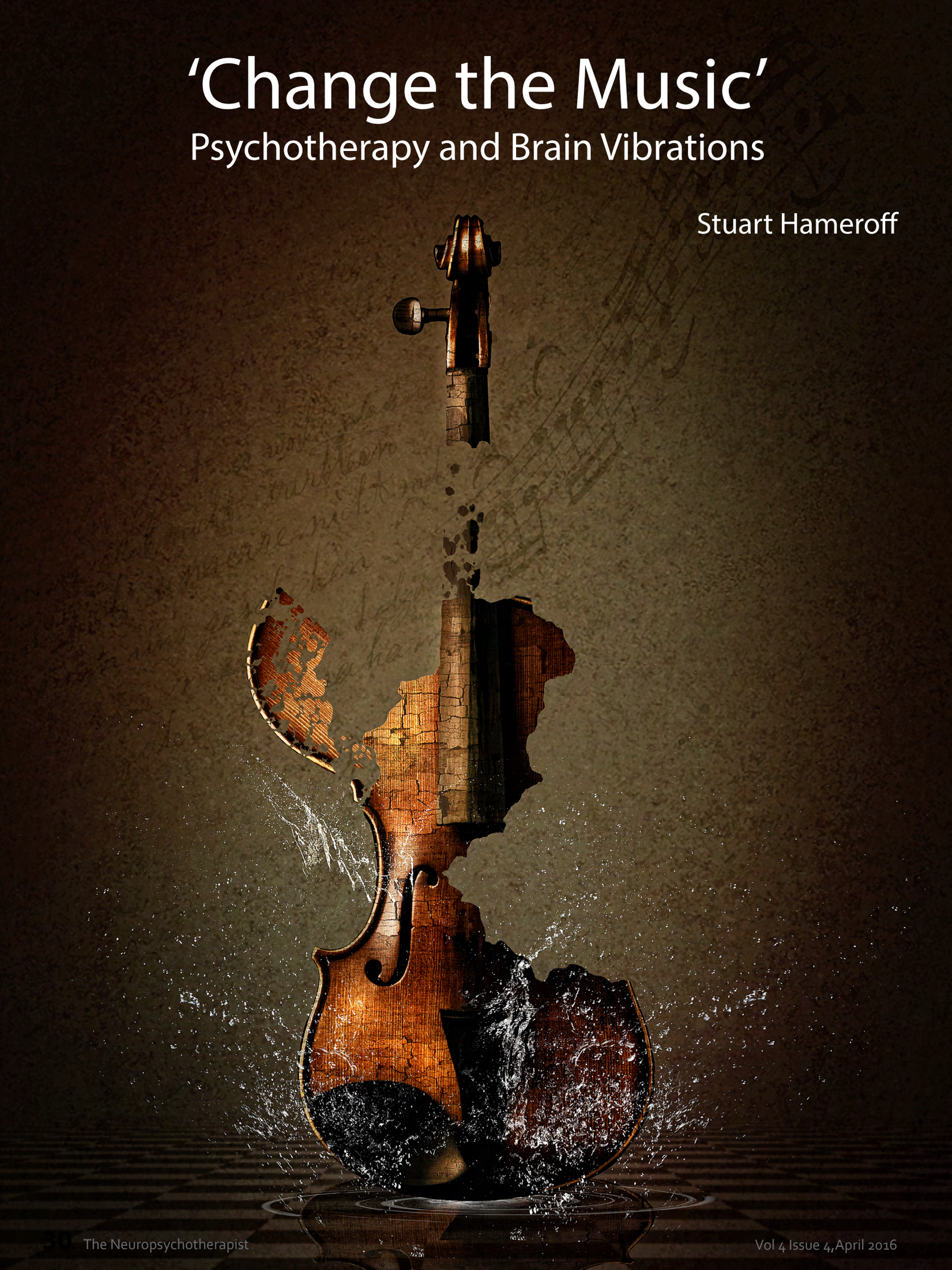
‘Change the Music’

Psychotherapy and Brain Vibrations

Stuart Hameroff



Psychotherapists have recommended treating certain mental disorders by soliciting traumatic memory and providing concomitant positive emotional experience to "re-consolidate" alternative memories—overwriting, if not erasing, mental trauma and leading to psychotherapeutic benefit (e.g., Lane, Ryan, Nadel, & Greenberg, 2015). However, these worthy efforts have lacked (as does science in general) actual neurobiological mechanisms for emotional experience (consciousness) and memory (encoding, consolidation/reconsolidation, storage, and recall). When asked why he robbed banks, the notorious criminal Willie Sutton famously answered, "Because that's where the money is!" To delete or overwrite traumatic memories, we need to know where and how they are encoded and consolidated. And improving conscious experience, the essential therapeutic goal, would be far easier if we knew how consciousness actually occurred in the brain.

