Meta-analysis on ketamine/pharmacological-induced neuromodulation to increased burst mode

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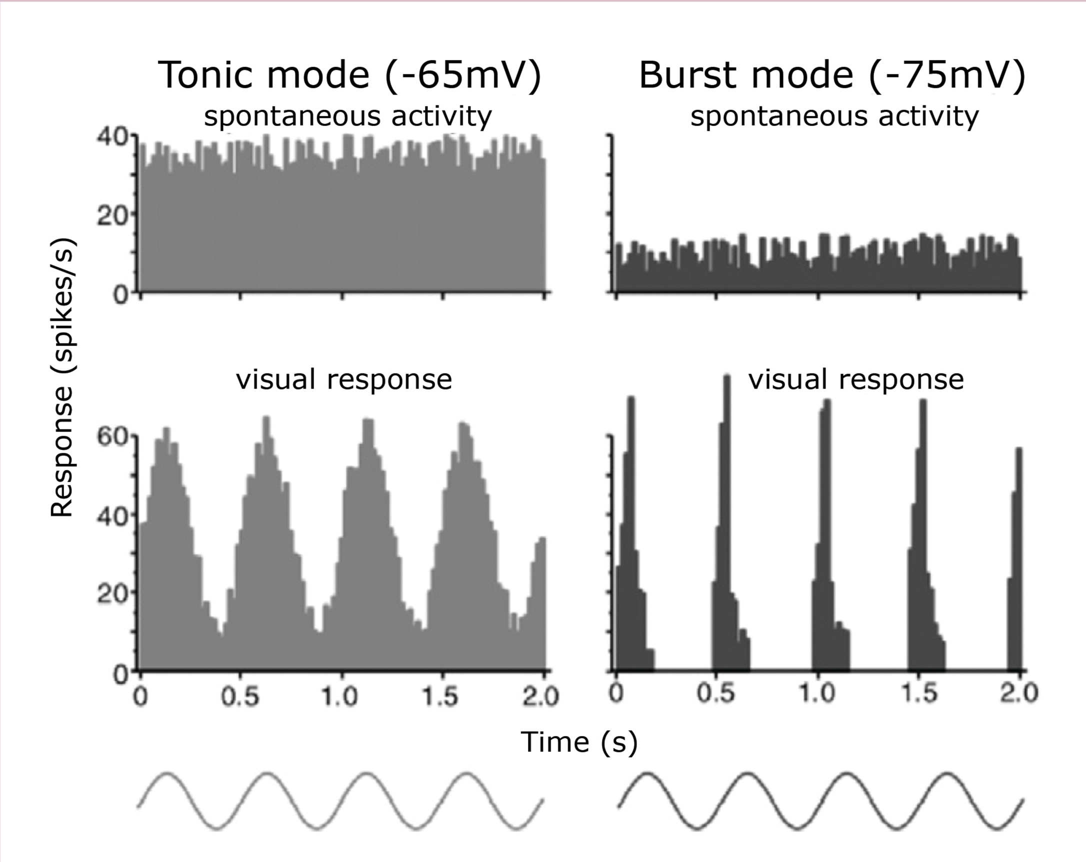
1. Increased **burst mode**: common effect across diverse agents (via hyperpolarization)?

Neurons with **T-channels** (thalamic relay cells)/**HCN-channels** (some cortical cells) switch to burst mode upon hyperpolarization. This bursting behavior has been associated with various pharmacological mechanisms, such as the **antagonism of NMDA receptors** (implicated w/ agents like *ketamine, alcohol, cannabinoids, and ibogaine*), the **agonism of GABA receptors** (e.g., by *muscimol and barbiturates*), and the **agonism of kappa-opioid receptors** (such as by *Salvia divinorum*).

