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Modulation of NMDA and GABA receptor binding in rat brain by the prolonged ventricular infusion of biotransformed ginsenosides

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Ginseng saponins are transformed by intestinal microflora and the transformants would be absorbed from intestine. In the present study, we have investigated the effects of biotranformed ginsenoside Rg3, Rh2 and compound K on the modulation of NMDA receptor and $GABA_A$ receptor binding in rat brain. The NMDA receptor binding was analyzed by quantitative autoradiography using [^{3}H]MK-801 binding, and $GABA_A$ receptor bindings were analyzed by using [^{3}H]muscimol and [^{3}H]flunitrazepam binding in rat brain slices. Ginsenoside Rg3, Rh2 and compound K were infused (10 ug/10 ul/ hr) into rat brain lateral ventricle for 7 days, through pre-implanted cannula by osmotic minipumps (Alzet, model 2ML). The levels of [^{3}H]MK-801 binding were highly decreased in almost all regions of frontal cortex and hippocampus by ginsenoside Rh2 and compound K. The levels of [^{3}H]muscimol binding were elevated in part of frontal cortex and granule layer of cerebellum by the treatment of ginsenoside Rh2 and compound K. However, the [^{3}H]flunitrazepam binding was not modulated by any tested ginsenosides.

Ginsenoside Rh2 and compound K induced the downregulation of the [^{3}H]MK-801 binding as well as upregulation of the and [^{3}H]muscimolbinding in a region-specific manner after prolonged infusion into lateral ventricle. However, ginsenoside Rg3 did not show the significant changes of ligand bindings. In addition, ginsenoside Rh2 and compound K modulated the expression of nNOS in hippocampus and striatum. These results suggest that prolonged infusion of ginsenosides could differentially modulate [^{3}H]MK-801 and [^{3}H]muscimol binding in a region-specific manner and ginsenoside Rh2 and compound K could play an important role in the biological activities in the central nervous systems and neurodegenerative disease.

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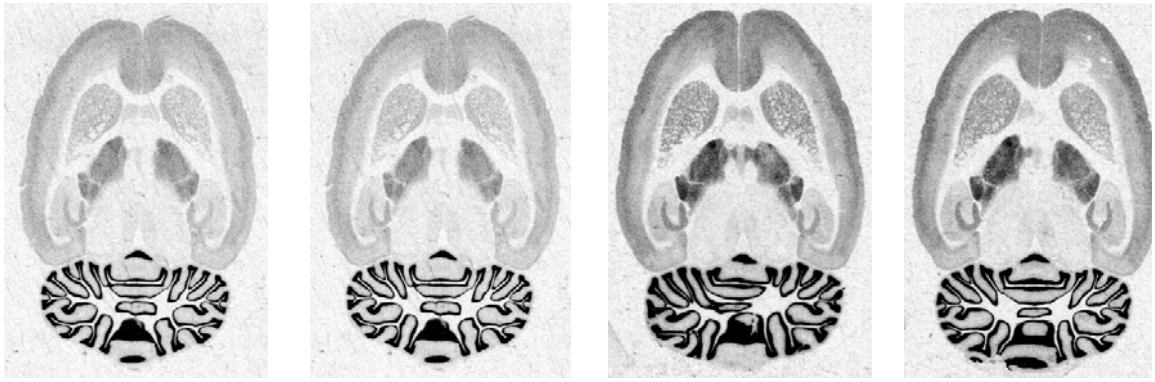
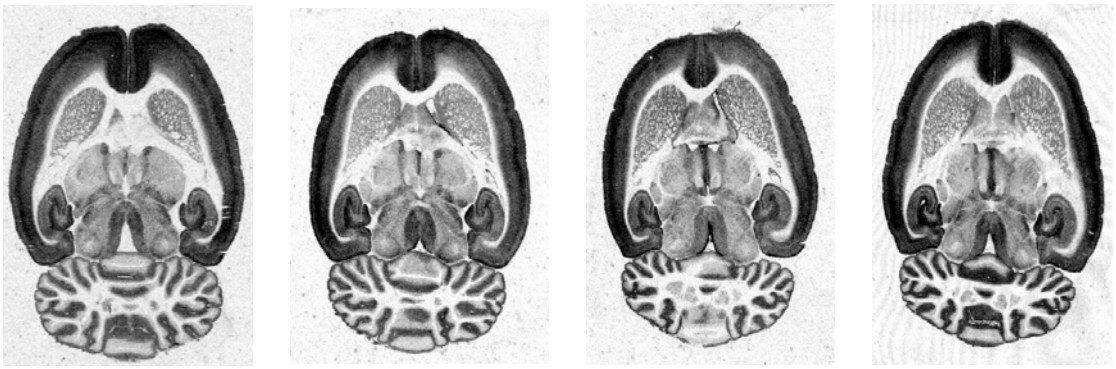
Changes of [^{3}H]Muscimol binding by ginsenoside infusion



Saline Rg3 Rh2 CK

Representative autoradiograms of [3H]muscimol in ginsenoside Rg3-, Rh- or compound K-infused rats. Ginsenoside or metabol
(Rg3, Rh2, compound K) was continuously infused (flow rate, 10 μg/10 μl/hr) into rat brain (icv) by osmotic minipump for 7 da

Changes of [^{3}H]Flunitrazapam binding by ginsenoside infusion



Saline Rg3 Rh2 CK

Representative autoradiograms of [3H]flunitrazepam in ginsenoside Rg3-, Rh- or compound K-infused rats. Ginsenoside or
metabolite (Rg3, Rh2, compound K) was continuously infused (flow rate, 10 μg/10 μl/hr) into rat brain (icv) by osmotic minipu
for 7 days. The tissue sections were incubated with 1 nM [3H]flunitrazepam in the presence of 150 mM NaCl for 90 min at 4 oC