

# Paradoxical Wakefulness: Inducing slow oscillations during wakefulness through psychedelics in mice

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## INTRODUCTION

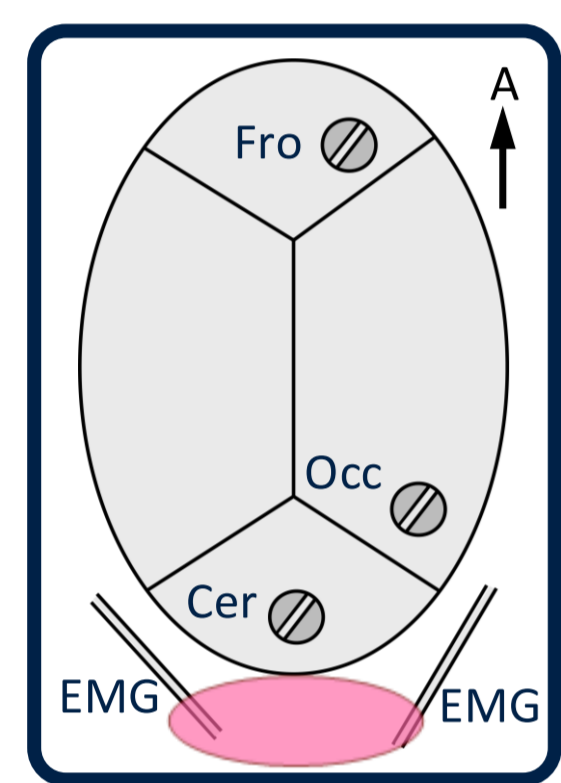
Vigilance states are defined using state-specific markers measurable with an electroencephalogram (EEG) or an electromyogram (EMG). For instance, the EEG during wake shows fast activity of low amplitude with and active EMG. During slow wave sleep, the EEG shows slow activity of high amplitude with a low EMG.

In rodents, the sleep wake cycle can be altered with 5-HT psychedelics notably through a significant suppressing of paradoxical sleep and increasing sleep fragmentation.<sup>1,2</sup>

Psychedelics can also promote EEG sleep-like slow wave activity (0.25 – 4 Hz) during wakefulness, resulting in a hybrid state of vigilance.<sup>1</sup>

These observations suggest that psychedelics control the quality of specific sleep-wake state rather than the quantity. However, little remains known on how much these modulations share with sleep regulatory processes.