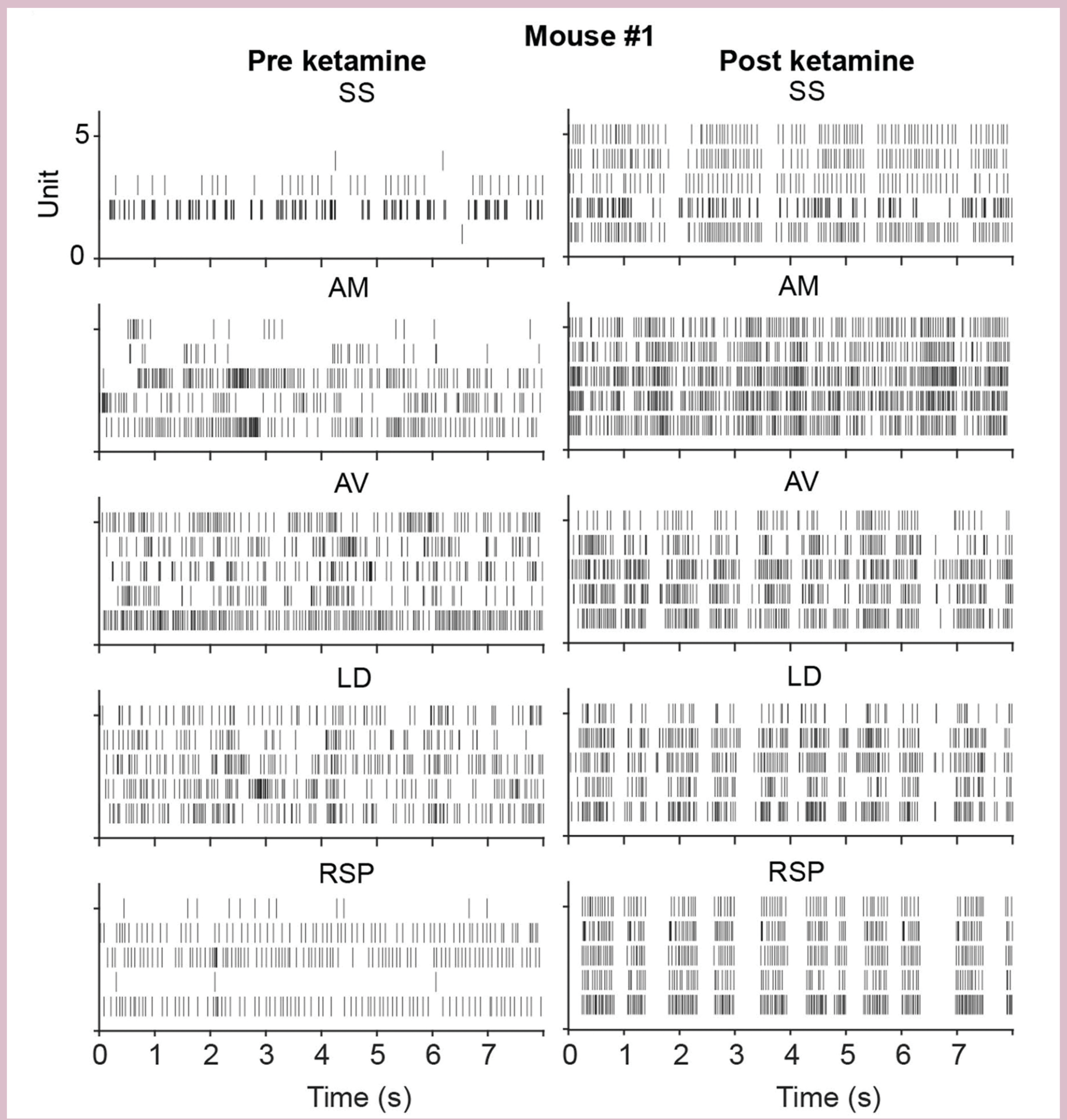
1a. Via **T-channels** in thalamic relay cells

Rodolfo Llinás and coworkers discovered that all relay cells in the thalamus have a sufficient density of T-channels to induce bursting upon hyperpolarization. Depicted here, artificial hyperpolarization was induced by electrode (cat LGN relay cell, bottom histograms depict a sinusoidal grating drifting through the receptive field).



1b. Via **HCN1-channels** in retrosplenial cortex

In the study "Deep Posteromedial Cortical Rhythms in Dissociation" by Deisseroth et al., it was discovered that ketamine triggers a burst mode of approximately **2 Hz** in layer 5 of the retrosplenial cortex (this phenomenon occasionally led to anti-correlation, such as between the somatosensory cortex and the retrosplenial cortex. The researchers propose that this might be associated with dissociative states, characterized by a temporary loss, to consciousness, of somatic input and control).



