Psilocybin selectively suppresses REM sleep in the Wistar Kyoto rat model of treatment-resistant depression

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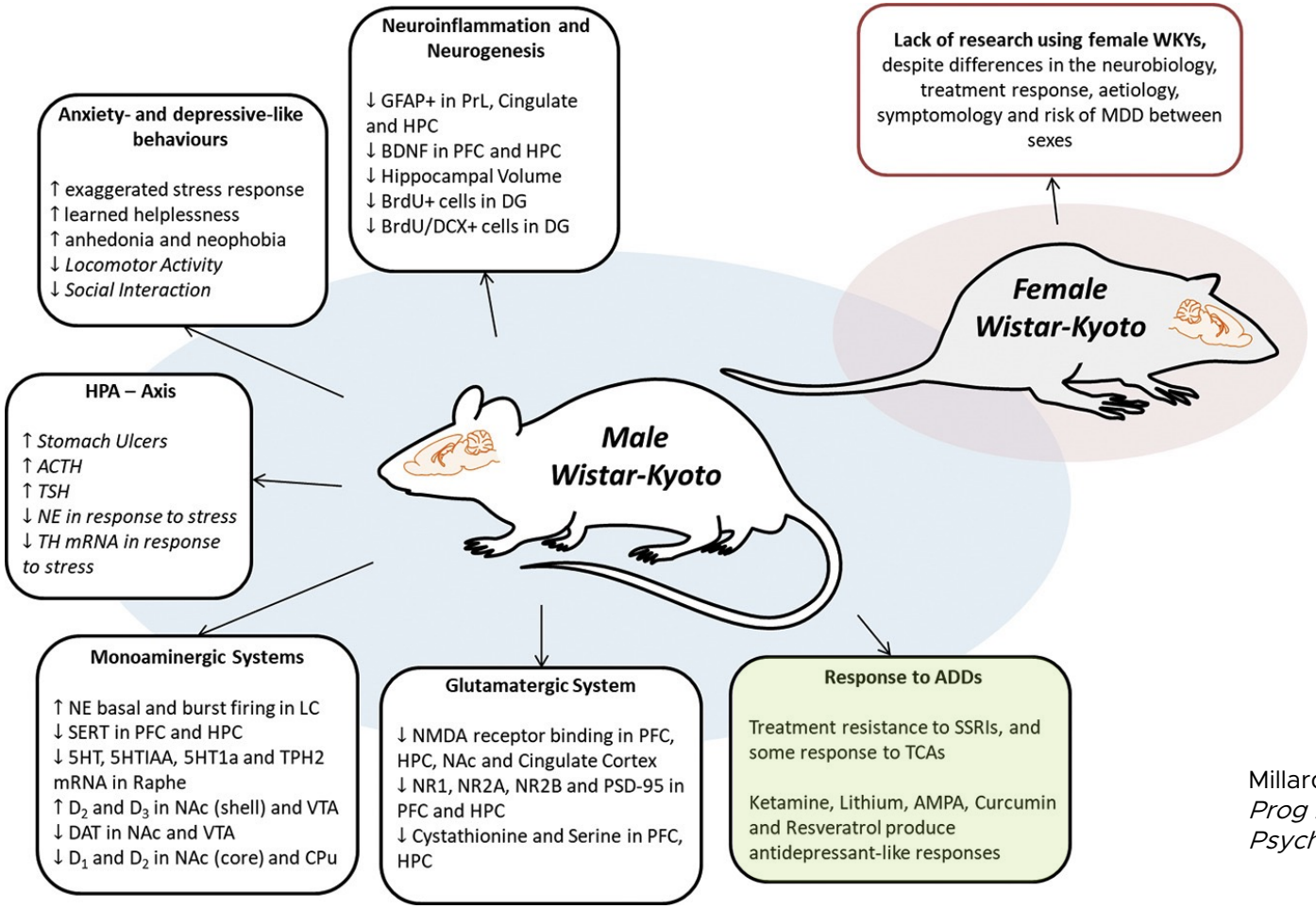
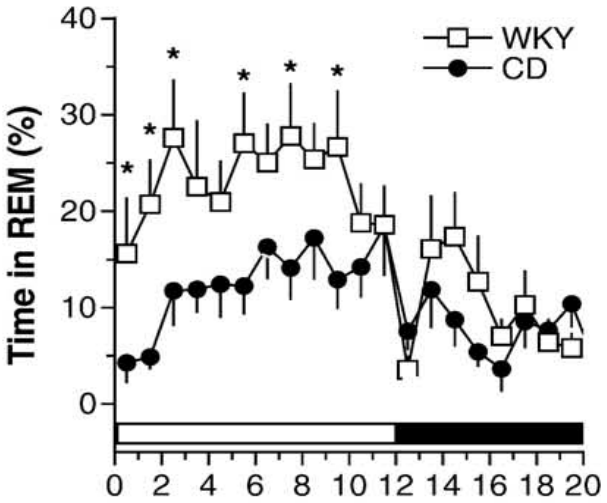
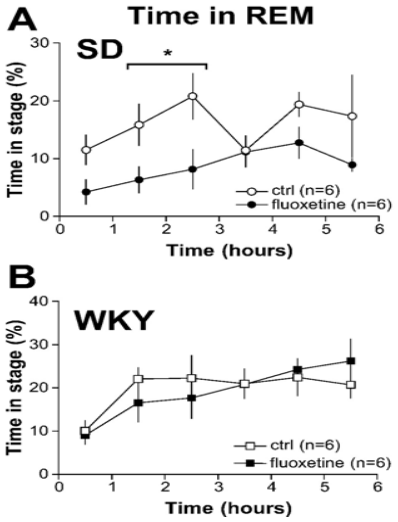
The Wistar-Kyoto (WKY) rat model of treatment resistant depression