## METHOD

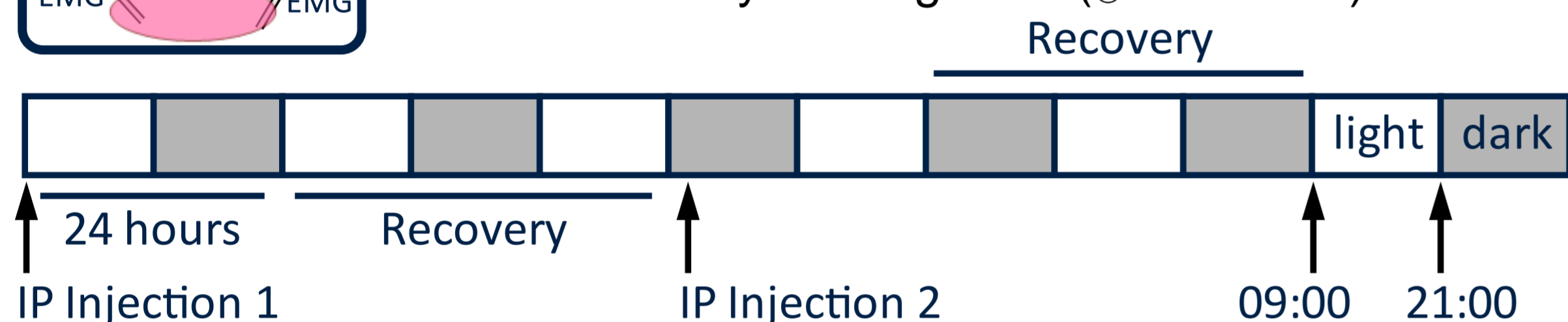


### Injections:

- 5 mg/kg 5-MeO-DMT (1 mg/mL saline)
- Vehicle: 5 ml/kg saline

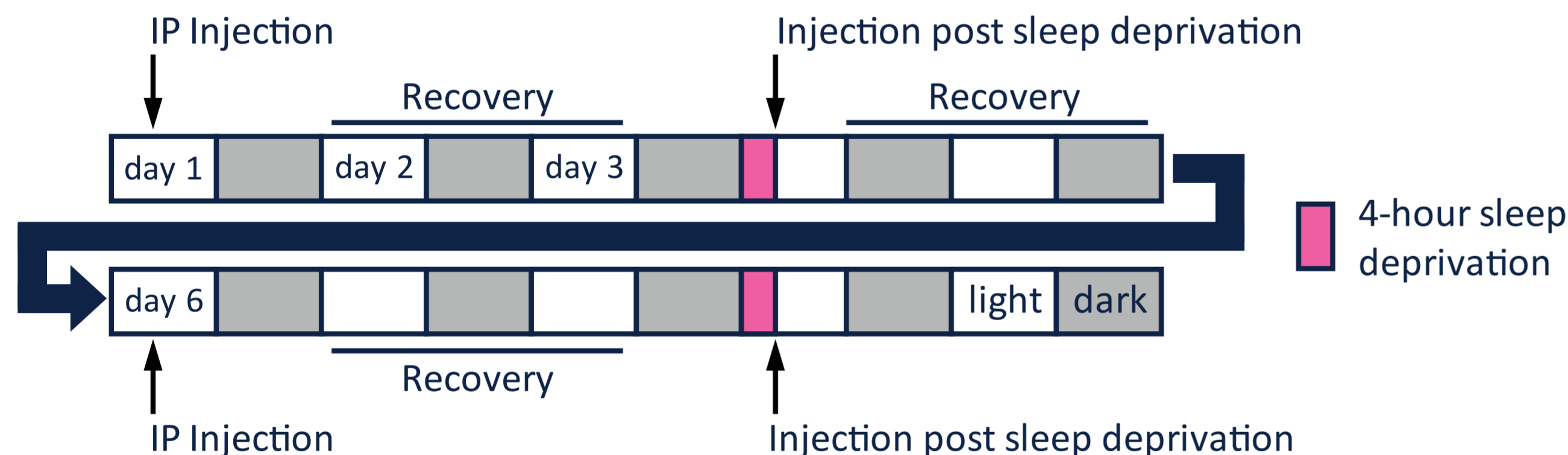
### Simple recording protocol

- n = 7 freely-moving mice (♂ C57Bl/6J)