It is my contention (definitely a minority contention, but one supported by evidence) that in contrast to conventional wisdom, both memory and consciousness are rooted *inside* brain neurons, in vibrational states of cytoskeletal protein polymers called microtubules.

Mainstream science considers consciousness to be an emergent product of synaptic computation among brain neurons, the state of each neuron acting as a fundamental unit of information, that is, a "bit". But computational views about consciousness lack specifics and fail to generate testable predictions. Without having synapses or participating in a network, single-cell organisms such as *paramecia* exhibit cognitive behaviors—finding food and mates, having sex, and learning, for example—using their internal microtubules for information processing and movement. These same microtubules are found inside all cells, including brain neurons, as major components of the cytoskeleton. Self-assembling lattice polymers of the protein "tubulin" (the brain's most prevalent protein), microtubules grow and shape neurons and form and regulate synapses. Stemming from a suggestion by famed neuroscientist Charles Sherrington in the 1950s, microtubules have been likened to the "cell's nervous system". Their lattice structure and organizational abilities have prompted suggestions that microtubules process and store information and perform computation (Hameroff & Watt, 1982; Rasmussen, Karampurwala, Vaidyanath, Jensen, & Hameroff, 1990). Microtubule disruption and loss of "tau", a microtubule-associated protein, correlates with cognitive dysfunction, for example in Alzheimer's disease.

A maverick theory of consciousness, the Penrose-Hameroff orchestrated objective reduction (Orch OR) theory (see, e.g., Penrose & Hameroff, 1995; Hameroff & Penrose, 2014) suggests quantum vibrational computations in microtubules inside brain neurons (a) produce conscious experience, and (b) regulate neuronal firings, behavior, and synaptic plasticity. In Orch OR, microtubule quantum vibrations are "orchestrated" (Orch) by synaptic inputs and memory (encoded in microtubules) and terminated by "objective reduction" (OR), Penrose's solution to the measurement problem in quantum mechanics (Penrose, 1989).

Orch OR has been viewed skeptically and harshly criticized, as the brain has been considered too "warm, wet, and noisy" for seemingly delicate quantum effects. But in recent years, functional quantum biology has been recognized at ambient temperatures in photosynthesis, bird navigation, olfaction, and in microtubules. Single, isolated microtubules and bundles of microtubules inside active neurons have been shown to have quantum resonant vibrations in megahertz and kilohertz frequencies (Ghosh et al., 2014; Sahu, Ghosh, Ghosh, et al., 2013; Sahu, Ghosh, Hirata, Fujita, & Bandyopadhyay, 2013). Orch OR further suggests microtubule vibrations (e.g., in megahertz) interfere to cause music-like (electrophysiological) "beats" seen as EEG rhythms (Hameroff & Penrose, 2014). Indeed, microtubule resonant vibrations, and consciousness, have been said to resemble music more than computation (Ghosh et al., 2014; Hameroff, 2015). Recent evidence also shows that anesthetics (which selectively erase consciousness) act on microtubules rather than membrane receptors as is generally assumed (Emerson et al., 2013). The maverick Orch OR theory has far more supportive evidence than any mainstream approaches to consciousness.

The mainstream view of memory is "synaptic plasticity", in which adjusted strengths of specific synapses guide information in particular pathways through neuronal networks. But the synaptic membrane proteins that determine synaptic strength are transient—recycled over hours—yet memories can last lifetimes. Again, microtubules play key roles, as synapses are formed, maintained, and regulated by microtubules and associated proteins. And microtubules may be the actual site for memory encoding. In long-term potentiation (LTP, a cellular model for memory), calcium influx