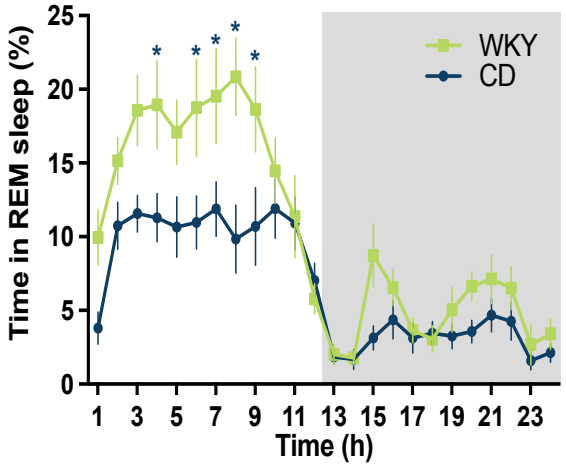
Millard, Weston-Green and Newell; *Prog Neuropsychopharmacol Biol Psychiatry* 101 (2020)

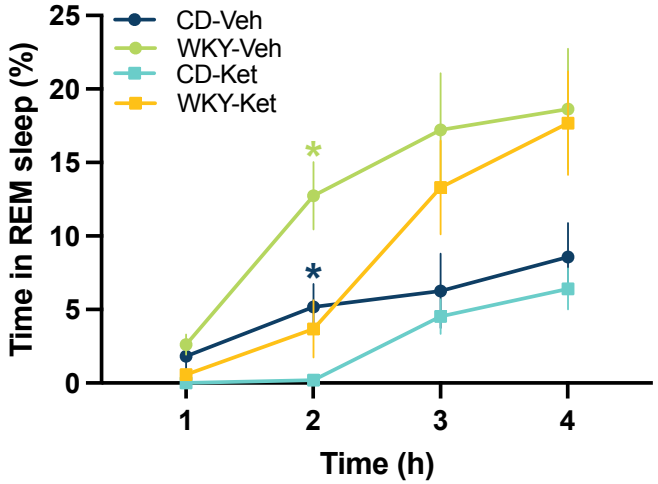
WKY rats have abnormally increased REM sleep that is suppressed by ketamine but not by SSRIs





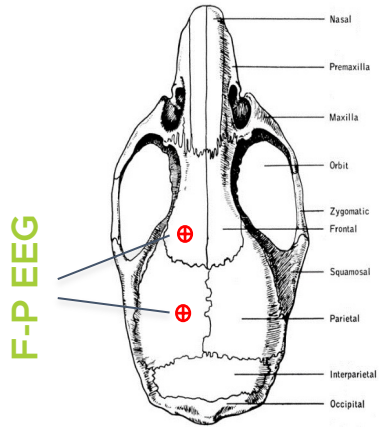
Ivarsson, Paterson and Hutson;
Eur J Pharmacol 522:63-71 (2005)