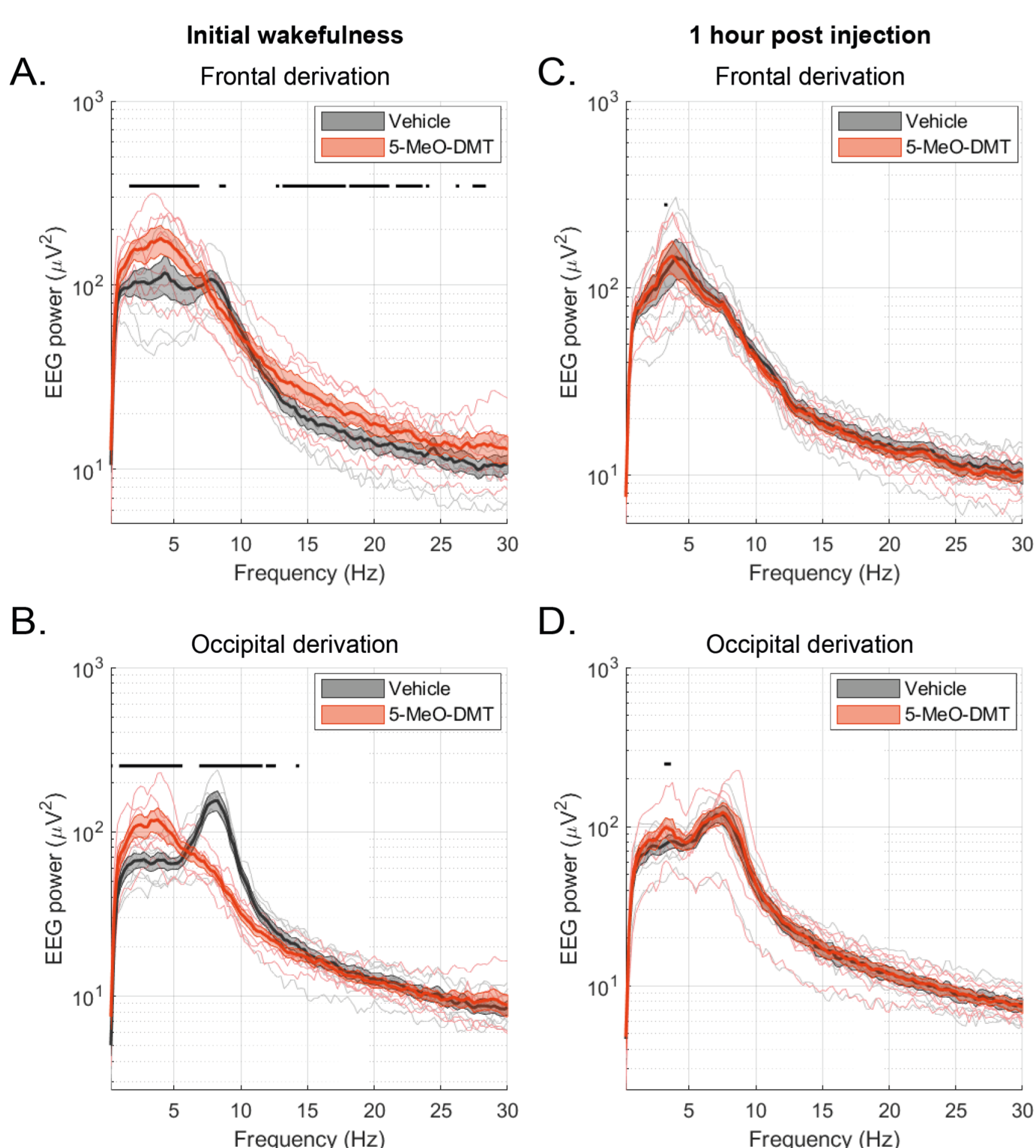


### Sleep deprivation protocol

- n = 7 freely-moving mice (♂ C57Bl/6J)



