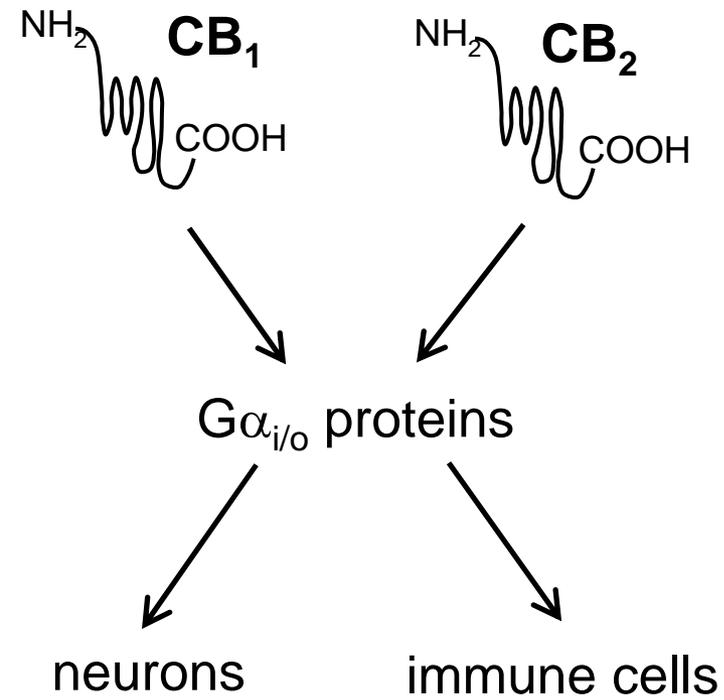


Effects of synthetic cannabinoids, identified in smoked herbal products, on synaptic transmission in the brain

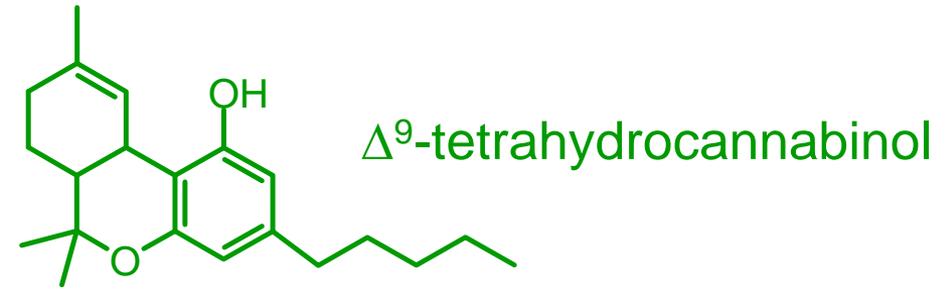
Bela Szabo, Mario Lederer,
Eszter Boros
Inst. f. Pharmakologie
Albert-Ludwigs-Universität
Freiburg

1) Cannabinoid receptors and their typical effects in the brain

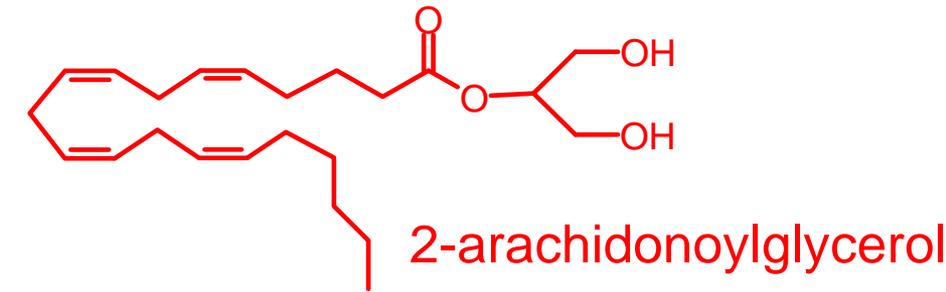
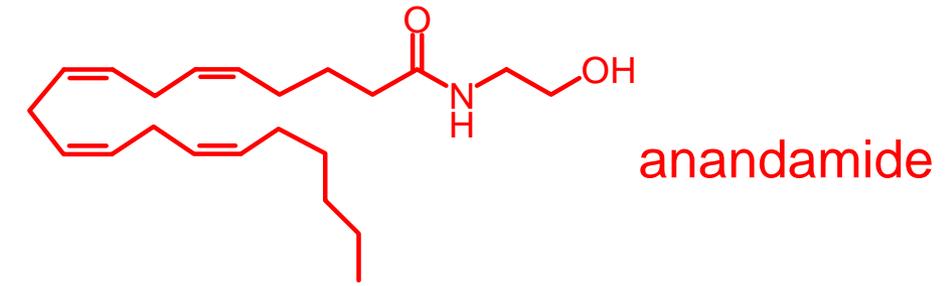
Cannabinoid receptors



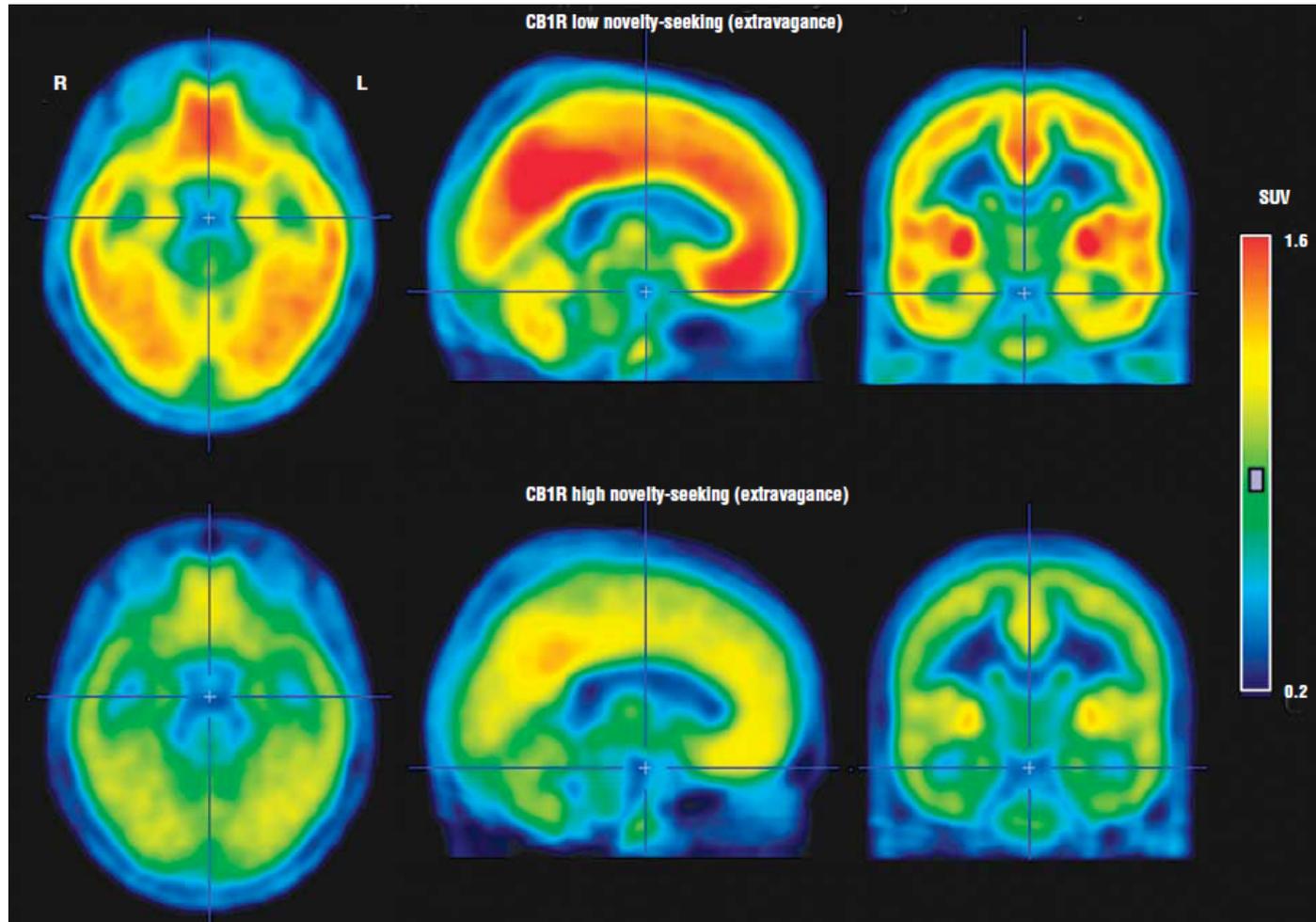
NATURAL



ENDOGENOUS



CB₁-Rezeptoren im menschlichen Gehirn: PET-Untersuchung mit [18F]MK-9470



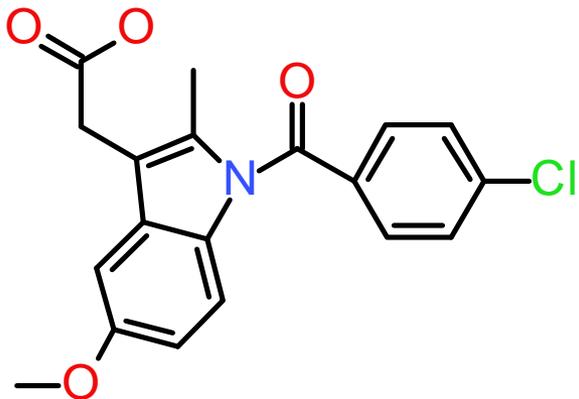
Negative correlation: extravagance – CB₁ receptor
disorderliness – CB₁ receptor

