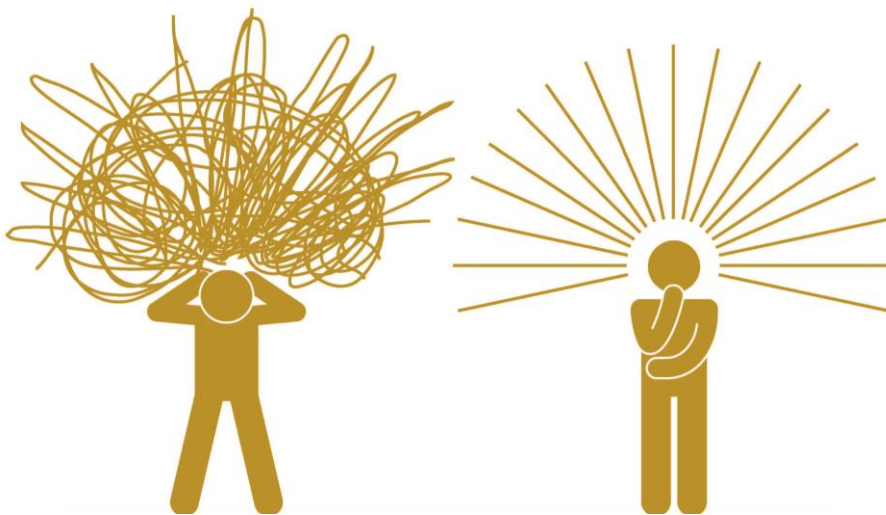




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# SYNCTUITION TECHNOLOGY SCIENTIFIC REFERENCES





## Brain synchronization through hearing

Synctuition is an audio tool for the synchronization of brain hemispheres through the entrainment and amplification of neural oscillations in the brain that mostly occur within the range of gamma frequency brain waves.

### **Synctuition works through the brain's auditory system.**

Hearing sound requires cooperation from many Brain regions that interact through a complex and dynamic neural network. Auditory signals initiate a cascade of neural activities throughout the whole brain - from the lowest to the highest level of cognitive actions.

### **This is how the brain perceives sound**

The auditory brainstem response begins at the cochlea - a sense organ in the inner ear that translates sound into nerve impulses. Sound processing continues in the central nervous system and occurs in three levels: in the brainstem as a reflex, in the auditory cortex (part of temporal lobe and located bilaterally in both brain hemispheres) and in other remote areas of the brain that are used to process the audio stimuli.

Auditory brainstem response occurs in the first 10 milliseconds. The arrival of auditory information to the brainstem triggers reflexes and subconscious processes.

In the brainstem, auditory information is decoded into basic components like frequency and duration. From the brainstem, the decoded auditory information is passed to the thalamus, which is situated in the cerebellum and acts as a neural information hub of the brain. The thalamus relays and integrates sensory and motor signals to the cerebral cortex and participates in the regulation of consciousness, sleep and alertness.

The thalamus passes auditory information to the brain's primary auditory cortex. The primary auditory cortex is part of the temporal lobe and it is located bilaterally in both brain hemispheres. In the auditory cortex, the wave signals are recognized and processed.

In addition to the primary pathway there are alternative non-primary auditory pathways which process all sorts of sensory messages. The function of these non-primary pathways is to "choose" the which sensory messages will be treated first (this gives us the ability to focus only on certain sounds or to ignore them, such as when we read a book while listening to music).

## **The auditory cortex provides distinct powerful responses in the gamma frequency range of sound**

The reason for this is that gamma frequencies are resonant frequencies of certain areas of the brain. The different gamma range binaural frequencies and entrainment patterns used in Synctuition affect the brain through the same auditory pathways and brain mechanisms that affect different neurons in the brain. This is because the auditory cortex and other brain centers which are directly or indirectly involved with auditory information processing use different sets of neurons to decode sounds with different pitch.

### **Why gamma range binaural beats?**

Neurons in local populations process information whereas larger neural assemblies, including neurons connected across separate brain areas, combine multiple processes that are important for higher-level cognitive tasks. These neural oscillations promote transient neural network interactions responsible for complex cognitive tasks.

Gamma range binaural beats and 3D sounds provide an extremely powerful synchronizing effect on neural oscillation brainwave patterns because the auditory cortices are located in different hemispheres of the brain and they have to work very closely together in order to decode the 40Hz binaural signal that you are listening to in the Synctuition journeys. The right auditory cortex is more sensitive to tonality and the left auditory cortex is more sensitive to minute sequential differences in sound. Synctuition uses these properties of the hearing system to provide for an even more immersive sound experience.

In addition, oscillators in one brain region can phase synchronize with oscillators in another region through these long range connections that are being created by listening to Synctuition. As neurons oscillate, they effectively open and close their window to both send and receive information. For information to be transferred from one neuronal group to another, the sending neuron must be excitable at the same time that the receiving group is excitable. This requires the coupling of oscillations between sending and receiving neurons through brainwave synchronization. This pattern of neural interactions allows for efficient neural communication transient coupling of neurons firing synchronously forming functional neural network.