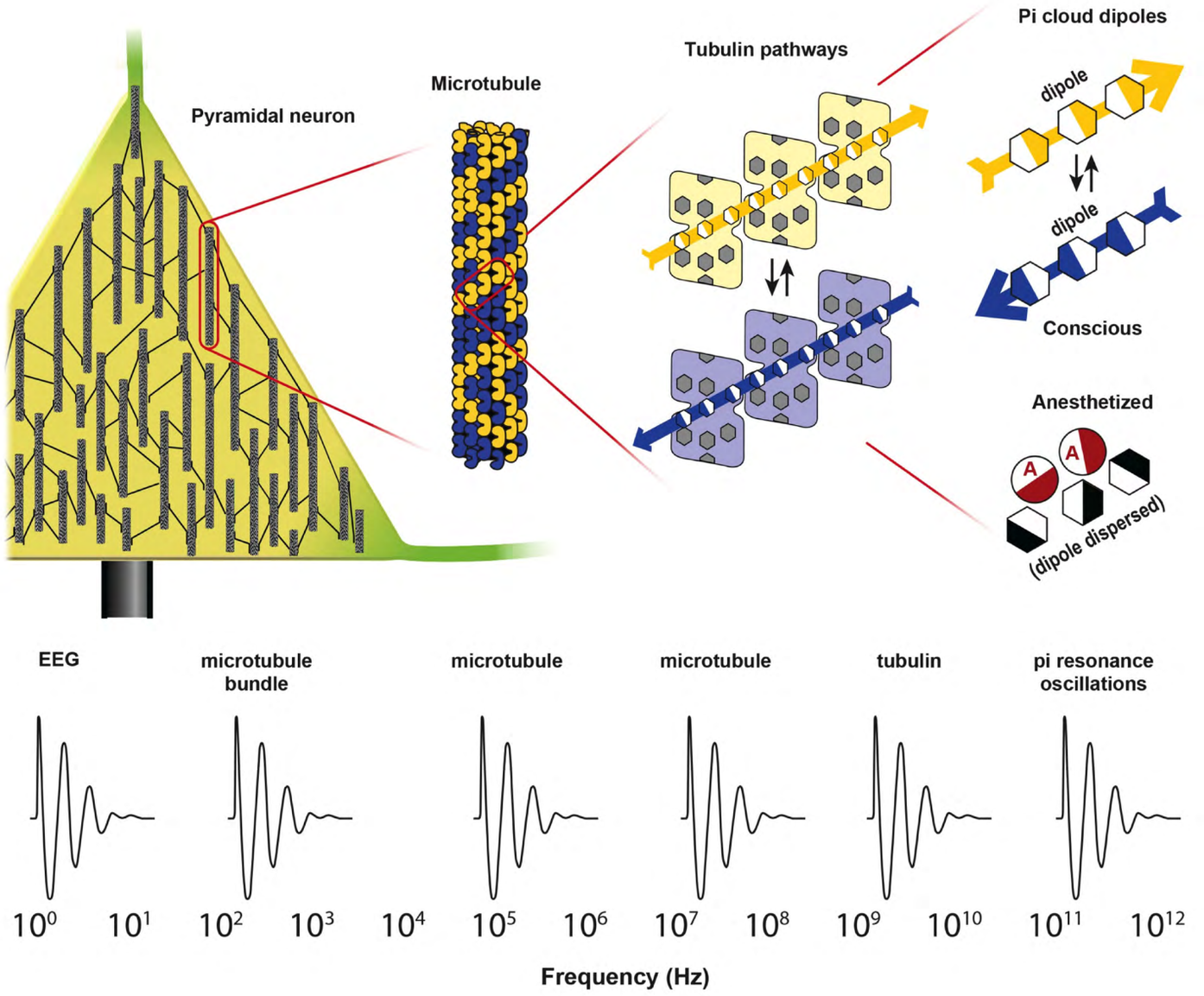


Figure 1. Brain multi-scalar vibrational hierarchy. Top row shows structure (left to right): pyramidal neuron cell body with interior microtubules, a single microtubule, tubulin pathways through pi resonance clouds, and dipole oscillations—resonance transfers and/or spin currents occur, with the upper image showing pi cloud dipole oscillations and the lower image showing anesthetics dispersing dipoles. Bottom row shows dynamics at frequency ranges matching structure in top row (Craddock et al., 2015; Sahu, Ghosh, Ghosh, et al., 2013; Sahu, Ghosh, Hirata, et al., 2013; Sahu, Ghosh, Fujita, & Bandyopadhyay, 2014).

activates CaMKII, a hexagonal holoenzyme that then extends sets of six kinase domains, with each domain able to phosphorylate a substrate). The CaMKIIs rapidly distribute to microtubules throughout dendritic trees and encode memory, presumably by phosphorylation (Lemieux et al., 2012). But CaMKII phosphorylation targets and sites of memory encoding remain unknown. It turns out that CaMKII precisely matches microtubule lattice geometry and size. The six CaMKII kinase domains can bind (and phosphorylate) precisely six tubulins in microtubule hexagonal lattices, and thus encode six "bits" of memory per CaMKII (Craddock, Tuszynski, & Hameroff, 2012) onto dendritic microtubules, which are uniquely stable and ideally positioned to encode memory. CaMKII phosphorylation of specific tubulins would modulate microtubule resonant vibrations like frets or nodes in a musical instrument, encoding memory, changing the tune and altering conscious experience.