Van Laere et al., Arch Gen
Psychiatry 66:196-204, 2009

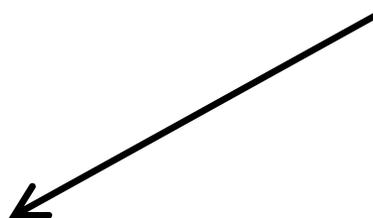
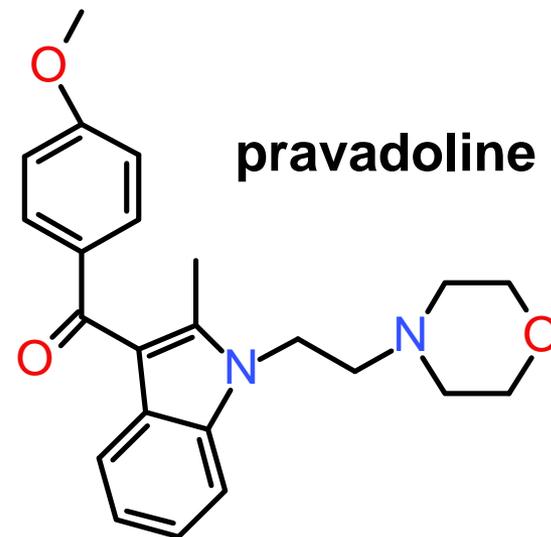
2) Synthetic cannabinoids

Synthetic cannabinoids from Sterling Winthrop

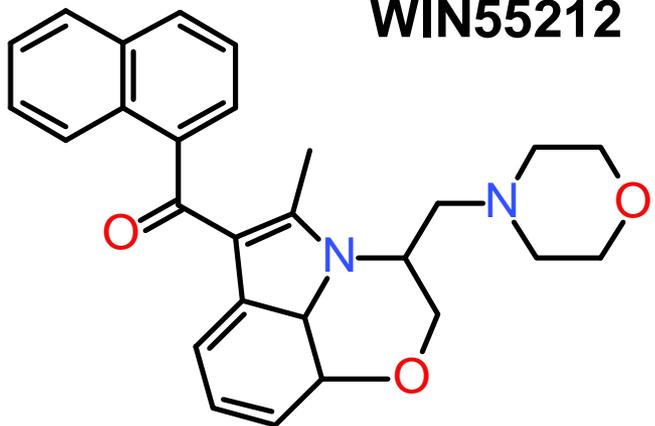
indomethacin



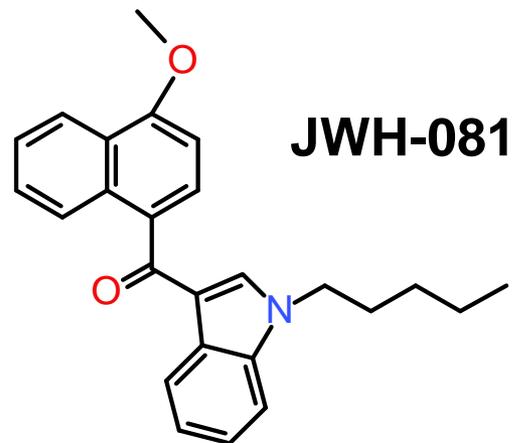
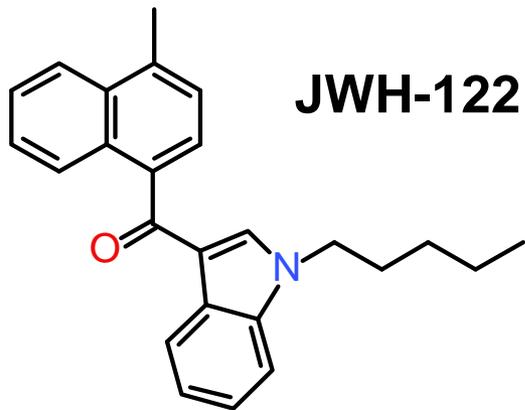
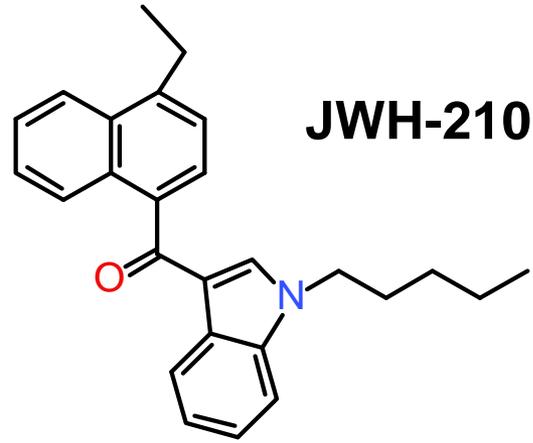
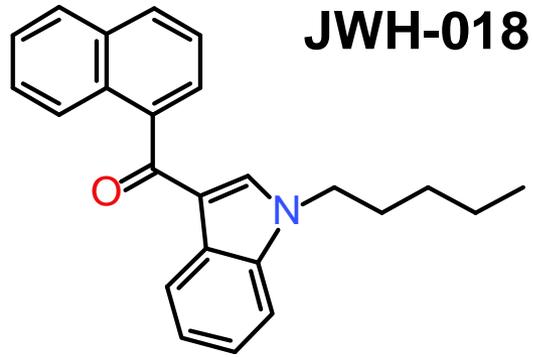
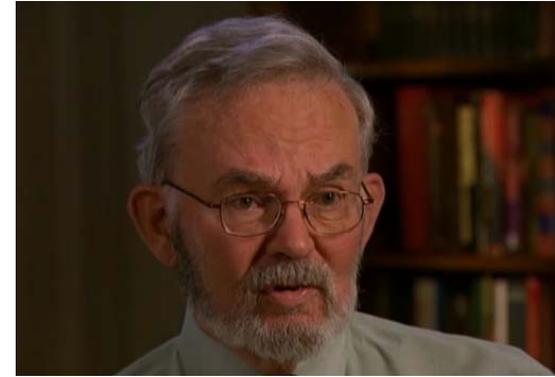
pravastatin