Listening to the gamma range binaural beat frequencies in Synctuition increases connections in the brain through neural plasticity by using the auditory cortex initiated phase synchronization of brain neural networks. As a result of enhanced neural plasticity Synctuition accelerates intuitive processes and communication processes by creating new synaptic connections between different regions of the brain.



## The Synctuition wave formula

The Synctuition wave formula is a composition of natural 3D sounds and rhythmic entrainment frequencies. Some of the component sounds are intentionally coinciding with the neural oscillations from the gamma band. The following will present a short description of the Synctuition wave formula:

$$S(n_1, n_2, n_3, \dots, n_n, t_1, t_2, t_3, \dots, t_n) = \sum_{i=1}^w \Psi(n_i, t_i) = \Psi(n_1, t_1) + \Psi(n_2, t_2) + \Psi(n_3, t_3) + \dots + \Psi(n_w, t_w)$$

The Synctuition wave formula or the representing function  $S(n_1, n_2, n_3, \dots, n_w, t_1, t_2, t_3, \dots, t_n)$  is a superposition of  $w$  number of component waves  $\Psi(n_x, t_x)$ . The  $\Psi(n_x, t_x)$  and represents an acoustic wave function (for 3D spherical waves) for the spatial position  $n$  of the component and it can be written as follows:

$$\Psi(n, t) = \int_{-\infty}^{\infty} \Psi(n, \omega) e^{-i\omega t} d\omega$$

As mentioned, the component waves  $\Psi_n$  (or  $\Psi(n_x, t_x)$ ) of the Synctuition wave (produced by the Synctuition wave formula) are from computer generated or natural sources such as rhythmic entrainment frequencies or natural sounds.

The difference between natural and artificial sound waves in the context of the Synctuition wave formula and the corresponding sound wave is the intrinsic dimensionality of the wave  $\Psi_n$ . Here, the intrinsic dimensionality of the sound wave is calculated as a Hausdorff dimension of the sound wave:

$$D = -\log_{\epsilon} N = -\frac{\log N}{\log \epsilon}$$

Where  $D$  - Hausdorff dimension (approximation),  $N$  - number of repeating units,  $\epsilon$  - scaling factor.

The value of  $D$  for the synthetic sound wave is approaching the integer while in the case of natural sounds the value of  $D$  is a fractional number. The Hausdorff dimension of the sound wave can also be seen as an entropy of the sound.

## Binaural beats

Binaural beats, or binaural tones, are auditory processing artifacts, or apparent sounds, caused by specific physical stimuli. A binaural beat is an auditory effect perceived when two different pure-tone sine waves, are presented to the ears of a listener.

The effect on brainwaves depends on the frequency difference in each tone: for example, if 300 Hz was played in one ear and 310 in the other, then the binaural beat would have a frequency of 10 Hz. Synctuition uses binaural beats in the Gamma ~40Hz range.

Binaural beats are not a physical property of the sound, but the convergence of neural activity from the two ears in the central binaural auditory pathways of the brain in response to the sound - intensity changes in the perceived sound are therefore called "binaural beats".

### **Research Summary on Binaural Beats:**

Human electroencephalography (EEG) activity can be entrained by rhythmic sensory stimulation.

A.-K Becher's research (Becher et al. 2015)

Stimulus-related responses are observed at modulation rates up to 200 Hz, with the largest responses being recorded at approximately 40 Hz.

Phase synchronization has been shown to play a major role in cognitive processes, in particular in memory operations. As a practical application of these findings, it has been demonstrated, for instance, that long-term memory performance can be modulated by weak electric in-phase vs. antiphase stimulation of the rhinal cortex and hippocampus for other deep brain stimulation approaches to memory enhancement.

These findings suggest a role for binaural beats for the purpose of memory enhancement.

### Binaural beats to relax and de-stress

McConnell et al has written (McConnell et al. 2014)

Findings from a double-blind placebo-controlled study by McConnell demonstrate a role for binaural beats in facilitating access to more restorative states of post-exercise relaxation with subtle, yet somewhat durable psychophysiological effects.

The results show that a 20-min of exposure to binaural beats significantly increases a known marker of parasympathetic activation that is driven by activity in regions of the anterior cingulate and medial prefrontal cortex.

McConnel research subjects reported being significantly more relaxed while listening to binaural beats then while listening to a placebo.

## Binaural Gamma waves

Science has discovered a strong correlation between transcendental mental states and gamma waves.

A gamma wave is a pattern of neural oscillation in humans with a frequency between 25 and 100 Hz. Gamma neural oscillations can act in the cortex to bind modality specific perceptual representations and in the hippocampus to bind the rich perceptual and contextual information from diverse brain regions into episodic representations. The impact of gamma waves can activate experiences of the past in the brain and can also reveal forgotten experiences stored in memory. The amount of available experiences, at least the ones we use for decision making, is smaller than the actual set of stored (existing) experiences in memory. The revealed experiences significantly increase the probability of the accuracy of correct intuitive decisions.

Gamma oscillations allow for the interaction between cortical structures and the hippocampus for the encoding and retrieval of (episodic) memories. Gamma phase synchronization between cortical and hippocampal neurons and between hippocampal neurons provide the mechanism by which individual episodic memory representations from diverse cortical regions get encoded into hippocampal representations.