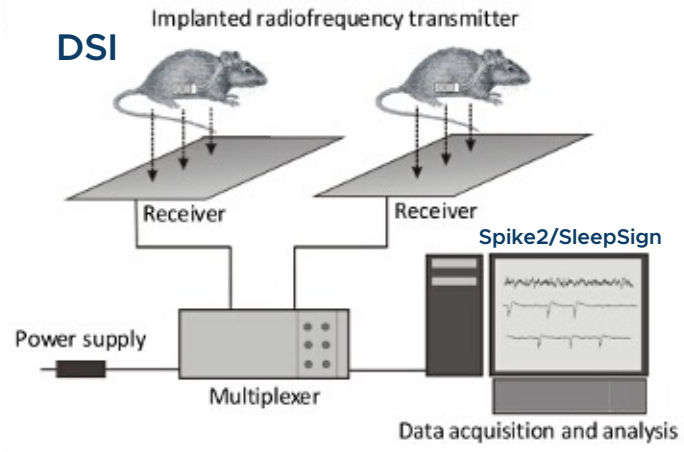


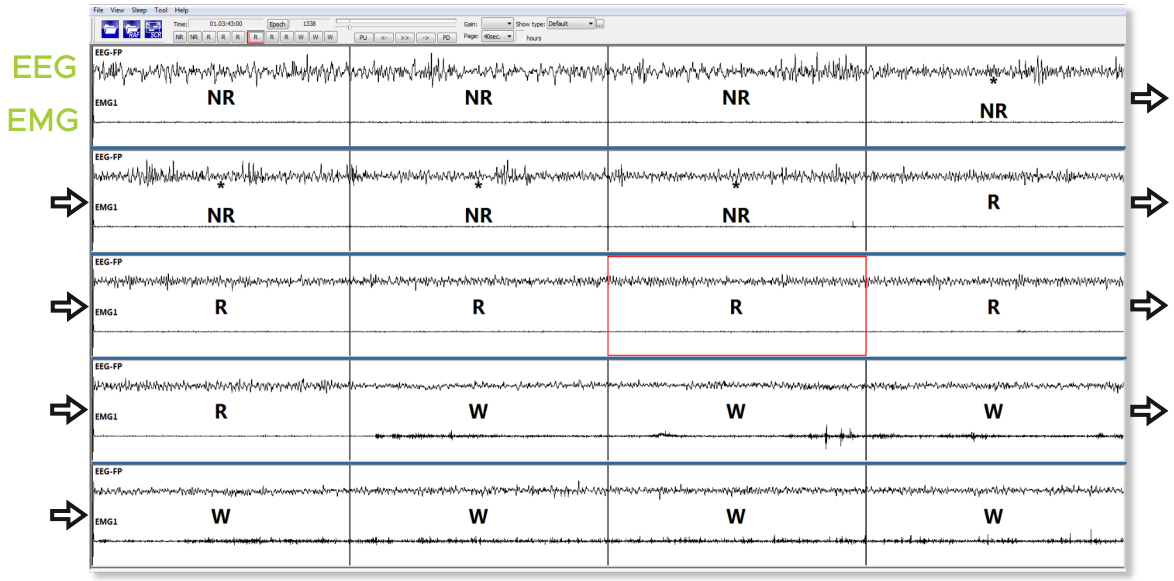
Upton, Duxon and Kantor;
SFN.org Neurosci Meeting Planner
289.27 (2019)

Sleep-wake behavior was recorded in SD and WKY rats after vehicle and psilocybin treatment



