute intoxicating action of ethanol, which mediate a fast synaptic transmission in the brain. Thus, studying the effects of ethanol on corticostriatal synaptic transmission is important in terms of understanding the mechanisms by which motor function is impaired during acute ethanol intoxication. Our results show that ethanol caused a decrease in striatal population spikes amplitude evoked by cortical stimulation, in a dose-dependent manner. It has been reported that ethanol exerts different potency depending on its target. For example, NMDA receptors are inhibited at 20~200 mM by about 20~40% (Wirkner et al, 1999). However, ethanol enhances the effect of GABA activity at relatively lower concentration (1~50 mM) in various brain regions (Mihic, 1999). The IC_{50} (189.0± 0.5 mM) and the test concentration in our study is pharmacologically relevant. The relatively modest effect of ethanol might be explained by brain regional differences in receptor sensitivity, or by experimental conditions, such as the age and species of animals and recording temperature. The inhibitory effects of ethanol in our study were not prevented by pretreatment with the $GABA_A$ receptor blocker, picrotoxin, but were completely blocked by pretreatment with APV, an NMDA receptor antagonist. These results suggest that ethanol inhibits corticostriatal synaptic transmission, and that these inhibitory actions require the activation of NMDA receptors, because APV blocked the action of ethanol in our experiments. There are two possible explanations for the NMDA receptor requirement for ethanol inhibition on corticostriatal synaptic transmission. In the first, NMDA receptors may significantly participate in glutamatergic corticostriatal synaptic transmission under normal conditions, and these NMDA-mediated synaptic transmissions were directly inhibited by the ethanol. A number of studies suggest that NMDA receptors are one of the major targets for ethanol among the various glutamate receptors in the CNS (Harrison et al, 1990; Lovinger et al, 1990; Peoples et al, 1997; Wirkner et al, 1999; Littleton et al, 2001). Thus, ethanol would inhibit NMDA receptor function via changes in NMDA receptor phosphorylation (Yaka et al, 2003) and compartmentalization (Maldve et al, 2002). However, it has been reported that the main synaptic transmission in the striatum is mediated by non-NMDA receptors, and that NMDA receptor-mediated synaptic transmission is significant only in the state of release from the voltage-dependent Mg^{2+} blocking of the NMDA receptor induced by strong repetitive cortical stimulation or pharmacological manipulation (Calabresi et al, 1992; Lovinger, 1993). In our experiments, the decreases in the population spikes as the result of ethanol were more than 20% of the baseline value, and these magnitudes were greater than the ratio of the population spikes amplitudes contributed by NMDA receptors in corticostriatal synapses, which have been reported in other studies (Jiang & North, 1991; Calabresi et al, 1992; Lovinger, 1993). Therefore, this explanation may not be valid. Secondly, ethanol inhibits NMDA receptors and then alters the corticostriatal synaptic transmission mediated by non-NMDA receptors, possibly through the changing of signaling mechanisms or neurotransmitter release mediated by the NMDA receptor activation. It has been reported that ethanol inhibits NMDA receptor-evoked dopamine release in the striatum (Woodward & Gonzales, 1990) and the dopamine modulates the activity of striatal medium spiny neurons (Cepeda et al, 1993; Cepeda et al, 1998). In addition, it has been reported that blocking NMDA receptors could impair the activity of AMPA receptors on glutamatergic synapse (Zhu & Malinow, 2002). Thus, in this scenario, ethanol inhibits corticostriatal synaptic transmission via a NMDA receptor-dependent cellular mechanism.

The inhibitory action of ethanol on non-NMDA receptors has also been suggested by the experiments showing that non-NMDA receptors may exhibit a relatively high sensitivity to ethanol and that ethanol inhibits both the peak current and the steady-state component of the AMPA-activated current (Wirkner et al, 2000; Moykkynen et al, 2003). However, it was not possible to test the non-NMDA receptor subtype selective antagonist, because 2,3-dioxo-6-nitro-1,2,3,4-tetrahydrobenzo[f]quinoxaline-7-sulfonamide (NBQX) and 6-cyano-7-nitroquinoxaline-2,3-dione (CNQX), non- NMDA receptor antagonists, completely abolished the population spikes (data not shown), thus the possible role of non-NMDA receptor on the effect of ethanol in these synapses cannot be completely excluded. Furthermore, the suppression of glutamate release by ethanol through inhibition of NMDA receptors was observed in the striatum in some in vivo microdialysis studies (Carboni et al, 1990). Moreover, Carboni et al. (1993) reported that ethanol prevents the release of glutamate induced by NMDA receptors in the striatum. Therefore, further study using protocols, such as paired-pulse ratios and spontaneous EPSC analysis might be helpful in clarifying the mechanisms of ethanol actions on the corticostriatal synaptic transmission electrophysiologically.