Vesuna, Sam, et al. "Deep Posteromedial Cortical Rhythm in Dissociation." Nature, U.S. National Library of Medicine, Oct. 2020, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7553818/. Paid use.

2. Does the **"frame + gap"** staccato experience (reported to a variety of hyperpolarizing agents) imply increased burst mode is a common cause?

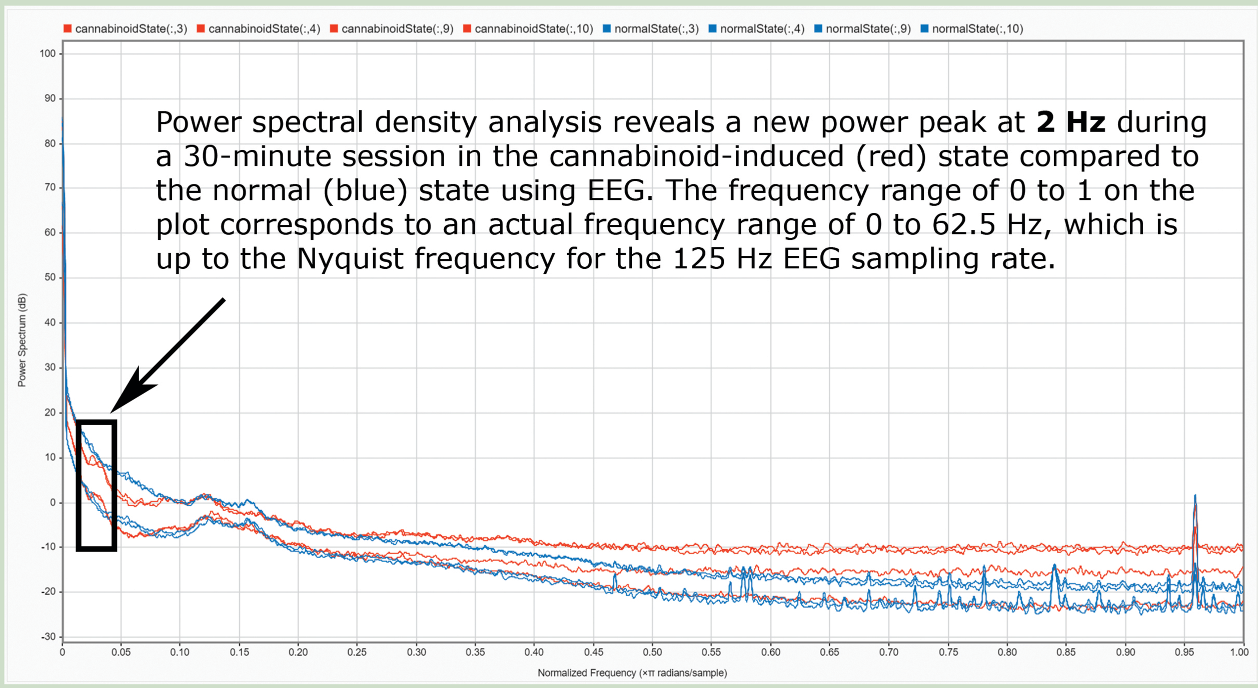
Many individuals, including from the general public and notable figures like Carl Sagan, have described conscious experiences as being segmented into frames and gaps, with frequencies ranging approximately from **1 to 12 Hz**, often around **2 Hz** (while in hyperpolarized, altered states). Given the similarity between these anecdotal reports and laboratory observations, this phenomenon warrants investigation as a potential connection between neural activity and phenomenal experience.

"Flash . . . Flash . . . Flash. The flashes came about once a heartbeat."
—*Carl Sagan*, https://www.organism.earth/library/document/mr-x.

During *burst mode gaps* in thalamic relay cells, sensory and attentional information fails to transmit, logically resulting in blackout periods where metacognition sees blackness (absence). A recent publication found that many relay cells in higher thalamus fire upon an attended stimulus, regardless of modality, suggesting that **conscious attention feeds through higher thalamus** just like sensory inputs do in lower thalamus.

Petty, G., & Bruno, R. M. (2024). Attentional Modulation of Secondary Somatosensory and Visual Thalamus of Mice. https://doi.org/10.1101/2024.03.22.586242.