### **Research by Nyhaus and Curran (Nyhus and Curran 2010)**

To understand how gamma oscillations contribute to episodic memory and cognitive ability, it is essential to first consider their basic underlying neural mechanisms of rhythmic activity. Studies using single unit and multiunit recording show that rhythmic firing can occur because of intrinsic firing patterns of excitatory principal cells or common input from a pacemaker like the thalamus. More commonly in the cortex and the hippocampal rhythmic firing is an emergent property of interactions between excitatory principal cells and inhibitory interneurons.

In the cortex and hippocampus the collective activity of excitatory principal cells and inhibitory interneurons leads to neurons firing together and being inhibited together—**creating rhythmic firing patterns**.

The neural mechanism responsible for gamma rhythmic firing occurs through the interaction of excitatory principle cells and fast basket cell inhibitory interneurons in the cortex and the hippocampus.

Gamma rhythmic firing modulates perceptual feature binding—just as visual perception consists of several visual features that must be integrated into a perceptual whole, episodic memory consists of several different individual memory representations that include several features that must be integrated into an individual memory representation.

Gamma oscillations lead to spike-timing-dependent plasticity—Research has shown that gamma oscillations provide the precise timing necessary for spike-timing-dependent plasticity.

During a cognitive task, gamma oscillations can allow for local neurons to fire synchronously at high frequencies to process information. Multiple processes can then be combined through large-scale brain networks whose oscillations become phase synchronized causing neurons within these large-scale brain networks to fire synchronously.

## 3D sounds

Synctuition has been created with a specially developed 3D recording technology, which allows for the listener to enjoy a spatially accurate soundscape through normal stereo headphones that provide the listener with a correct dimensional perception of the sound source in the recording field. The broad mechanism of 3D sound perception consists of two parts: the detection of timing differences between the ears, and spectral differences between the ears.

## 3D sound

### **Natural 3D sounds**

Natural 3D sounds are sounds which are recorded spatially in wild nature without synthetic components. Natural sounds are restricted to natural sources in their normal soundscape and presented to the listener with the correct timing and spectral differences as are found in nature, thereby delivering an authentic experience of the sound that makes the brain react as if the audio stimulus is coming live from nature.

### **3D music**

3D music recordings include human produced sounds which are made using instrumental or vocal techniques, or sounds derived from other anthropogenic sources.

### **Intuitive instrumental and vocal music used in Synctuition**

Synctuition's music is based on intuitive improvisations of instrumental and vocal music that are performed extemporaneously in a meditative state of the mind.

Intuitive instrumental and vocal music is a creative activity of immediate musical composition, which combines performance with communication of emotions and instrumental techniques as well as spontaneous responses to inspiration. The manifestations of intuitive music creation are spontaneous actions of meditative mindsets, but they can also be initiated or affected by external stimuli. All music used in Synctuition is intuitive music - a performance without any pre-set structure or harmonic limitations, all flowing straight from the subconscious.

In terms of cognitive processes, improvisation can be defined as the spontaneous generation, selection, and execution of novel auditory–motor sequences. (*Berkowitz and Ansari 2008*)

## Rhythmic entrainment frequencies

### Rhythmic entrainment constitutes a key source of emotions experienced during music listening.

From 2004 Trost research

Different bodily rhythms can synchronize to those present in music, consequently generating emotional feelings via proprioceptive feedback mechanisms. Recent scientific works have reported that corticospinal excitability is increased during metrically strong rhythmical sequences. The basal ganglia integrate rhythmical information with both cognitive and affective components of musical experience. On the other hand, cross-modal influences on attention and its deployment over time are known to recruit cortical areas in posterior parietal lobule, including for synchronization of motor responses with auditory (non-musical) sequences. Therefore, parietal attention systems can contribute to the effect musical rhythm has on attention and entrainment.

Further Research by Thaut, Peterson, and McIntosh (2005)

The effect of temporal entrainment on motor function through rhythmic auditory stimuli has been well established in motor learning and therapeutic rehabilitation.

Temporally structured learning templates (as inherent in most music) enhance learning and may involve different plastic processes in the brain. Rhythm and music have been associated with providing the temporal structure for information encoding.

Previous scientific research has shown that rhythmic motor synchronization involves changes in activation patterns of prefrontal and parietal networks, depending on the nature of the temporal tracking task. During isochronous synchronization, prefrontal areas are activated, whereas tracking of tempo-modulated rhythmic patterns shows a gradually expanding involvement of medio-, ventro-, and dorsolateral areas in the prefrontal cortex (PFC), contingent upon the modulation amplitude of the tempo changes and degree of conscious awareness of the tempo fluctuations.

Research data has provided evidence that spatial patterns of neural synchronizations change with the duration of working memory, possibly indicating a progressive shift from phonological to semantic encoding.

Long-term recall in music (memory trial after 20-min delay) has shown additional significant local network coherence in the gamma band in right anterior and posterior networks.

Neuronal synchronization processes are involved in assembling coupled neuronal networks associated with effective learning and training. Brain plasticity associated with behavioral learning is thus critically dependent on precise temporal coding of neuronal responses.

The data suggest that special melodic–rhythmic structures in music, enhance memory performance by mapping the temporal order on learning information.