Early studies reported that activation of the NMDA receptor is not only involved in neural excitation (Collingridge et al, 1988), but is critically involved in certain forms of synaptic plasticity in the various regions of the brain (Collingridge et al, 1983; Harris et al, 1984; Calabresi et al, 1992). It has been also reported that the acute administration of ethanol alters striatal function (Schreckenberger et al, 2004), which is considered to be a region specific for habitual learning. Our data provide evidence to show that acute ethanol exposure could inhibit corticostriatal synaptic transmission via a NMDA receptor-dependent mechanism, and that these inhibitory effects of ethanol on the striatal synapses, may contribute to the impaired behavioral and cognitive consequences that are associated with acute alcohol intoxication.

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REFERENCES

Anderson WW, Collingridge GL. The LTP Program: a data acquisition program for on-line analysis of long-term potentiation and other synaptic events. *J Neurosci Methods* 108: 71−83, 2001

Calabresi P, Pisani A, Mercuri NB, Bernardi G. Long-term potentiation in the striatum is unmasked by removing the voltage-dependent magnesium block of nmda receptor channels. *Eur J Neurosci* 4: 929−935, 1992

Carboni S, Isola R, Gessa GL, Rossetti ZL. Ethanol prevents the glutamate release induced by N-methyl-D-aspartate in the rat striatum. *Neurosci Lett* 152: 133−136, 1993

Carboni S, Melis F, Pani L, Hadjiconstantinou M, Rossetti ZL. The non-competitive NMDA-receptor antagonist MK-801 prevents

the massive release of glutamate and aspartate from rat striatum induced by 1-methyl-4-phenylpyridinium (MPP+). *Neurosci Lett* 117: 129–133, 1990

Cepeda C, Buchwald NA, Levine MS. Neuromodulatory actions of dopamine in the neostriatum are dependent upon the excitatory amino acid receptor subtypes activated. *Proc Natl Acad Sci USA* 90: 9576–9580, 1993

Cepeda C, Colwell CS, Itri JN, Chandler SH, Levine MS. Dopaminergic modulation of NMDA-induced whole cell currents in neostriatal neurons in slices: contribution of calcium conductances. *J Neurophysiol* 79: 82–94, 1998

Cherubini E, Herrling PL, Lanfumey L, Stanzione P. Excitatory amino acids in synaptic excitation of rat striatal neurones in vitro. *J Physiol* 400: 677–690, 1988

Collingridge GL, Herron CE, Lester RA. Synaptic activation of N-methyl-D-aspartate receptors in the Schaffer collateral-commissural pathway of rat hippocampus. *J Physiol* 399: 283–300, 1988

Collingridge GL, Kehl SJ, McLennan H. Excitatory amino acids in synaptic transmission in the Schaffer collateral-commissural pathway of the rat hippocampus. *J Physiol* 334: 33–46, 1983

Gerdeman GL, Partridge JG, Lupica CR, Lovinger DM. It could be habit forming: drugs of abuse and striatal synaptic plasticity. *Trends Neurosci* 26: 184–92, 2003

Graybiel AM. Neurotransmitters and neuromodulators in the basal ganglia. *Trends Neurosci* 13: 244–254, 1990

Graybiel AM, Aosaki T, Flaherty AW, Kimura M. The basal ganglia and adaptive motor control. *Science* 265: 1826–1831, 1994

Harris EW, Ganong AH, Cotman CW. Long-term potentiation in the hippocampus involves activation of N-methyl-D-aspartate receptors. *Brain Res* 323: 132–137, 1984

Harrison NL, Lovinger DM, Lambert NA, Teyler TJ, Prager R, Ong J, Kerr DI. The actions of 2-hydroxy-saclofen at presynaptic GABAB receptors in the rat hippocampus. *Neurosci Lett* 119: 272–276, 1990