WIN55212



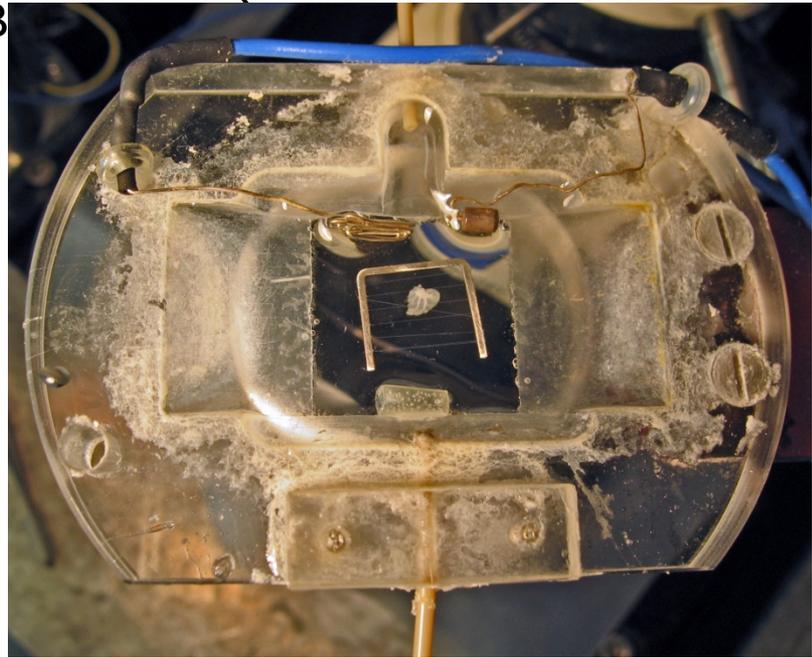
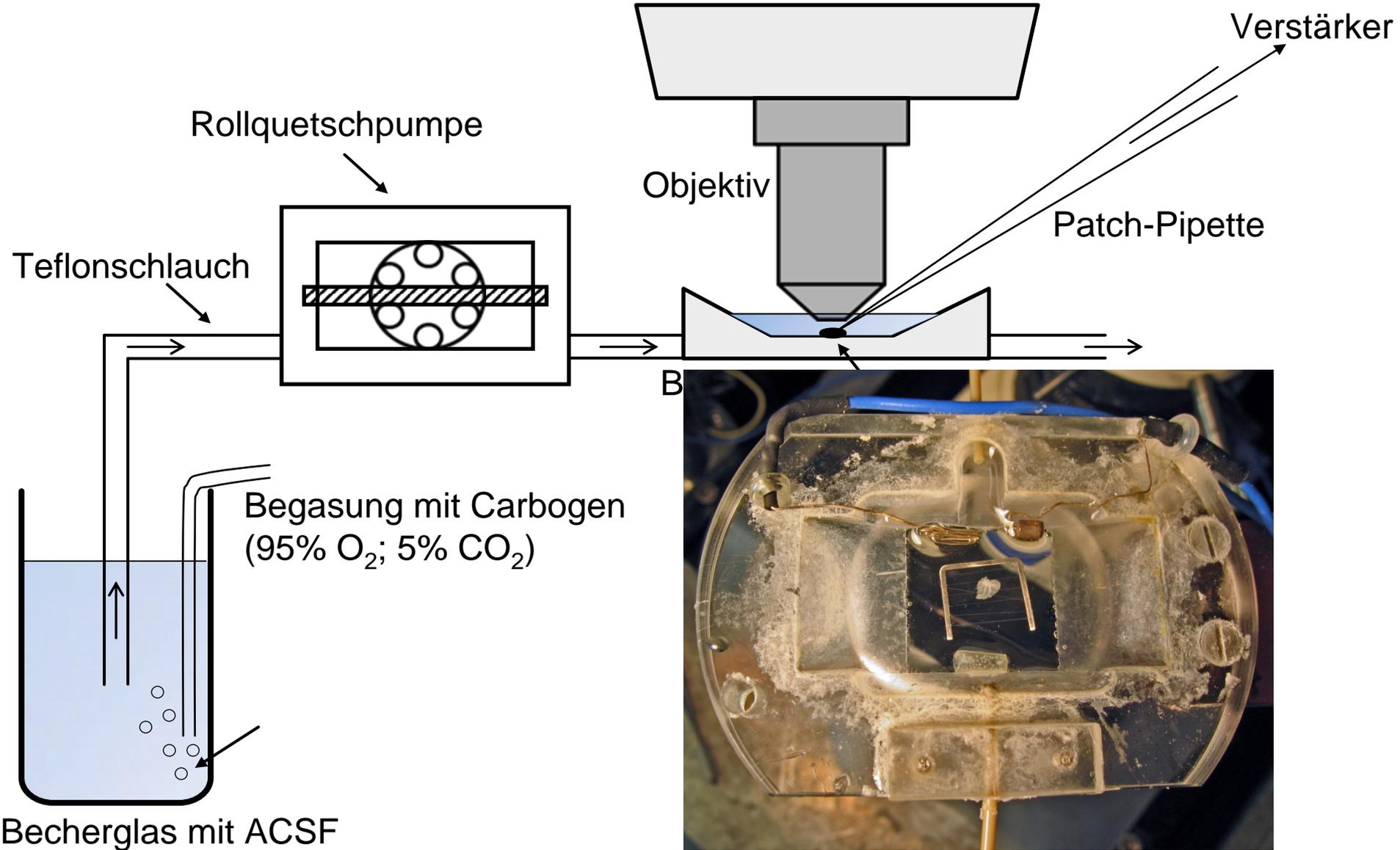
Synthetic cannabinoids from John William Huffman: JWH-compounds



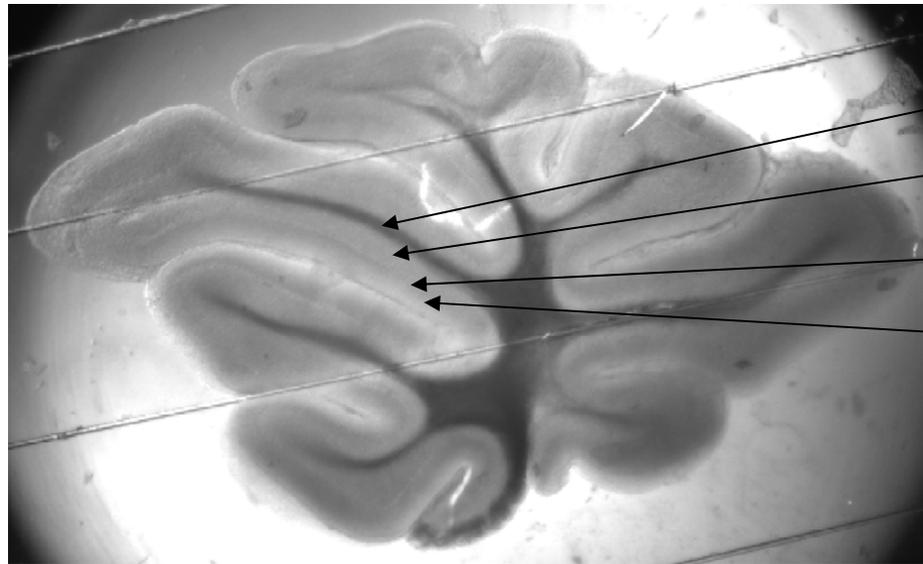
Aung et al., Drug Alcohol Depend 60: 133-140, 2000
Huffman JW, Cannabimimetic indoles, pyrroles, and indenes: structure-activity relationships and receptor Interactions. In: Reggio PH (ed), The Cannabinoid Receptors, The Receptors, Humana Press, 2009, pp 49-94