## Combination of the waves

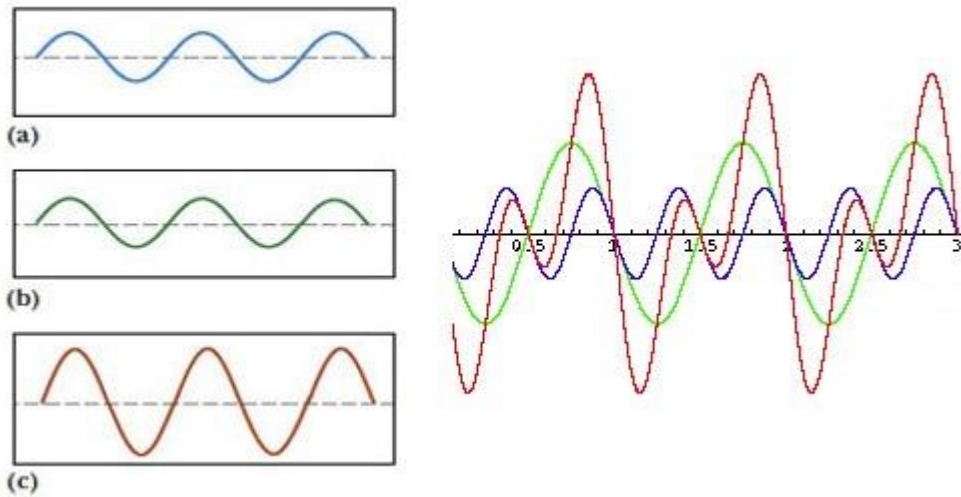


Illustration of the Synctuition formula operation principle. The input sound waves (a), (b) and (c) are combined into the composite Synctuition sound wave.

## Why listen before sleep

Why we need to sleep seems clear: without sleep, we become tired, irritable, and our brain functions less well. After a good night of sleep, brain and body feel refreshed and we are restored to normal function. The synaptic homeostasis hypothesis (SHY) proposes that the fundamental function of sleep is the restoration of synaptic homeostasis, which is challenged by synaptic strengthening triggered by learning during wake and by synaptogenesis during development. In other words, sleep is “the price we pay for neuroplasticity.” By renormalizing synaptic strength, sleep reduces the burden of plasticity on neurons and other cells while restoring neuronal selectivity and the ability to learn, and in doing so enhances signal-to-noise ratios (S/Ns), leading to the consolidation and integration of memories. Sleep is also an essential process that supports learning and memory by acting on synapses through molecular mechanisms. (Diering GH)

Synctuition’s audio technology helps the listener to fully relax the body and calm the electrical storm in the brain before sleep through binaural 3D audio meditation - this helps in achieving considerably better rest during the night.

Sleeping protects memories and makes them easier to access. It is common knowledge that after sleep we are more likely to recall different facts and memories which are usually tricky to remember during awake time.

A good night's sleep is shown to promote access to memory traces that had initially been too weak to be retrieved. Compared to wakefulness, sleep helps to recall and reprocess unrecalled memories for usage or long time storage. While we are asleep, the brain actively repeats information which is considered important. Sleep allows memories to be accessible in a wider range of contexts, hence making them more useful. Sleeping is known to help us

remember the things we did or heard the previous day. The main factor for the sleep related memory boost is the hippocampus which stores recently experienced information.

## What is intuition?

As magical as intuition seems, it is actually a set of complex neural processes which involve the whole brain – from sensory inputs and low-level reflex actions to high-level cognitive processes. Intuition is the brain's ability to solve difficult or seemingly impossible problems as very complex logical inferences, where sensory inputs in conjunction with existing memories work as premises and the intuitive thoughts are the results of these logical inferences.

Here's just one example. For every problem-solving task the brain needs "computational" capability, but intuition needs it remarkably more despite the fact that it usually all happens unconsciously. For problem solving, the brain uses neural networks. Usually, neural networks specialized for certain tasks are grouped together in specific brain areas. The composition of neural networks in the brain is not constant and it changes throughout life. The brain builds new neural connections and alters or removes existing ones - this happens, for example, when we learn, and the process is called neuroplasticity.

In order to solve some problems, neural networks from different areas of the brain must cooperate. Cooperating neural networks must act as synchronously as possible to solve problems efficiently. In case of intuition, the neural processes behind it are more complex and both brain hemispheres should be equally involved in problem solving. Brain hemispheres are like mirror images, but not completely. Usually they work nearly in sync, but they tend to have subtle differences which reduce the communication between the hemispheres and intuitive thinking.

## What is neuroplasticity?

Neuroplasticity is the process how experiences reorganize neural pathways in the brain. Long lasting functional changes in the brain occur when we learn new things or memorize new information. These changes in neural connections are what we call neuroplasticity.

Neuroplasticity is the idea that individual synaptic connections are constantly being removed or recreated, largely dependent upon the activity of the neurons that bear them. The activity-dependence of synaptic plasticity is captured in the aphorism which is often used to summarize Hebbian theory: "neurons that fire together, wire together"/"neurons that fire out of sync, fail to link". If two nearby neurons often produce an impulse in close temporal proximity, their functional properties may converge. Conversely, neurons that are not regularly activated simultaneously may be more likely to functionally diverge.