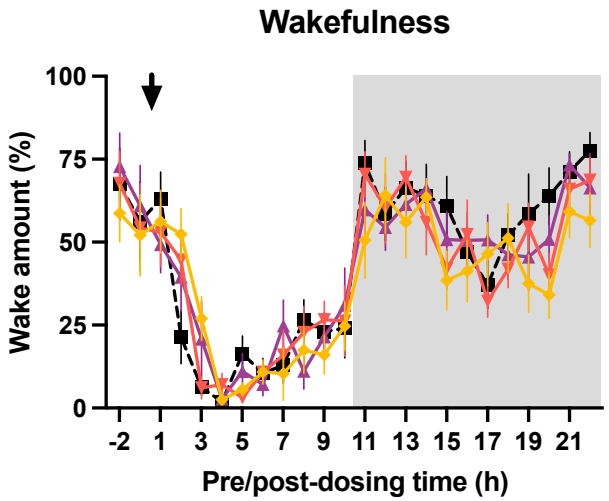
Test Article	Dose level	Dose Volume, Route	N
Vehicle*	N.A.	3 ml/kg, i.p.	8 SD / 8 WKY
Psilocybin	1 mg/kg	3 ml/kg, i.p.	8 SD / 8 WKY
Psilocybin	3 mg/kg	3 ml/kg, i.p.	8 SD / 8 WKY
Psilocybin	10 mg/kg	3 ml/kg, i.p.	8 SD / 8 WKY
*Saline			

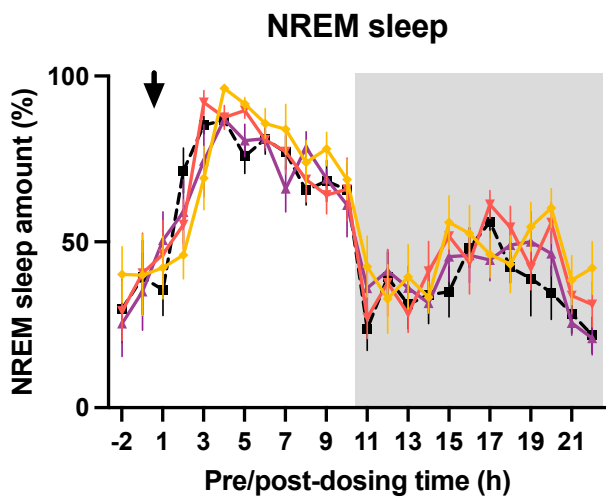


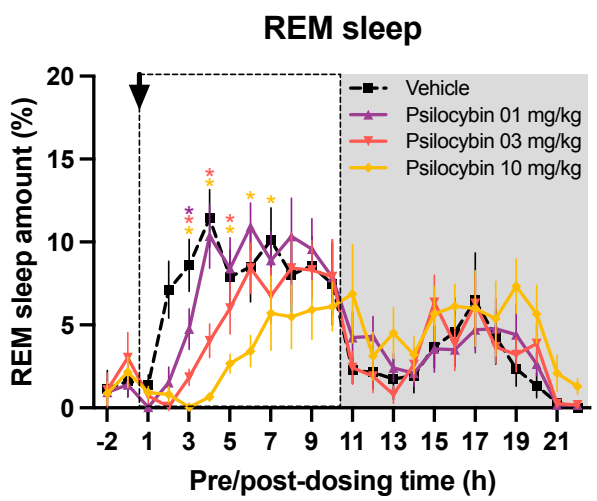


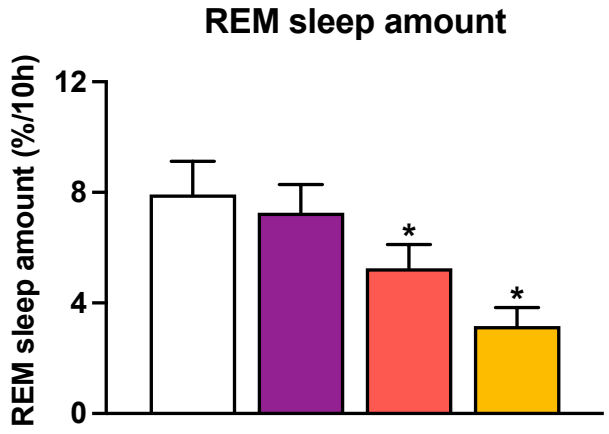
NR - NREM sleep, R – REM sleep, W - wakefulness