Stroboscopic motion, ~12 Hz (cf. "frame + gap" experience). Shutterstock. Paid use.



FFT of EEG recordings suggesting induction of burst mode telegraphed through. Data obtained via OpenBCI 16-channel EEG electrode cap (processed with Matlab Analyzer).

2a. Pharmacological dose–response relation

Increasing doses of any of the mentioned pharmacological agents shows increasing response and apparently increased burst mode, both in laboratory observations, and in experience (**frames + gaps become more pronounced or evident**). Shown above is a relatively mild dose–level producing an observable, but mild, effect spectrally.

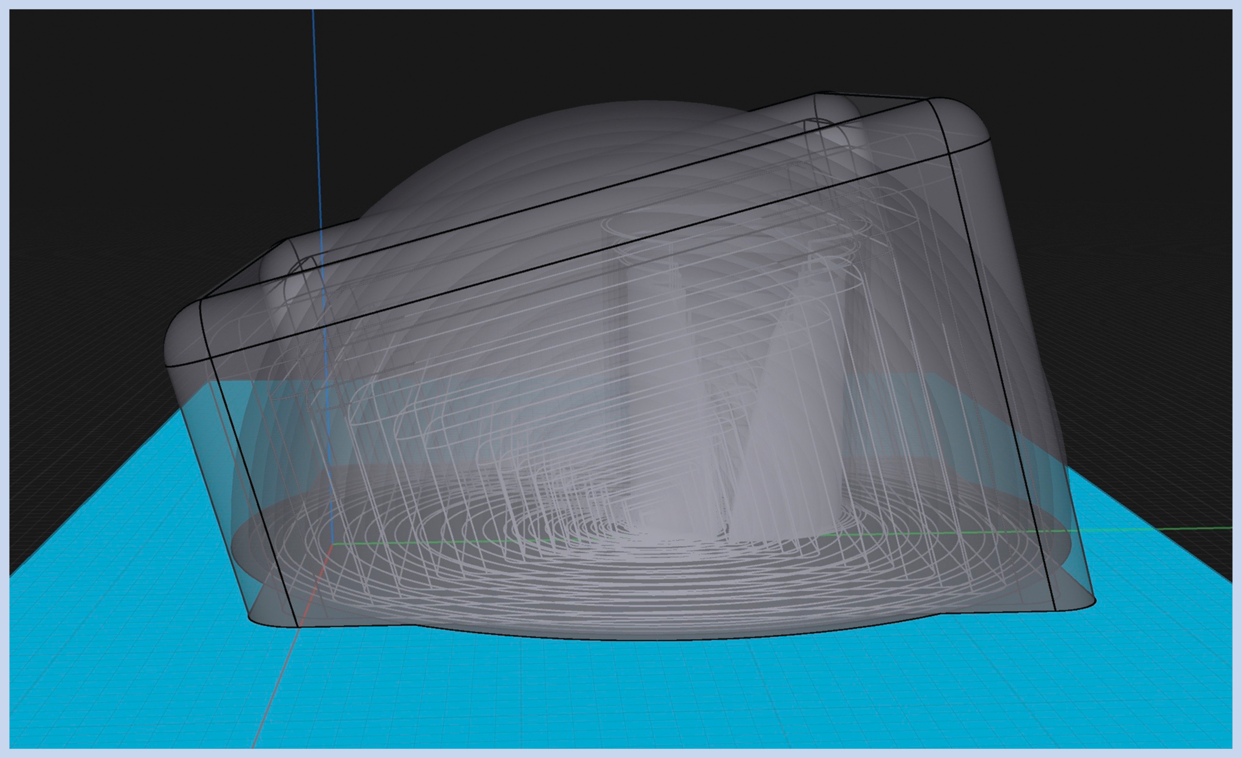
2b. Increase of cross-channel temporal synchrony at low frequency (~2 Hz)

Also observed in real-time EEG is **increased cross–channel temporal synchrony of EEG peaks** at low (~2 Hz) frequency. This seems to be a fairly well–observed phenomenon, that **lower frequencies of LFP go hand-in-hand with more globality of synchrony**. In summary, the idea is that perhaps just as burst mode highlights the timing of gratings drifting past a visual receptive field, so it reveals the timing of attention frames as outlines/surfaces, drifting or walking through perceptual space, which are fed into higher thalamus for metacognitive observation.