Correlated activation in both neurons strengthens the connection between them, or as summarized by the world's leading neuroscientist Siegrid Löwel "cells that fire together, wire together". Therefore, neuroplasticity can be viewed as either strengthening of a connection or as an increase in efficiency, where we consider synaptic strength as the ability to elicit a

response (either excitation or inhibition) in the postsynaptic cell and synaptic efficiency as the ability of the postsynaptic cell to be excited by the presynaptic cell.

### **Homeostatic synaptic plasticity**

One can view homeostatic plasticity as a phenomenon that stabilizes activity of a single neuron or a neuronal circuit, when faced with perturbations that alter excitability, by keeping its action potential output within an optimal range (e.g., change in size of cells, strength of connections or synapse number). The process is believed to operate at least at two levels. The first, residing at the individual synapse, whereas the second is operating cell-wide for maintaining the metabolic stability while keeping constant the synaptic connections. The principal models that are considered to be involved in the process of homeostatic plasticity are: synaptic scaling, the Bienenstock-Cooper-Munro (BCM) synapse, spike timing-dependent plasticity (STDP), the regulation of intrinsic excitability and synaptic redistribution.

Synaptic scaling is a process that adjusts the strength of all synapses on a postsynaptic neuron in response to modifications in average postsynaptic activity. The term “synaptic scaling” was implemented after the observation that a perturbation to network activity generates compensations in terms of synaptic strength that return, or “scale”, the average firing rates back to control values. (Cohen EJ 2017)

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### Abstract

The plastic character of brain synapses is considered to be one of the foundations for the formation of memories. There are numerous kinds of such phenomenon currently described in the literature, but their role in the development of information pathways in neural networks with recurrent architectures is still not completely clear. In this paper we study the role of an activity-based process, called pre-synaptic dependent homeostatic scaling, in the organization of networks that yield precise-timed spiking patterns. It encodes spatio-temporal information in the synaptic weights as it associates a learned input with a specific response. We introduce a correlation measure to evaluate the precision of the spiking patterns and explore the effects of different inhibitory interactions and learning parameters. We find that large learning periods are important in order to improve the network learning capacity and discuss this ability in the presence of distinct inhibitory currents.

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### Abstract

Neuroplasticity has been subject to a great deal of research in the last century. Recently, significant emphasis has been placed on the global effect of localized plastic changes throughout the central nervous system, and on how these changes integrate in a pathological context. Specifically, alterations of network functionality have been described in various pathological contexts to which corresponding structural alterations have been proposed. However, considering the amount of

literature and the different pathological contexts, an integration of this information is still lacking. In this paper we will review the concepts of neural plasticity as well as their repercussions on network remodeling and provide a possible explanation to how these two concepts relate to each other. We will further examine how alterations in different pathological contexts may relate to each other and will discuss the concept of plasticity diseases, its models and implications.

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Affiliation

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Abstract

Plastic changes occurring during wakefulness aid in the acquisition and consolidation of memories. For some memories, further consolidation requires sleep, but whether plastic processes during wakefulness and sleep differ is unclear. We show that, in rat cortex and hippocampus, GluR1-containing AMPA receptor (AMPA) levels are high during wakefulness and low during sleep, and changes in the phosphorylation states of AMPARs, CamKII and GSK3beta are consistent with synaptic potentiation during wakefulness and depression during sleep. Furthermore, slope and amplitude of cortical evoked responses increase after wakefulness, decrease after sleep and correlate with changes in slow-wave activity, a marker of sleep pressure. Changes in molecular and electrophysiological indicators of synaptic strength are largely independent of the time of day. Finally, cortical long-term potentiation can be easily induced after sleep, but not after wakefulness. Thus, wakefulness appears to be associated with net synaptic potentiation, whereas sleep may favor global synaptic depression, thereby preserving an overall balance of synaptic strength.

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Affiliation

Department of Psychiatry, University of Wisconsin, Madison, WI 53719, USA.

Abstract

Sleep is universal, strictly regulated, and necessary for cognition. Why this is so remains a mystery, although recent work suggests that sleep, memory, and plasticity are linked. However, little is known about how wakefulness and sleep affect synapses. Using Western blots and confocal microscopy in *Drosophila*, we found that protein levels of key components of central synapses were high after waking and low after sleep. These changes were related to behavioral state rather than time of day and occurred in all major areas of the *Drosophila* brain. The

decrease of synaptic markers during sleep was progressive, and sleep was necessary for their decline. Thus, sleep may be involved in maintaining synaptic homeostasis altered by waking activities.

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Abstract

Sleep is universal, tightly regulated, and its loss impairs cognition. But why does the brain need to disconnect from the environment for hours every day? The synaptic homeostasis hypothesis (SHY) proposes that sleep is the price the brain pays for plasticity. During a waking episode, learning statistical regularities about the current environment requires strengthening connections throughout the brain. This increases cellular needs for energy and supplies, decreases signal-to-noise ratios, and saturates learning. During sleep, spontaneous activity renormalizes net synaptic strength and restores cellular homeostasis. Activity-dependent down-selection of synapses can also explain the benefits of sleep on memory acquisition, consolidation, and integration. This happens through the offline, comprehensive sampling of statistical regularities incorporated in neuronal circuits over a lifetime. This Perspective considers the rationale and evidence for SHY and points to open issues related to sleep and plasticity.