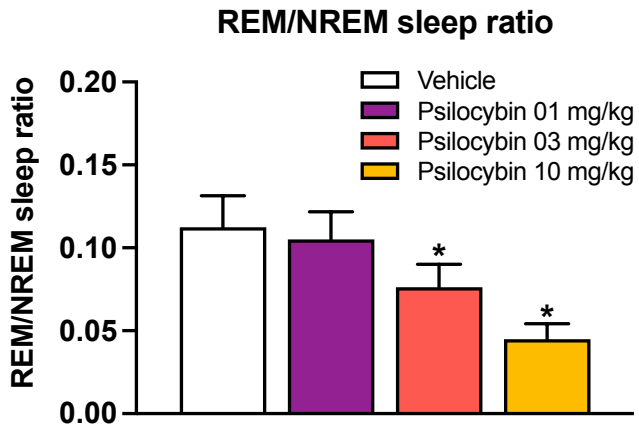
Psilocybin suppressed REM sleep in SD rats without affecting wakefulness or NREM sleep

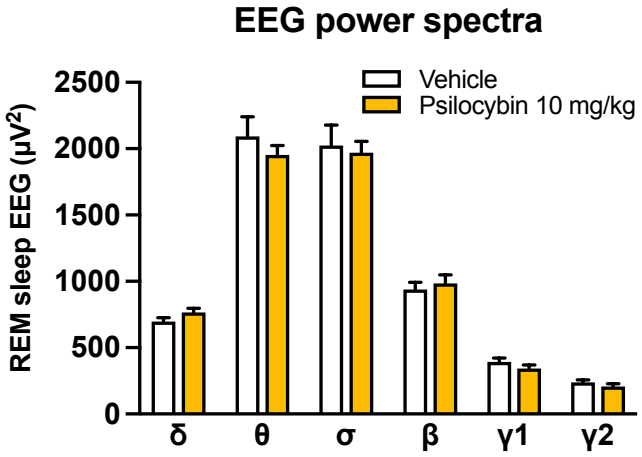








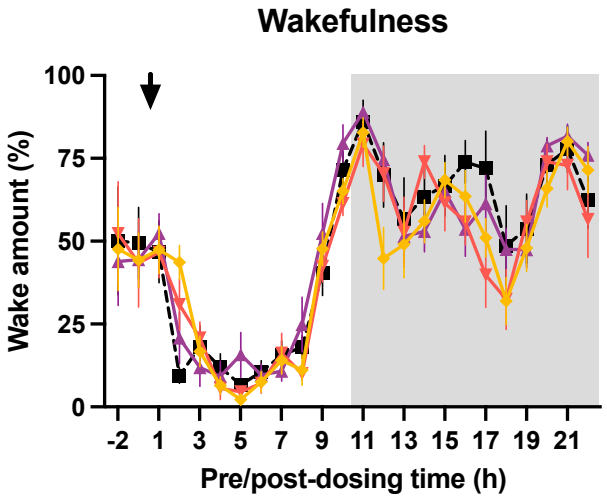


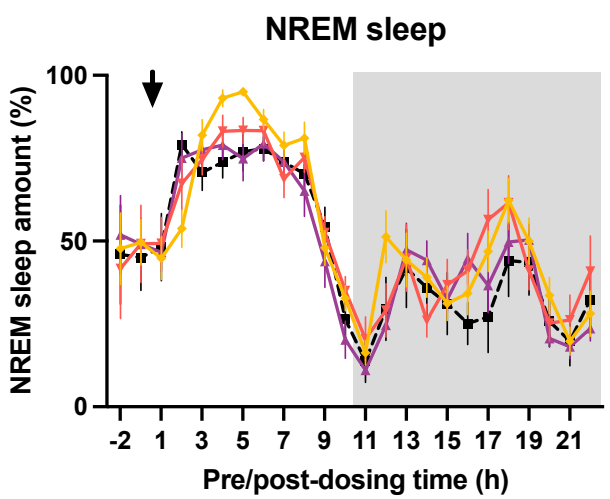


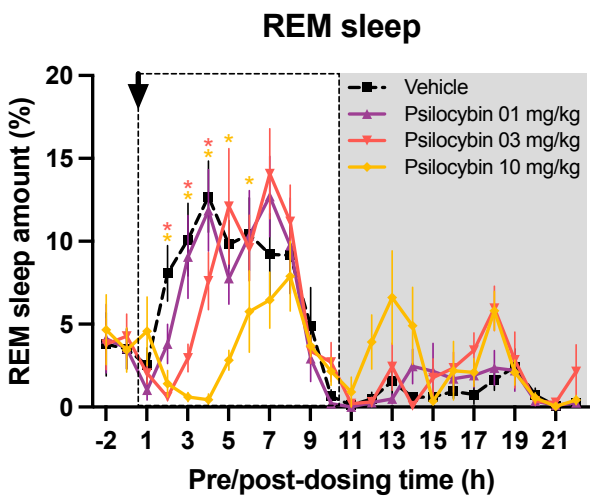