## 5-MeO-DMT alters wake EEG

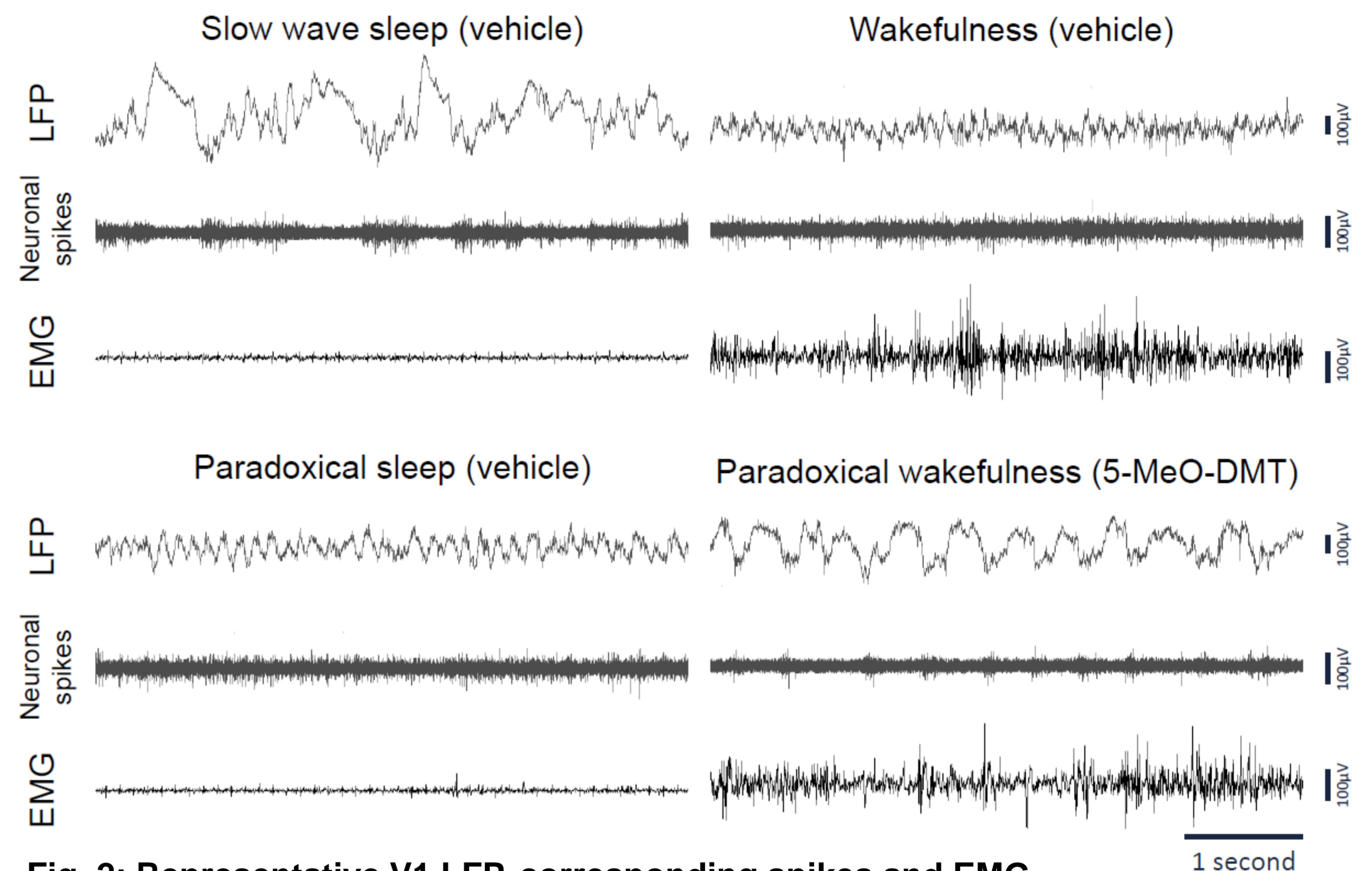


**Fig. 1: EEG power spectra.** Black horizontal lines denote a significant difference between the two conditions at a given frequency. **A-B.** During the initial wake episodes following an injection in the frontal (A) and occipital (B) derivation. **C-D.** During wake episodes occurring 1 hour following an injection in the frontal (C) or occipital (D) derivation. *Note the significant increase in slow frequencies in both derivations and decrease in theta frequency in the occipital derivation.*

## REFERENCES

1. B.J.B. Bréant et al., Acute paradoxical wake state induced by psychedelic 5-MeO-DMT in mice. *bioRxiv*. 2022
2. C.W. Thomas et al., Psilocin acutely alters sleep-wake architecture and cortical brain activity in laboratory mice. *Transl Psychiatry*. 2022;12(1), 77.