Keywords: Neuroscience;

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Keywords: Neuroscience;

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Abstract

Sleep appears to be a universal phenomenon in the animal kingdom (1) and lack of sleep leads to severe cognitive disruption (2). Yet, the biological function of sleep is unknown. On pages 507 and 511 of this issue, de Vivo et al. (3) and Diering et al. (4), respectively, provide a peek into the nightlife of synapses, the neural connections in the nervous system. The studies reveal substantial alterations in the structure and molecular machinery of synapses during sleep.

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Affiliation

Institute of Psychology, University of Leipzig, Leipzig, Germany.

Abstract

Modulations of oscillatory electroencephalogram (EEG) activity in the induced gamma and theta frequency ranges (induced gamma and theta band responses; iGBRs: >30 Hz; iTBRs: approximately 6 Hz) have been associated with retrieval of information from long-term memory. However, the specific functional role of these two forms of oscillatory activity remains unclear. The present study examines theta- and gamma-oscillations within a dual-process framework, which defines “familiarity” and “recollection” as the two component processes of recognition memory. During encoding, participants were instructed to make “bigger/smaller than a shoebox” or “living/nonliving” decisions for different object pictures. During retrieval “old/new” recognition was followed (for items judged old) by a source discrimination task regarding the decision made for each item at encoding. iGBRs (35-80 Hz; 210-330 msec) were higher for correctly identified “old” relative to “new” objects. Importantly, they did not distinguish between successful and unsuccessful source judgments. In contrast, iTBRs (4-7.5 Hz; 600-1200 msec) were sensitive to source discrimination. We propose that iGBRs mirror early associative processes linked to familiarity-related retrieval processes, whereas iTBRs reflect later onsetting, episodic, recollection-related mechanisms.

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Affiliation

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Abstract

In two experiments we tested the hypothesis that music, in the form of a familiar melody, can serve as an effective mnemonic device. Prior research has provided very little support for this commonly held belief. In both studies, participants learned a list of names that they heard either spoken or sung to a familiar tune. In Experiment 1, the melody was “Pop Goes the Weasel”; in Experiment 2, the melody was “Yankee Doodle.” We measured the number of trials to learn the list initially and the number of trials to relearn the list a week later. In both studies, there was no advantage in initial learning for those who learned the names to the musical accompaniment. However, in both studies, participants who heard the sung version required fewer trials to relearn the list of names a week later than did participants who heard the spoken version.

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Affiliation

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Abstract

The sense of agency is the experience of initiating and controlling one's voluntary actions and their outcomes. Intentional binding (i.e., when voluntary actions and their outcomes are perceived to occur closer together in time than involuntary actions and their outcomes) is increased in intentional action but requires no explicit reflection on agency. The reported experience of involuntariness is central to hypnotic responding, during which strategic action is experienced as involuntary. We report reduced intentional binding in a hypnotically induced experience of involuntariness, providing an objective correlate of reports of involuntariness. We argue that this reduced binding results from the diminished influence of motor intentions in the generation of the sense of agency when beliefs about whether an action is intended are altered. Thus, intentional binding depends on awareness of intentions. This finding shows that changes in metacognition of intentions affect perception.

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Affiliation

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Abstract

In this article, we summarize the state-of-science knowledge regarding the associations between hypnosis and brain oscillations. Brain oscillations represent the combined electrical activity of neuronal assemblies, and are usually measured as specific frequencies representing slower (delta, theta, alpha) and faster (beta, gamma) oscillations. Hypnosis has been most closely linked to power in the theta band and changes in gamma activity. These oscillations are thought to play a critical role in both the recording and recall of declarative memory and emotional limbic circuits. Here we propose that it is this role that may be the mechanistic link between theta (and perhaps gamma) oscillations and hypnosis; specifically that theta oscillations may facilitate, and that changes in gamma activity observed with hypnosis may underlie, some hypnotic responses. If these hypotheses are supported, they have important implications for both understanding the effects of hypnosis, and for enhancing response to hypnotic treatments.



- [11] A Mofredj, S Alaya, K Tassaïoust, H Bahloul, and A Mrabet. Music therapy, a review of the potential therapeutic benefits for the critically ill. *J. Crit. Care*, 35:195-199, October 2016.

Intensive care units are a stressful milieu for patients, particularly when under mechanical ventilation which they refer to as inhumane and anxiety producing. Anxiety can impose harmful effects on the course of recovery and overall well-being of the patient. Resulting adverse effects may prolong weaning and recovery time. Music listening, widely used for stress release in all areas of medicine, tends to be a reliable and efficacious treatment for those critically ill patients. It can abate the stress response, decrease anxiety during mechanical ventilation, and induce an overall relaxation response without the use of medication. This relaxation response can lower cardiac workload and oxygen consumption resulting in more effective ventilation. Music may also improve sleep quality and reduce patient's pain with a subsequent decrease in sedative exposure leading to an accelerated ventilator weaning process and a speedier recovery.

- [12] Shirley Fecteau, Pascal Belin, Yves Joanette, and Jorge L Armony. Amygdala responses to nonlinguistic emotional vocalizations. *Neuroimage*, 36(2):480--487, June 2007.