3) Methods

Patch-Clamp-Setup



Cerebellum: microscopic views

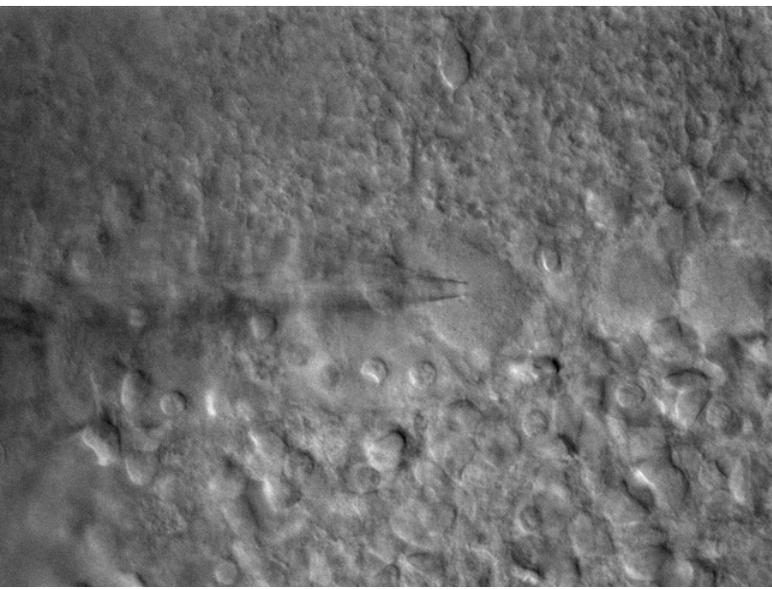


white matter

granule cell layer

Purkinje cell layer

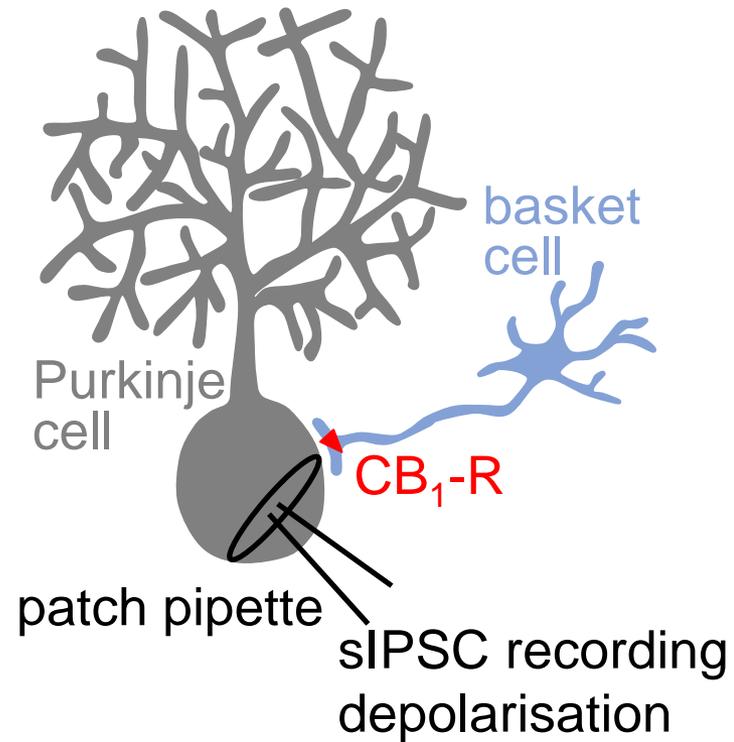
molecular layer



molecular layer

Purkinje cell layer

granule cell layer



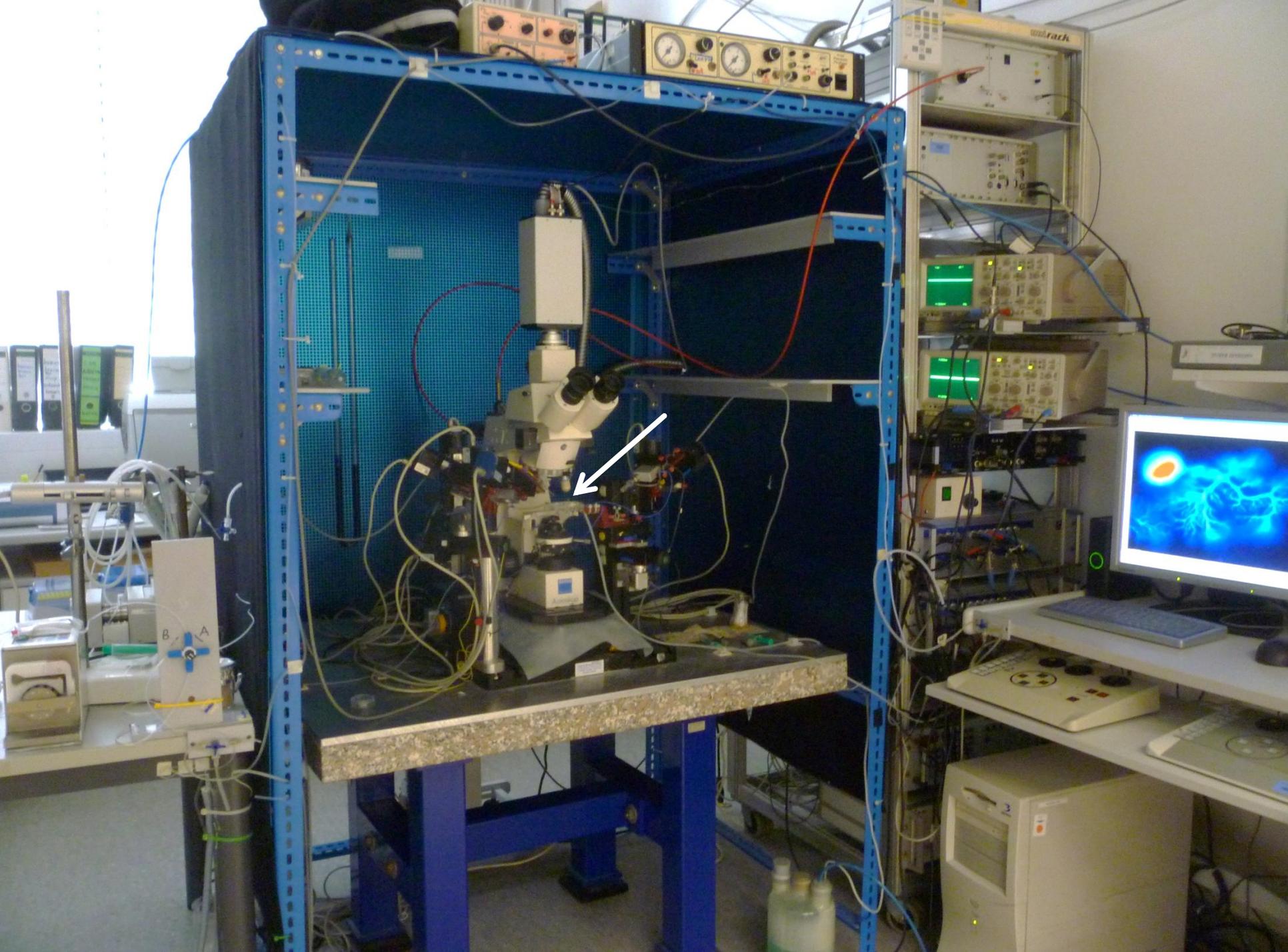
basket cell

Purkinje cell

CB₁-R