3. Are clues to **conscious mechanisms** seen in the **"frame + gap"** experience, such as the locational/morphological aspects of attention, as well as subliminal schema dynamics?

Carl Sagan proposed that "frame + gap" experiences might reveal the mechanisms of conscious experience. Embracing the idea that our perceptions are brain-constructed within a representational space, as supported by David Eagleman, leads to discovering that attention/rendering inherently involves translation, scaling, rotation in 3D, and morphing. These dynamics are pivotal for the rendering process, facilitating focus transitions from bodily posture to visual objects, to precise actions like striking a shuttlecock in Badminton, illustrated centrally. This suggests that our *conscious experience is most vividly rendered through a series of rotating, translating, and morphing content-linked outlines.*

Building on this, I suggest the concept of an attention **"bank"** schema, responsible for maintaining the morphological memory of these focal outlines/surfaces. Additionally, a **"fusing"** schema could underpin the spatio-temporal integration of attention with awareness, serving as a *"flowing time window,"* with a typical span of 0.1 to 3 seconds.



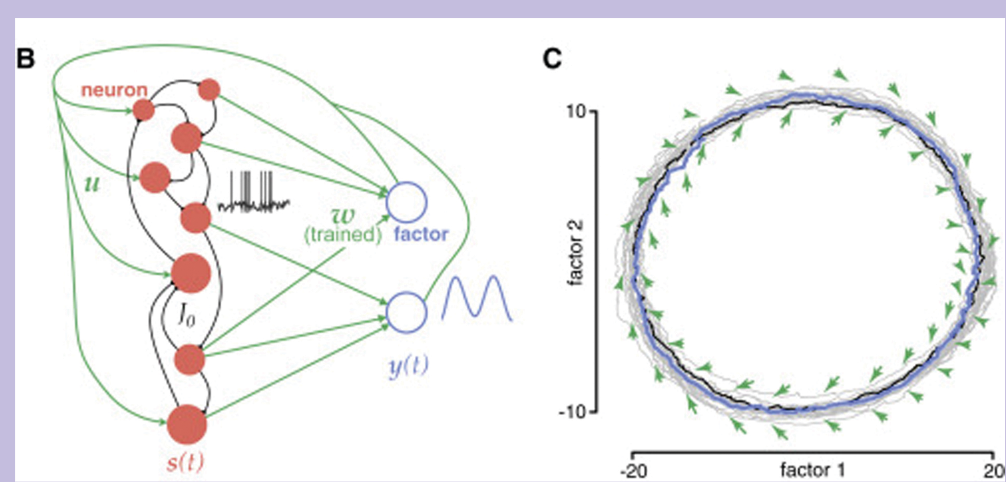
Depiction of proposed **"bank"** schema. All shape understanding is thought to be stored in this separate schema which carries attention within and across schemas (such as reality schema and imagination type schemas, used for understanding music, speech, and abstract thought). It is thought to "print" the frames of consciousness in an all-integrating "fusing" schema.

4. Explanatory power of **brain RNNs** if their **latent space** is what constitutes consciousness

Recurrent neural networks (RNNs) possess the notable ability to form **attractors** that embody abstract limit cycles, integrating present inputs with future states.

Envisioning consciousness as the emergent latent space of the brain's RNNs offers intriguing solutions to several longstanding problems in cognitive neuroscience: the binding problem of integrating multiple sensory inputs, the agency problem of initiating action, and the driving force of meaning within mental imagery on behavior.

Distinct but interlinked RNNs may be specialized for handling real-world sensory input, various modes of imagination, and shape information, all orchestrated by working memory. The integrated activity across these networks could culminate in a coherent, unified conscious experience. This framework can also account for phenomena like dissociation and the experiences of split-brain patients, suggesting scenarios where these RNNs become compartmentalized or siloed.



Depiction of how recurrent neural nets can learn attraction to trajectories and shapes.
DePasquale, B., Sussillo, D., Abbott, L. F., & Churchland, M. M. (2023). The centrality of population-level factors to network computation is demonstrated by a versatile approach for training spiking networks. Neuron, 111(5). https://doi.org/10.1016/j.neuron.2022.12.007