Whereas there is ample evidence for a role of the amygdala in the processing of visual emotional stimuli, particularly those with negative value, discrepant results have been reported regarding amygdala responses to emotional auditory stimuli. The present study used event-related functional magnetic resonance imaging to investigate cerebral activity underlying processing of emotional nonlinguistic vocalizations, with a particular focus on neural changes in the amygdala. Fourteen healthy volunteers were scanned while performing a gender identification task. Stimuli, previously validated on emotional valence, consisted of positive (happiness and sexual pleasure) and negative (sadness and fear) vocalizations, as well as emotionally neutral sounds (e.g., coughs). Results revealed bilateral amygdala activation in response to all emotional vocalizations when compared to neutral stimuli. These findings suggest that the generally accepted involvement of the amygdala in the perception of emotional visual stimuli, such as facial expressions, also applies to stimuli within the auditory modality. Importantly, this amygdala response was observed for both positive and negative emotional vocalizations.

- [13] Kari Suzanne Kraus and Barbara Canlon. Neuronal connectivity and interactions between the auditory and limbic systems. effects of noise and tinnitus. *Hear. Res.*, 288(1-2):34--46, June 2012.

Acoustic experience such as sound, noise, or absence of sound induces structural or functional changes in the central auditory system but can also affect limbic regions such as the amygdala and hippocampus. The amygdala is particularly sensitive to sound with valence or meaning, such as vocalizations, crying or music. The amygdala plays a central role in auditory fear conditioning, regulation of the acoustic startle response and can modulate auditory cortex plasticity. A stressful acoustic stimulus, such as noise, causes amygdala-mediated release of stress

hormones via the HPA-axis, which may have negative effects on health, as well as on the central nervous system. On the contrary, short-term exposure to stress hormones elicits positive effects such as hearing protection. The hippocampus can affect auditory processing by adding a temporal dimension, as well as being able to mediate novelty detection via theta wave phase-locking. Noise exposure affects hippocampal neurogenesis and LTP in a manner that affects structural plasticity, learning and memory. Tinnitus, typically induced by hearing malfunctions, is associated with emotional stress, depression and anatomical changes of the hippocampus. In turn, the limbic system may play a role in the generation as well as the suppression of tinnitus indicating that the limbic system may be essential for tinnitus treatment. A further understanding of auditory-limbic interactions will contribute to future treatment strategies of tinnitus and noise trauma.

- [14] Y Du, Q Wang, Y Zhang, X Wu, and L Li. Perceived target-masker separation unmasks responses of lateral amygdala to the emotionally conditioned target sounds in awake rats. *Neuroscience*, 225:249--257, 6 December 2012.
- In a (simulated) reverberant environment, both human listeners and laboratory rats are able to perceptually integrate the direct wave of a sound source with the reflections of the source, leading to a fused image as coming from the location around the source (the precedence effect). This perceptual grouping effect produces perceived spatial separation between sound sources and facilitates selective attention to the target source. However, the neural correlates of the unmasking effects of perceived spatial separation have not been reported in the literature. The lateral nucleus of the amygdala (LA) is critical for processing ecologically salient sensory signals (e.g., threatening sounds) and mediating auditory fear conditioning. LA neuronal responses to a sound increase if the sound is fear conditioned. This study investigated whether in awake rats the perceptual fusion-induced separation between a fear-conditioned target sound and a noise masker enhances LA responses to the target. The results show that frequency-following responses (FFRs, i.e., sustained potentials based on phase-locked firing of neuron populations to periodical sound waveforms) recorded in the LA to a tone-complex, which was masked by a wideband noise, were enhanced after the tone-complex became fear conditioned. More importantly, the fear-conditioned tone-complex, but not the pseudo-conditioned tone-complex, elicited further larger LA FFRs when it was perceived as separated from the masker than when it was perceived as co-located with the masker. The results suggest that in the LA there exists a neural correlate of selective attention to ecologically significant sounds with a high degree of stimulus specificity.