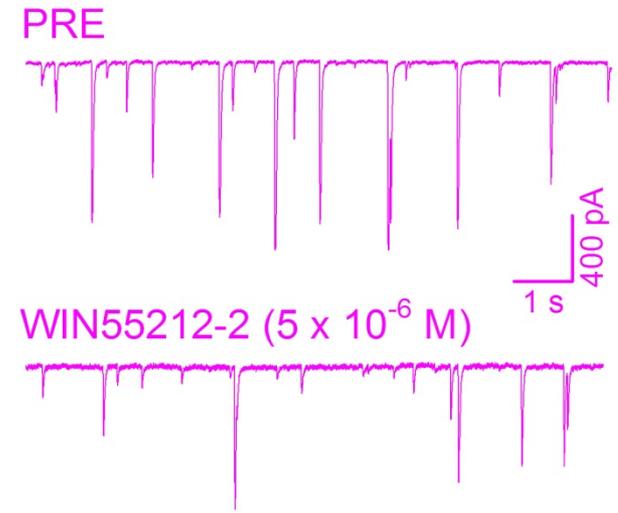
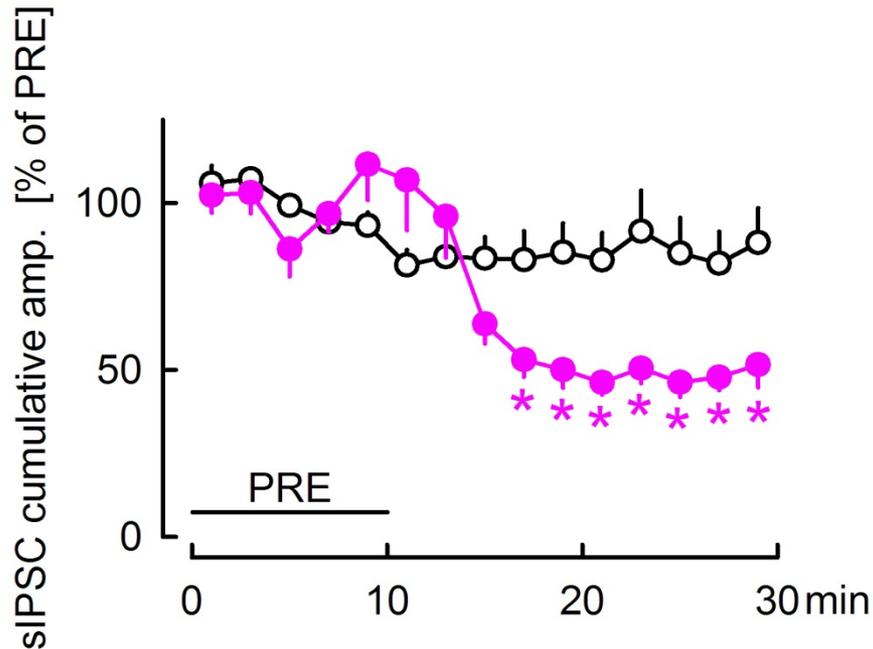
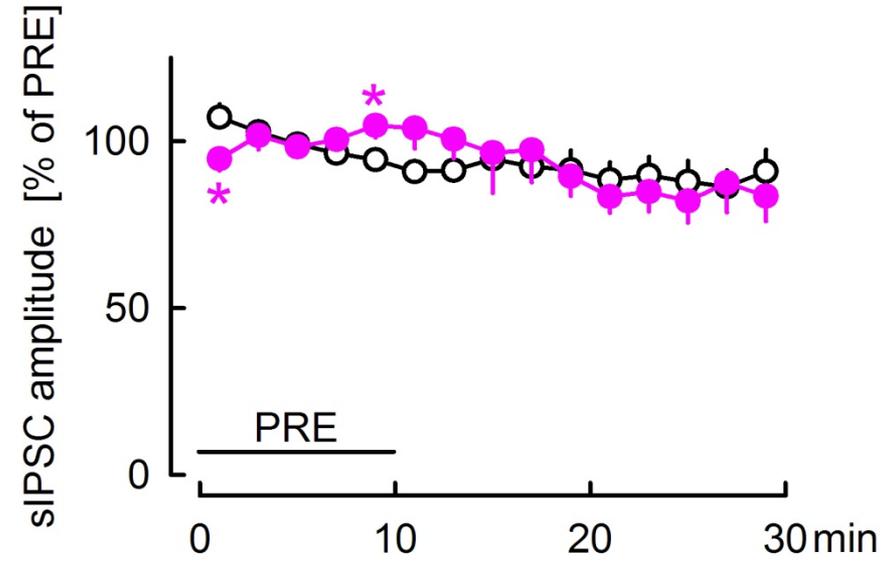
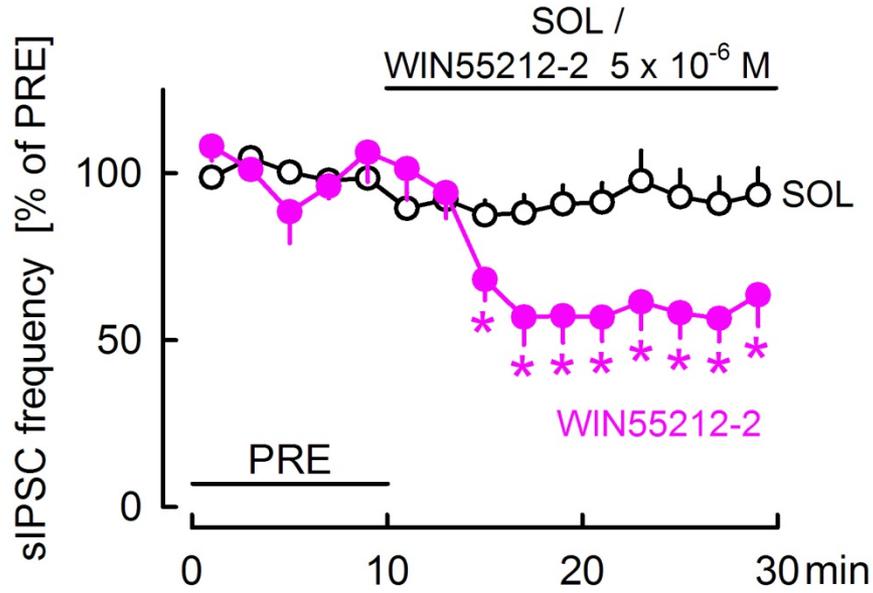
patch pipette

sIPSC recording
depolarisation

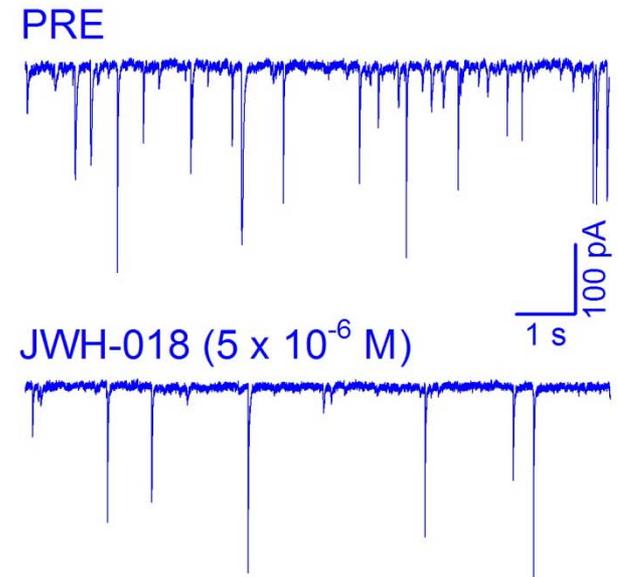
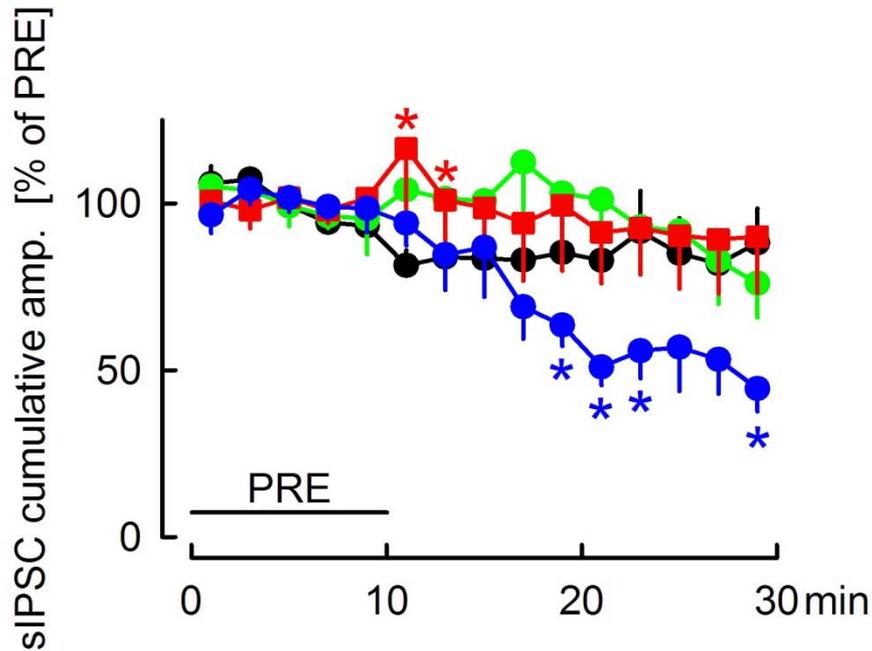
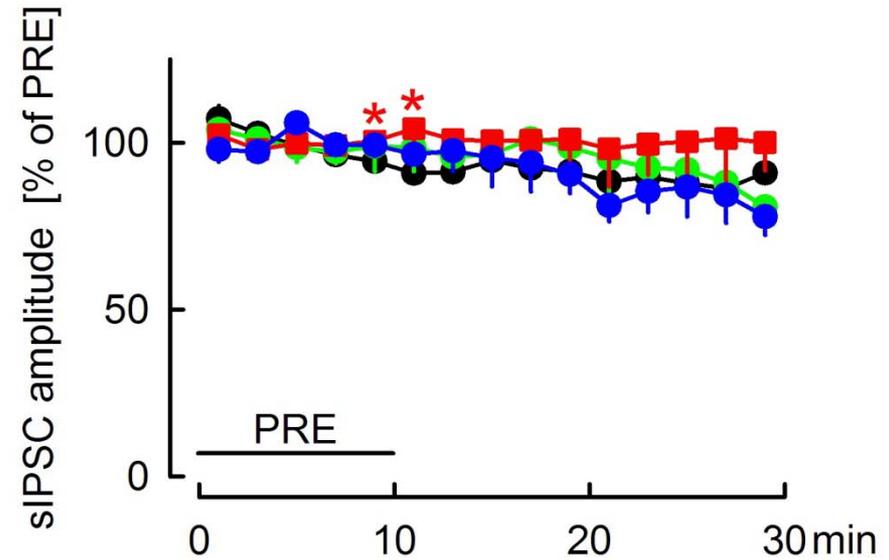
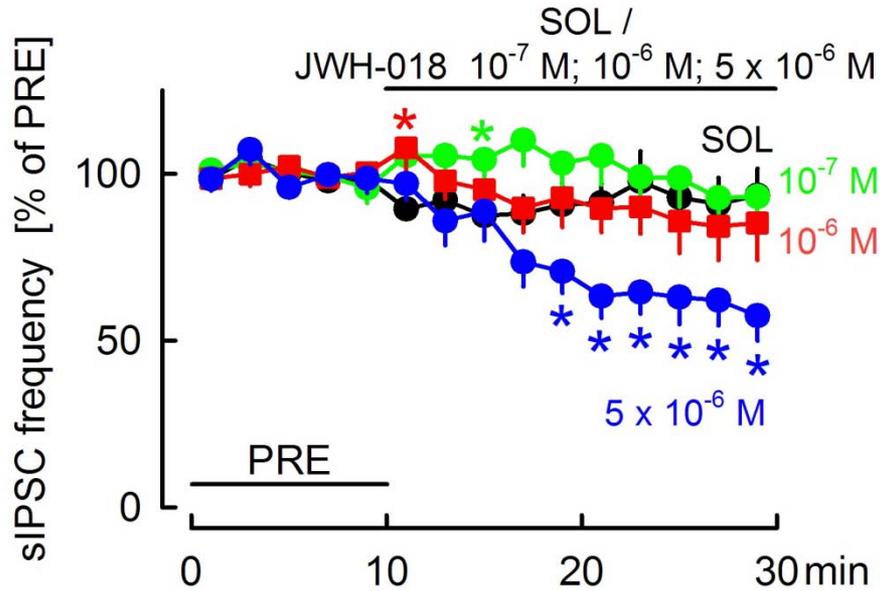