In a psychotherapy paradigm roughly similar to that proposed for human subjects by Lane et al. (2015), Cao et al. (2008) elicited specific fear memories in mice and then transiently overexpressed CaMKII, erasing (or overwriting) the fear memory. CaMKII overexpression presumably increased memory turnover but required invasive genetic manipulation.

It may be possible to noninvasively stimulate memory turnover (and mood enhancement) by direct effects on brain microtubules. The action of antidepressants, for example, fluoxitene (Prozac), appears to involve

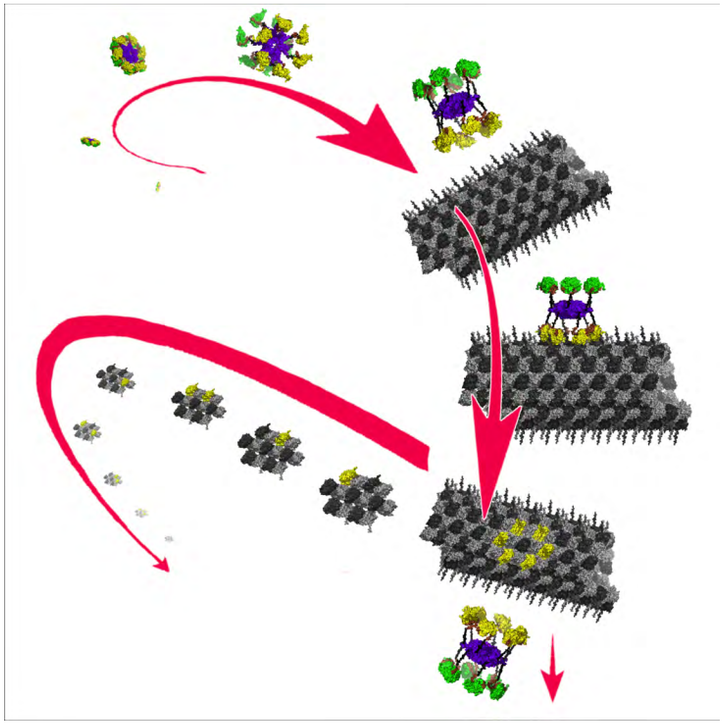


Figure 2. Calcium-calmodulin kinase II (CaMKII), a hexagonal holoenzyme activated by synaptic calcium influx, extends six leg-like kinase domains above and below an association domain. The six kinase domains precisely match hexagonal size and geometry in both A-lattice and B-lattice microtubules. (Image used with permission from Travis Craddock)

restructuring of cytoskeletal microtubules over several weeks (Bianchi et al., 2009). More immediate effects may be addressed through noninvasive transcranial modalities. Among these are transcranial magnetic stimulation (TMS), transcranial electrical, direct-current stimulation (TDcS), and transcranial ultrasound stimulation (TUS), consisting of megahertz mechanical vibrations which, at low intensity, sub-thermal levels, can safely penetrate skull and brain. As microtubules have megahertz vibrational resonances, TUS with proper settings might be expected to enhance microtubule resonance, and thereby affect cognition and mental states. In neuronal cell culture, ultrasound increases neuronal growth and synaptic formation (Bocchi et al., 2015). In mice with genetically-induced Alzheimer's disease (in which microtubules destabilize and tau protein is released), TUS improves pathology and cognitive function (Leinenga & Götz, 2015). In humans, focused TUS enhances sensory discrimination (Legon et al., 2014), and unfocused TUS improves mood in chronic pain patients (Hameroff et al., 2013).

To erase or overwrite traumatic memory, to change the music and re-tune the brain's tubules, combinations of pharmacology, psychotherapy and TUS (e.g., aimed at microtubule vibrations in the amygdala, hippocampus and prefrontal cortex) may be optimal. As the Beatles sang, "Take a sad song and make it better."

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Figure 3. Transcranial ultrasound (TUS) with General Electric Logique imaging device. Subject's skull and brain tissue are shown on screen, demonstrating penetration into brain.

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