δ: 0.5-4Hz
θ: 4-10Hz
σ: 6-15Hz
β: 12-30Hz
γ1: 30-50Hz
γ2: 50-100Hz

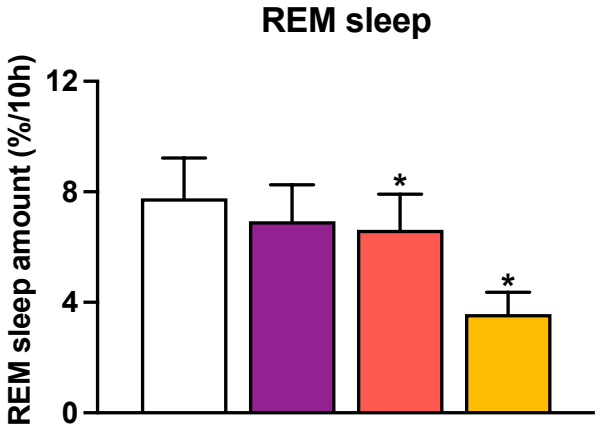
*p < 0.05 vs Vehicle treatment (Dunnett post-test)

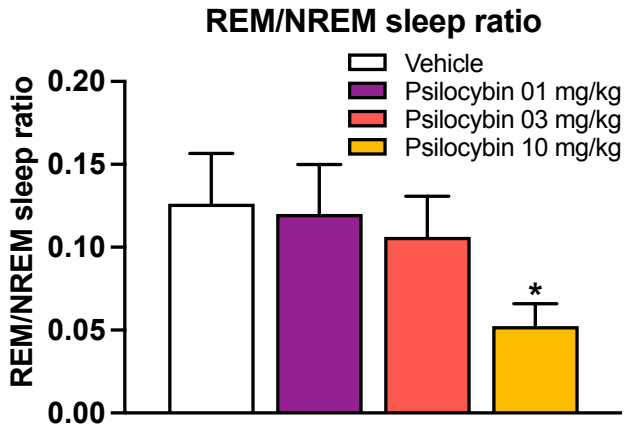
Psilocybin effectively and selectively suppressed REM sleep in WKY rats