4) Synthetic cannabinoids inhibit synaptic transmission

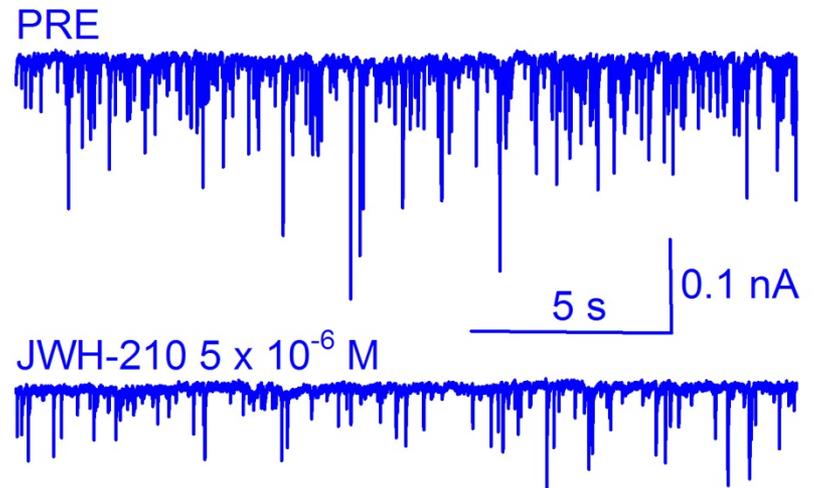
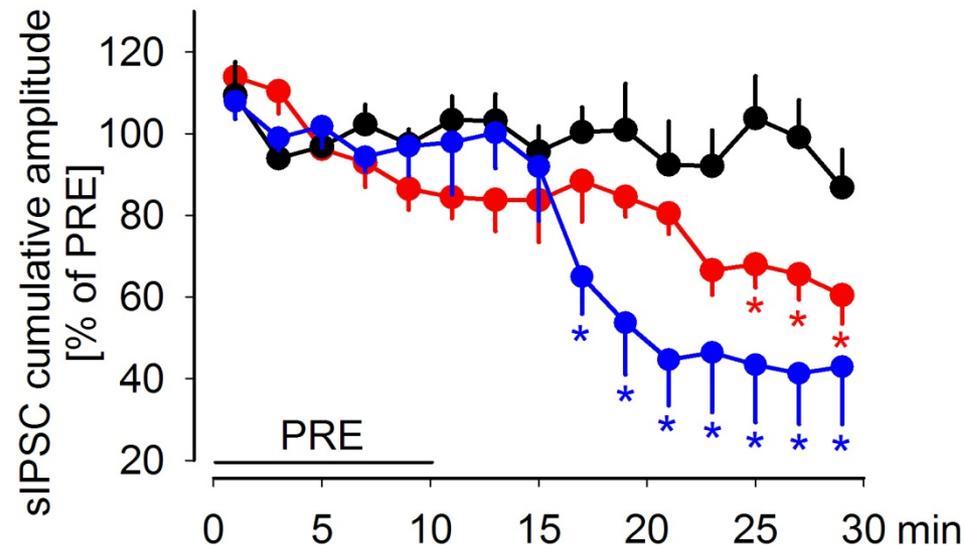
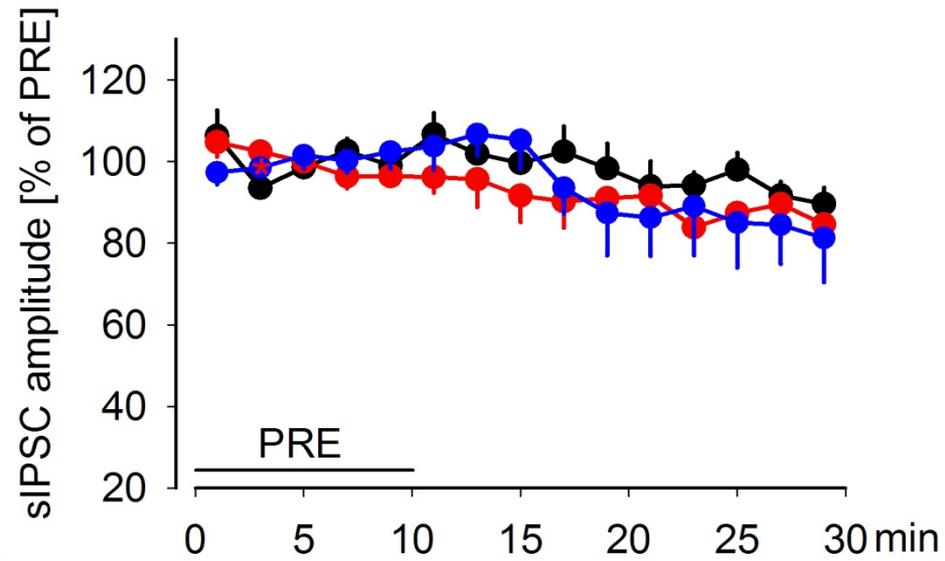
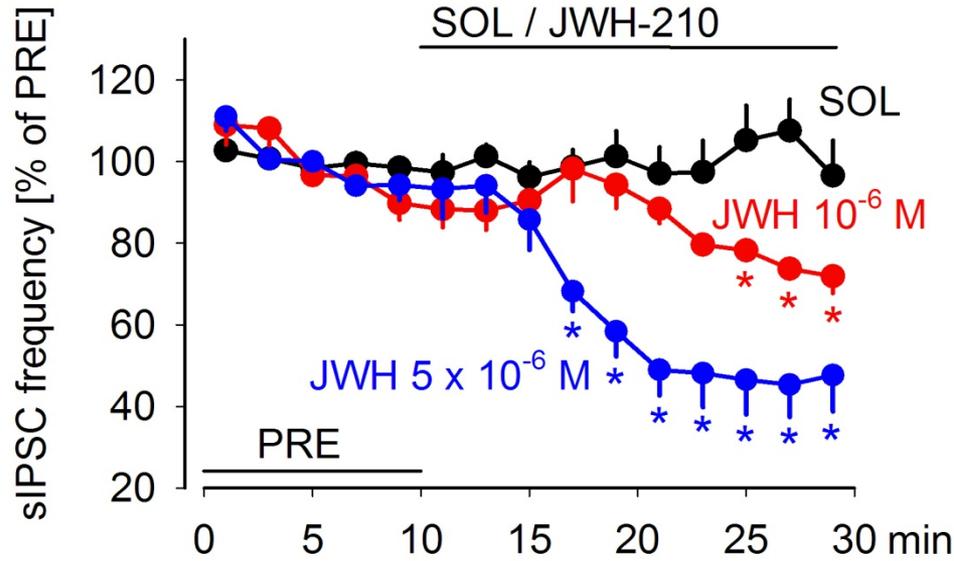
WIN55212-2 inhibits GABAergic synaptic transmission