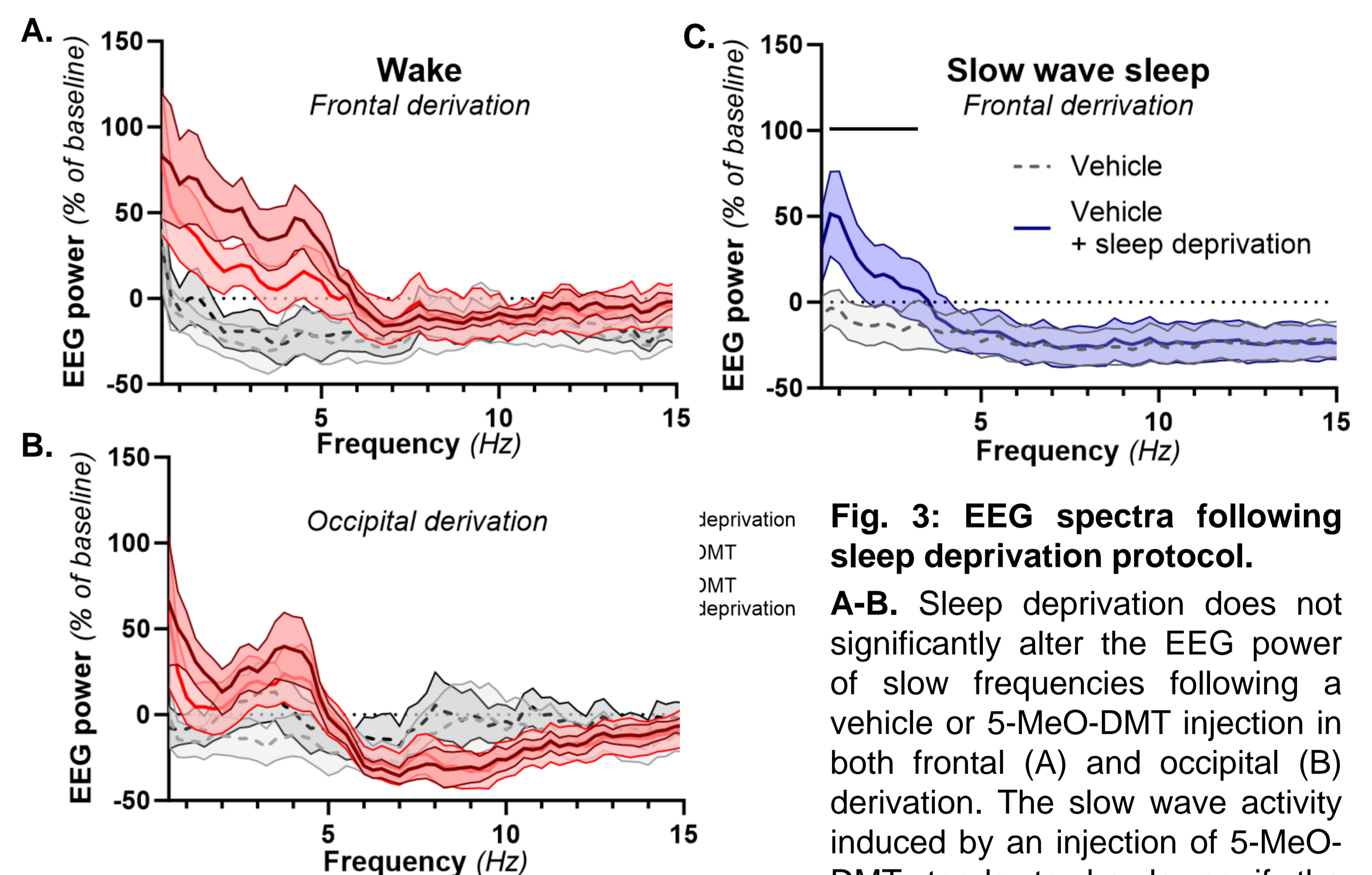
## 5-MeO-DMT induces sleep-like slow waves



**Fig. 2: Representative V1 LFP, corresponding spikes and EMG.**

Following 5-MeO-DMT injection, the mouse enters a state with clear markers of wakefulness, such as an active EMG denoting an animal behaviourally active. Paradoxically, LFP recordings and MUA shows off-periods, pattern of activity previously described during sleep. As Paradoxical Sleep is defined as a state with an inactive EMG corresponding to sleep and a wake-like EMG, Paradoxical Wakefulness is a mirror state, with sleep-like neuronal activity and an active EMG.

## Sleep pressure has low impact on wake slow activity



**Fig. 3: EEG spectra following sleep deprivation protocol.**

**A-B.** Sleep deprivation does not significantly alter the EEG power of slow frequencies following a vehicle or 5-MeO-DMT injection in both frontal (A) and occipital (B) derivation. The slow wave activity induced by an injection of 5-MeO-DMT tends to be lower if the injection follows a period of sleep deprivation. **C.** The same protocol of sleep deprivation significantly increases slow wave activity during slow wave sleep.

## CONCLUSION

- 5-MeO-DMT injections induces a sleep-like pattern of activity paradoxically in a behaviourally active animal.
- However, the activity of these sleep-like slow waves is not affected by sleep pressure in the same way true sleep slow waves are.

Paradoxical wakefulness is a short-lasting state of vigilance induced by 5-MeO-DMT and sleep pressure have little to no effect on the sleep-like features occurring during this state of wakefulness.

## ACKNOWLEDGEMENTS



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