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Short Communication

Trace amines reduce $GABA_B$ receptor-mediated presynaptic inhibition at GABAergic synapses of the rat substantia nigra pars compacta

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Abstract

Trace amines (TAs) act in the mammalian brain through amphetamine-like effects and as endogenous agonists of specific receptors. We now show that tyramine and β-phenylethylamine, in the presence of specific dopamine (DA) receptor antagonists, inhibit the $GABA_B$-dependent presynaptic inhibition of GABAergic inputs to midbrain DA neurons. Our results further extend the role of TAs as neuromodulators and propose a novel mechanism by which they modulate DA neurons.

Theme: Neurotransmitters, modulators, transporters, and receptors
Topic: Other neurotransmitters

Keywords: Trace amine; GABAB; Substantia nigra; Presynaptic mechanism

Trace amines (TAs) are endogenous amines present at low levels in the mammalian brain. They include tyramine (TYR), β-phenylethylamine (β-PEA), tryptamine and octopamine and are related to classical monoamine transmitters [1,3]. In recent years, growing attention has been directed towards TAs, especially following the discovery of a family of G-protein coupled receptors, including TA_1 and TA_2, selectively activated by TYR and β-PEA [2,4,8]. Several lines of evidence suggest a link between the mesencephalic dopamine (DA) system and TAs. TAs are probably synthesized by nigro-striatal DA neurons [1], in addition, a high expression of TA_1 mRNA has been detected in both the pars compacta (SNc) and the pars reticulata (SNr) of the substantia nigra [2].

The role of TAs has long been confined to amphetamine-like actions [3]. However, growing evidence propose TAs as neuromodulators that modify the action of coexisting neurotransmitters [1]. In the SNc, in particular, both TYR and β-PEA reduce the postsynaptic hyperpolarisation due to $GABA_B$ receptor-mediated inhibition by a G-protein coupled postsynaptic mechanism [5].

$GABA_B$ receptor activation also causes presynaptic inhibition of GABA release to SNc DA neurons [7], thus, we addressed the possibility that TYR and β-PEA, besides affecting postsynaptic $GABA_B$ responses, may also interfere with the presynaptic function of the same receptor.

Horizontal slices (250 μm) of the ventral midbrain, containing the substantia nigra, were obtained from 18 to 25 days old Wistar rats using standard procedures, in an artificial cerebrospinal fluid solution (ACSF) composed of (in mM): NaCl (126), KCl (2.5), $MgCl_2$ (1.2), $CaCl_2$ (2.4), NaH_2PO_4 (1.2), $NaHCO_3$ (24), glucose (11); saturated with 95% O_2, 5% CO_2. Slices were transferred to a submerged recording chamber (2.5–3 ml min^{-1}, 33.5 °C), on the stage of an upright microscope, equipped for infrared video microscopy. Whole-cell patch-clamp recordings were obtained using glass electrodes (3–4 MΩ) filled with (in mM): CsCl (133), $MgCl_2$

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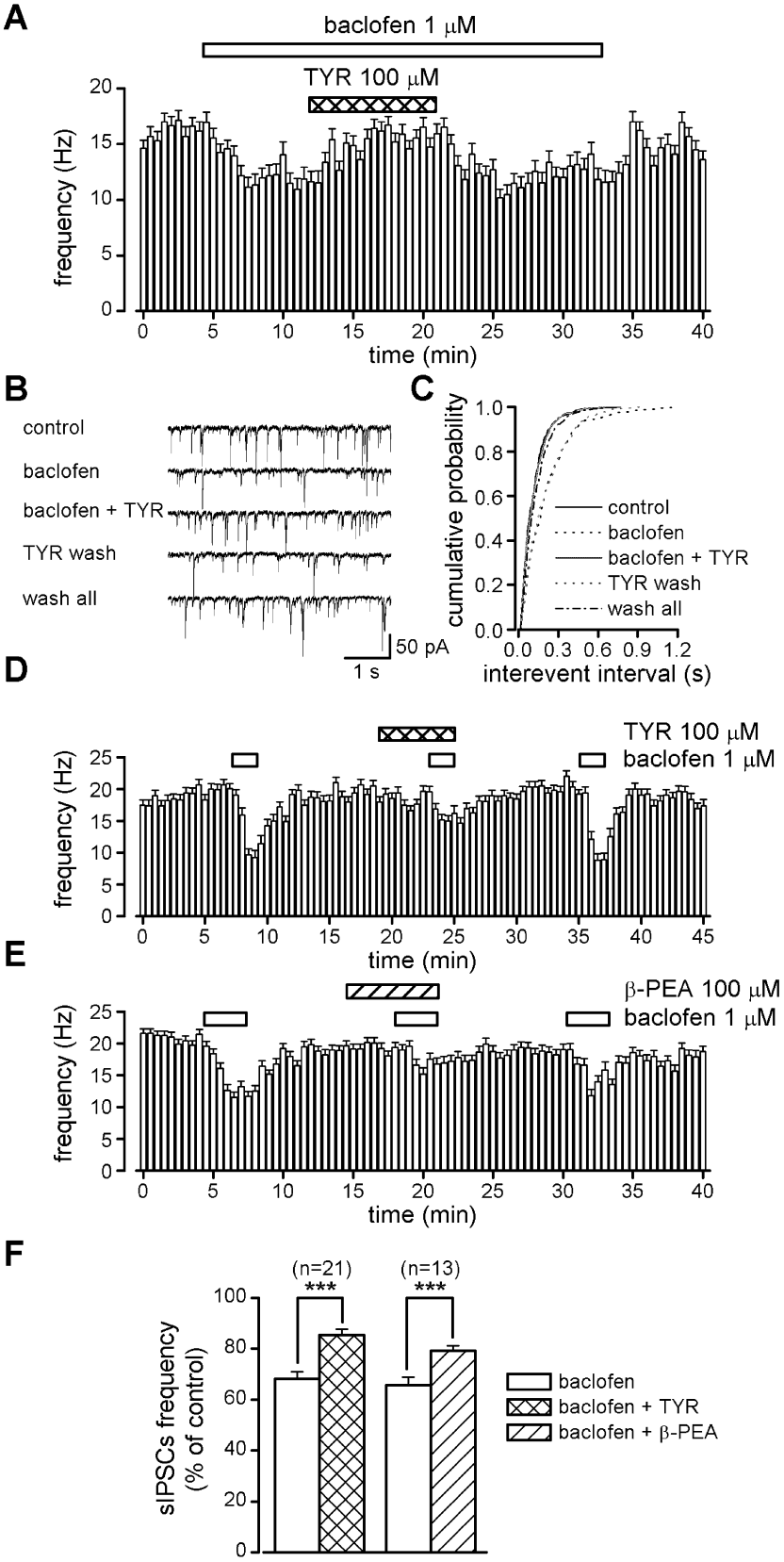
A
baclofen 1 μM
TYR 100 μM
frequency (Hz)
time (min)
B
control
baclofen
baclofen + TYR
TYR wash
wash all
50 pA
1 s
C
cumulative probability
interevent interval (s)
control
baclofen
baclofen + TYR
TYR wash
wash all
D
TYR 100 μM
baclofen 1 μM
frequency (Hz)
time (min)
E
β-PEA 100 μM
baclofen 1 μM
frequency (Hz)
time (min)
F
(n=21)
(n=13)
***
***
sIPSCs frequency (% of control)
baclofen
baclofen + TYR
baclofen + β-PEA