JWH-018 inhibits GABAergic synaptic transmission

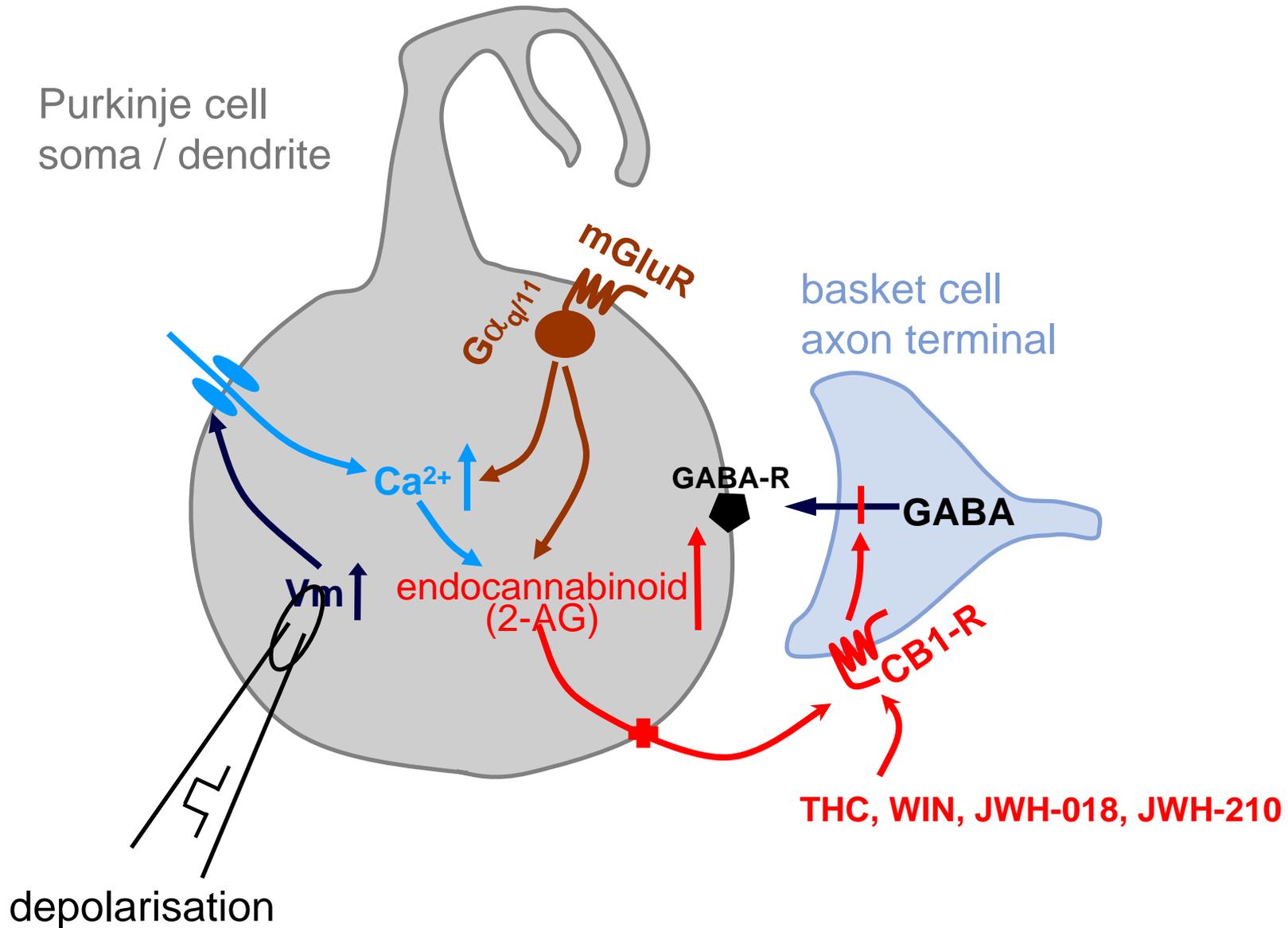


JWH-210 inhibits GABAergic synaptic transmission

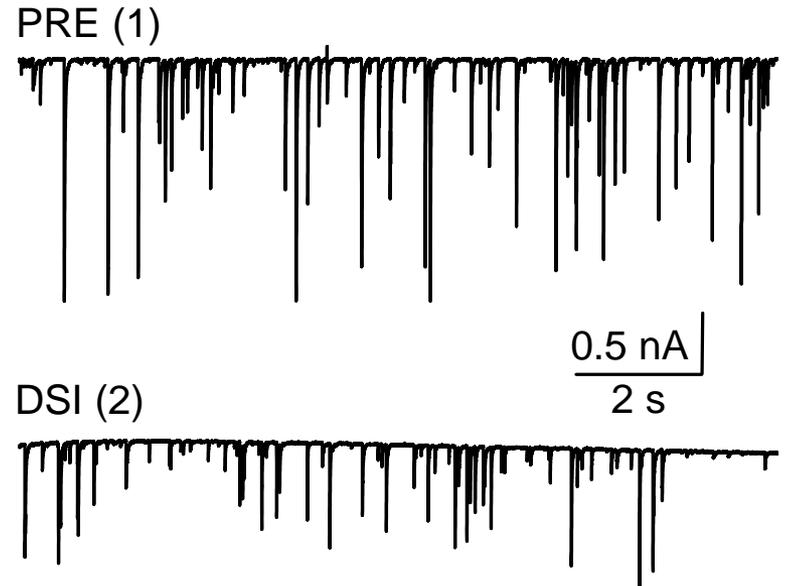
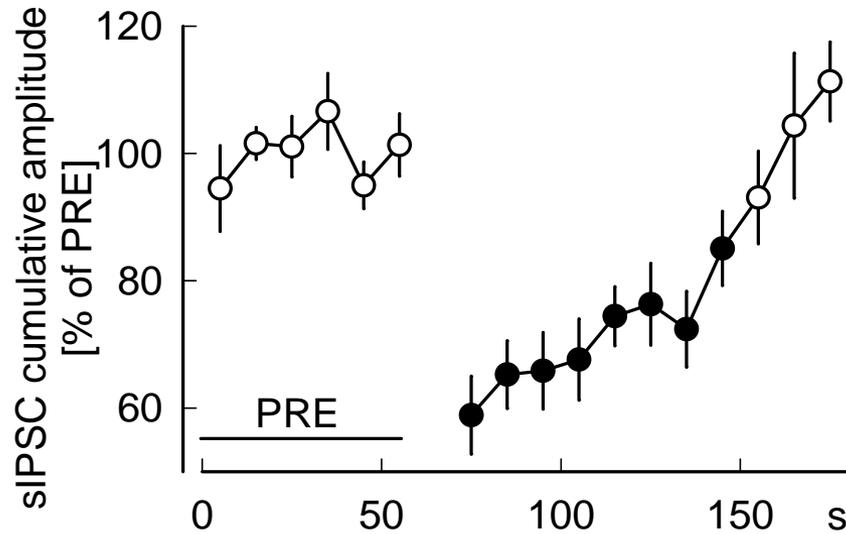
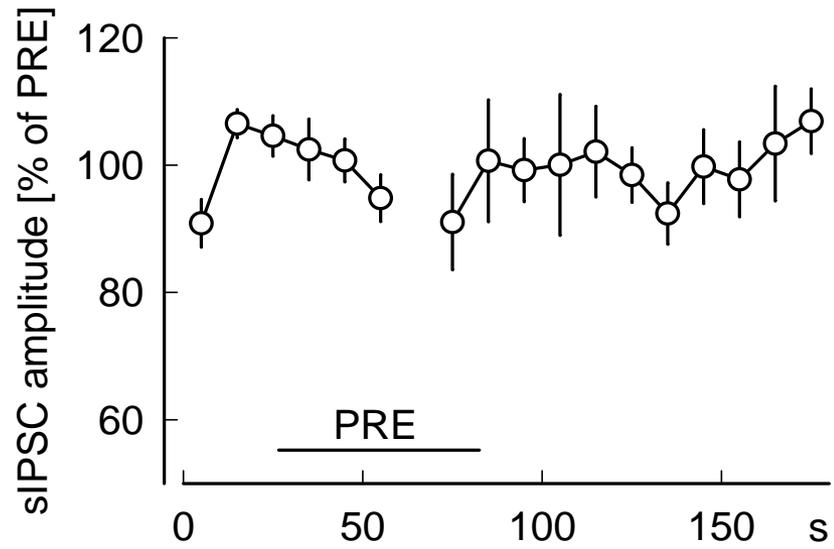
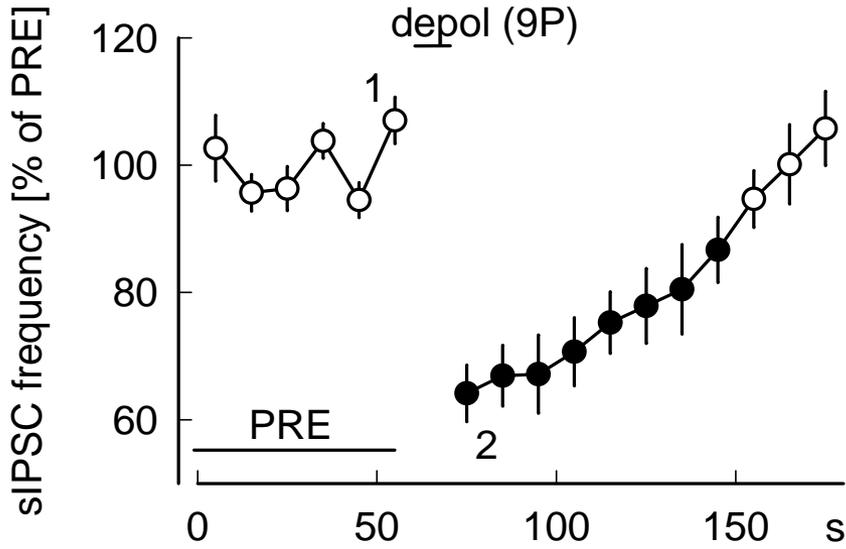