Jiang ZG, North RA. Membrane properties and synaptic responses of rat striatal neurones in vitro. *J Physiol* 443: 533–553, 1991

Jog MS, Kubota Y, Connolly CI, Hillegaart V, Graybiel AM. Building neural representations of habits. *Science* 286: 1745–1749, 1999

Littleton JM, Lovinger D, Liljequist S, Ticku R, Matsumoto I, Barron S. Role of polyamines and NMDA receptors in ethanol dependence and withdrawal. *Alcohol Clin Exp Res* 25: S132–S136, 2001

Lovinger DM. High ethanol sensitivity of recombinant AMPA-type glutamate receptors expressed in mammalian cells. *Neurosci Lett* 159: 83–87, 1993

Lovinger DM. Alcohols and neurotransmitter gated ion channels: past, present and future. *Naunyn Schmiedebergs Arch Pharmacol* 356: 267–282, 1997

Lovinger DM, White G, Weight FF. NMDA receptor-mediated synaptic excitation selectively inhibited by ethanol in hippocampal slice from adult rat. *J Neurosci* 10: 1372–1379, 1990

Maldve RE, Zhang TA, Ferrani-Kile K, Schreiber SS, Lippmann MJ, Snyder GL, Fienberg AA, Leslie SW, Gonzales RA, Morrisett RA. DARPP-32 and regulation of the ethanol sensitivity of NMDA receptors in the nucleus accumbens. *Nat Neurosci* 5: 641–648, 2002

Mihic SJ. Acute effects of ethanol on GABAA and glycine receptor function. *Neurochem Int* 35: 115–123, 1999

Moykkynen T, Korpi ER, Lovinger DM. Ethanol inhibits alpha-amino-3-hydyroxy-5-methyl-4-isoxazolepropionic acid (AMPA) receptor function in central nervous system neurons by stabilizing desensitization. *J Pharmacol Exp Ther* 306: 546–555, 2003

Nieber K, Poelchen W, Sieler D, Illes P. Inhibition by ethanol of excitatory amino acid receptors in rat locus coeruleus neurons in vitro. *Naunyn Schmiedebergs Arch Pharmacol* 357: 299–308, 1998

Peoples RW, White G, Lovinger DM, Weight FF. Ethanol inhibition of N-methyl-D-aspartate-activated current in mouse hippocampal neurones: whole-cell patch-clamp analysis. *Br J Pharmacol* 122: 1035–1042, 1997

Schreckenberger M, Amberg R, Scheurich A, Lochmann M, Tichy W, Klega A, Siessmeier T, Grunder G, Buchholz HG, Landvogt C, Stauss J, Mann K, Bartenstein P, Urban R. Acute alcohol effects on neuronal and attentional processing: striatal reward system and inhibitory sensory interactions under acute ethanol challenge. *Neuropsychopharmacology* 29: 1527–1537, 2004

Sung KW, Choi S, Lovinger DM. Activation of group I mGluRs is necessary for induction of long-term depression at striatal synapses. *J Neurophysiol* 86: 2405–2412, 2001

Wirkner K, Assmann H, Koles L, Gerevich Z, Franke H, Norenberg W, Boehm R, Illes P. Inhibition by adenosine A (2A) receptors of NMDA but not AMPA currents in rat neostriatal neurons. *Br J Pharmacol* 130: 259–269, 2000

Wirkner K, Poelchen W, Koles L, Muhlberg K, Scheibler P, Allgaier C, Illes P. Ethanol-induced inhibition of NMDA receptor channels. *Neurochem Int* 35: 153–162, 1999

Woodward JJ, Gonzales RA. Ethanol inhibition of N-methyl-D-aspartate-stimulated endogenous dopamine release from rat striatal slices: reversal by glycine. *J Neurochem* 54: 712–715, 1990

Yaka R, Phamluong K, Ron D. Scaffolding of Fyn kinase to the NMDA receptor determines brain region sensitivity to ethanol. *J Neurosci* 23: 3623–3632, 2003

Zhu JJ, Malinow R. Acute versus chronic NMDA receptor blockade and synaptic AMPA receptor delivery. *Nat Neurosci* 5: 513–514, 2002