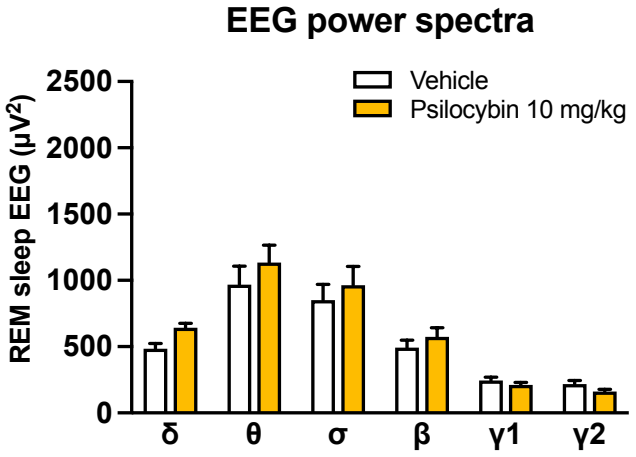












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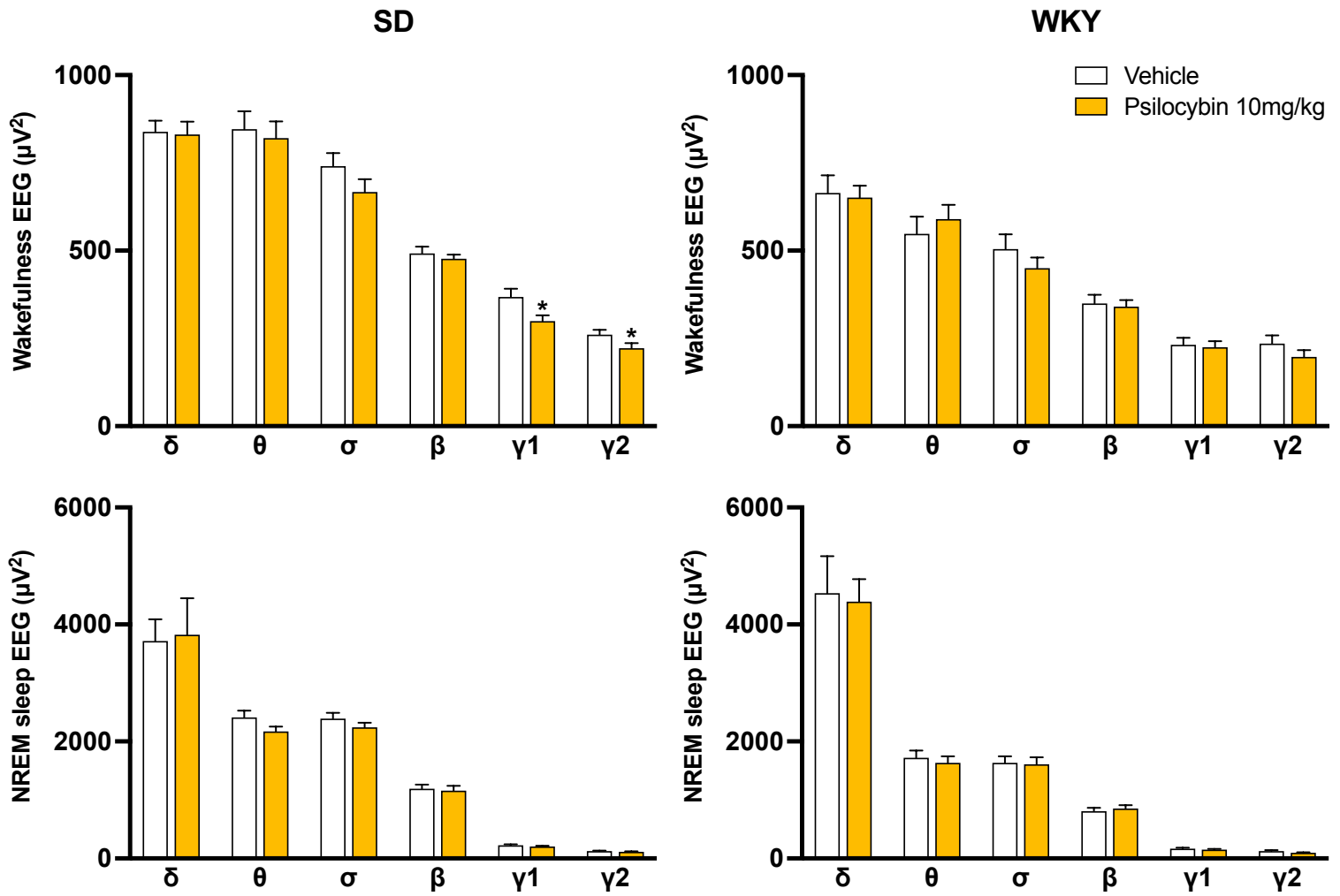
Psilocybin suppressed EEG gamma oscillations during wakefulness in SD rats



δ: 0.5-4Hz
θ: 4-10Hz
σ: 6-15Hz
β: 12-30Hz
γ1: 30-50Hz
γ2: 50-100Hz

*p < 0.05 vs Vehicle treatment (Dunnett post-test)

Conclusions

- Suppression of REM sleep by antidepressants is one of the most consistent findings in patients with depression.
- Therefore, the decreased amount of REM sleep after psilocybin treatment could indicate antidepressant-like properties of the drug in WKY rats.
- Changes in REM sleep in WKY rats may serve as a key translational tool in an effort to discover novel therapeutics against TRD.

Thank you

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