5) Synthetic cannabinoids interfere with
endocannabinoid-mediated retrograde signal
transmission

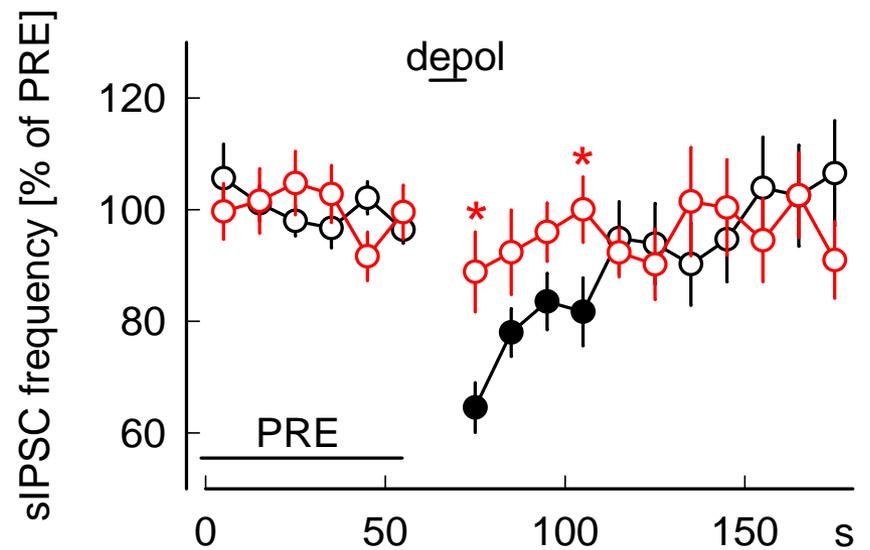
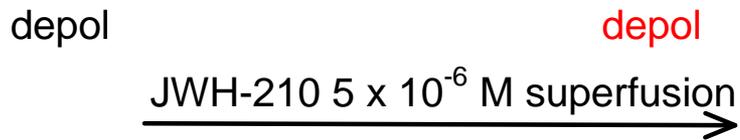
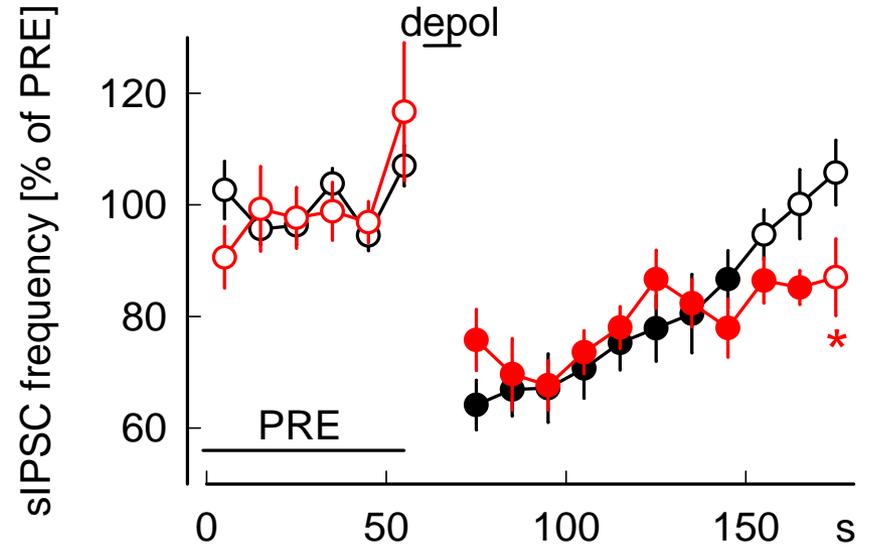
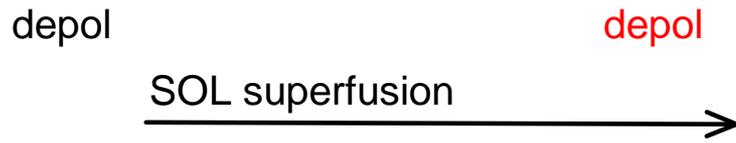
Retrograde signaling by cannabinoids



Depolarisation-induced suppression of inhibition (DSI)

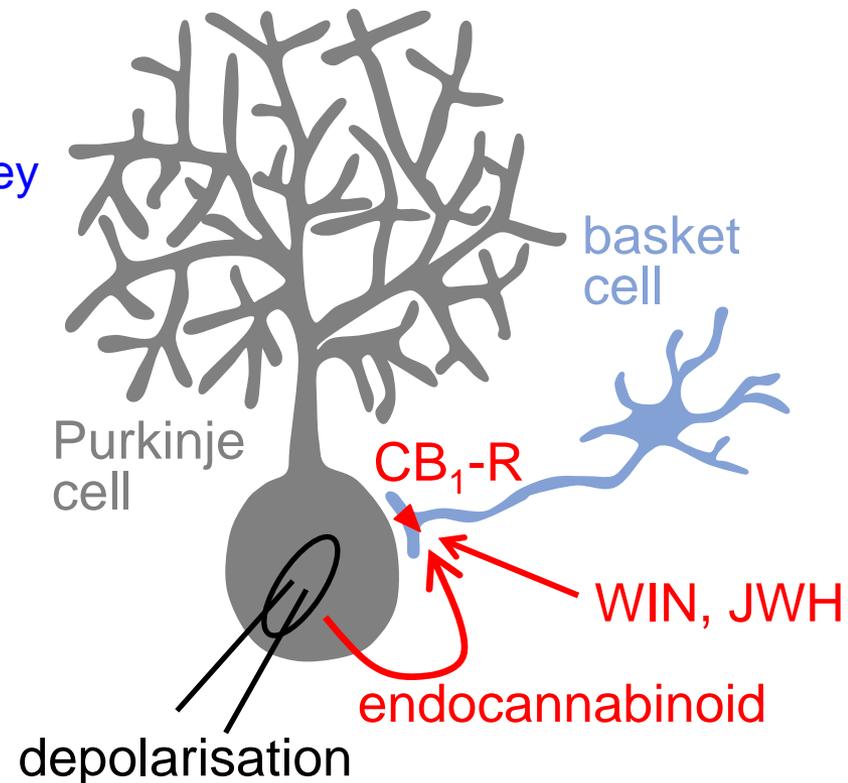


JWH-210 occludes DSI



Effects of synthetic cannabinoids, identified in smoked herbal products, on synaptic transmission in the brain

- 1) The synthetic aminoalkylindole cannabinoids WIN5512-2, JHW-018 and JWH-210 inhibit GABAergic synaptic transmission in the cerebellar cortex
- 2) The basis of the inhibition is very likely inhibition of GABA release from the presynaptic axon terminals
- 3) The synthetic cannabinoids occlude endocannabinoid-mediated retrograde signal transmission between neurons, indicating that they can interfere with elementary neuronal learning processes



End