- [15] Joel A Lopata, Elizabeth A Nowicki, and Marc F Joanisse. CREATIVITY AS a DISTINCT TRAINABLE MENTAL STATE: AN EEG STUDY OF MUSICAL IMPROVISATION. *Neuropsychologia*.  
Abstract Alpha-band EEG was used to index how creative mental states relate to the creation of artistic works in skilled musicians. We contrasted differences in frontal upper alpha-band activity between tasks with high and low creativity demands by recording EEGs while skilled musicians listened to, played back, and improvised jazz melodies. Neural responses were compared for skilled musicians with training in musical improvisation versus those who had no formal improvisation training. Consistent with our hypotheses, individuals showed increased frontal upper alpha-band activity during more creative tasks (i.e., improvisation) compared to during less creative tasks (i.e., rote playback). Moreover, this effect was greatest for musicians with formal improvisation training. The strength of this effect also appeared to modulate the quality of these improvisations, as evidenced by significant correlations between upper alpha EEG power and objective post-hoc ratings of individuals'™ performances. These findings support a conceptualization of creativity as a distinct mental state and suggest spontaneous processing capacity is better nurtured through formal institutional training than informal.
- [16] Roger E Beaty. The neuroscience of musical improvisation. *Neurosci. Biobehav. Rev.*, 51:108--117, April 2015.  
Researchers have recently begun to examine the neural basis of musical improvisation, one of the most complex forms of creative behavior. The emerging field of improvisation neuroscience has implications not only for the study of artistic expertise, but also for understanding the neural underpinnings of domain-general processes such as motor control and language production. This review synthesizes functional magnetic resonance imaging (fMRI) studies of musical improvisation, including vocal and instrumental improvisation, with samples of jazz pianists, classical musicians, freestyle rap artists, and non-musicians. A network of prefrontal brain regions commonly linked to improvisatory behavior is highlighted, including the pre-supplementary motor area, medial prefrontal cortex, inferior frontal gyrus, dorsolateral prefrontal cortex, and dorsal premotor cortex. Activation of premotor and lateral prefrontal regions suggests that a seemingly unconstrained behavior may actually benefit from motor planning and cognitive control. Yet activation of cortical midline regions points to a role of spontaneous cognition characteristic of the default network. Together, such results may reflect cooperation between large-scale brain networks associated with cognitive control and spontaneous thought. The improvisation literature is integrated with Pressing's theoretical model, and discussed within the broader context of research on the brain basis of creative cognition.

- [17] Antoine J Shahin, Larry E Roberts, Wilkin Chau, Laurel J Trainor, and Lee M Miller. Music training leads to the development of timbre-specific gamma band activity. *Neuroimage*, 41(1):113--122, 15 May 2008.
- Oscillatory gamma band activity (GBA, 30-100 Hz) has been shown to correlate with perceptual and cognitive phenomena including feature binding, template matching, and learning and memory formation. We hypothesized that if GBA reflects highly learned perceptual template matching, we should observe its development in musicians specific to the timbre of their instrument of practice. EEG was recorded in adult professional violinists and amateur pianists as well as in 4- and 5-year-old children studying piano in the Suzuki method before they commenced music lessons and 1 year later. The adult musicians showed robust enhancement of induced (non-time-locked) GBA, specifically to their instrument of practice, with the strongest effect in professional violinists. Consistent with this result, the children receiving piano lessons exhibited increased power of induced GBA for piano tones with 1 year of training, while children not taking lessons showed no effect. In comparison to induced GBA, evoked (time-locked) gamma band activity (30-90 Hz, approximately 80 ms latency) was present only in adult groups. Evoked GBA was more pronounced in musicians than non-musicians, with synchronization equally exhibited for violin and piano tones but enhanced for these tones compared to pure tones. Evoked gamma activity may index the physical properties of a sound and is modulated by acoustical training, while induced GBA may reflect higher perceptual learning and is shaped by specific auditory experiences.
- [18] Joydeep Bhattacharya and Hellmuth Petsche. Phase synchrony analysis of EEG during music perception reveals changes in functional connectivity due to musical expertise. *Signal Processing*, 85(11):2161--2177, November 2005.
- Differences in functional and topographical connectivity patterns between two groups, musicians and non-musicians, during attentively listening to three different pieces of music and to a text of neutral content, were presented by means of EEG phase synchrony analysis in five standard frequency bands: delta (30 Hz). The degree of phase synchrony or phase coherence between EEG signals was measured by a recently developed index, which is more suitable than classical indices, like correlation or coherence, when dealing with nonlinear and nonstationary signals like EEG. Comparing the music listening task to rest or control condition, musicians showed increase in phase synchrony over distributed cortical areas, both near and distant, in delta, and most conspicuously in gamma frequency band, whereas non-musicians showed enhancement only in delta band. Further, the degree of phase synchrony in musicians was reduced during listening to text as compared to listening to music. Comparing the two groups during the listening tasks, the clear-cut difference was found in gamma band phase synchrony, which was significantly stronger in musicians while listening to every chosen piece of music, yet no large difference between these two groups was found while listening to the chosen text. Musicians also showed stronger higher order inter-frequency phase synchrony between delta band oscillations in anterior regions and gamma band oscillations in posterior regions. In addition, consistent left hemispheric dominance, in terms of the strength of phase synchrony, was

observed in musicians while listening to music, whereas right hemispheric dominance was observed in non-musicians. These results suggest that professional training in music is able to elicit context-sensitive functional connectivity between multiple cortical regions resulting in different listening strategies to music.

- [19] Cristhian Potes, Peter Brunner, Aysegul Gunduz, Robert T Knight, and Gerwin Schalk. Spatial and temporal relationships of electrocorticographic alpha and gamma activity during auditory processing. *Neuroimage*, 97:188--195, 15 August 2014.

Neuroimaging approaches have implicated multiple brain sites in musical perception, including the posterior part of the superior temporal gyrus and adjacent perisylvian areas. However, the detailed spatial and temporal relationship of neural signals that support auditory processing is largely unknown. In this study, we applied a novel inter-subject analysis approach to electrophysiological signals recorded from the surface of the brain (electrocorticography (ECoG)) in ten human subjects. This approach allowed us to reliably identify those ECoG features that were related to the processing of a complex auditory stimulus (i.e., continuous piece of music) and to investigate their spatial, temporal, and causal relationships. Our results identified stimulus-related modulations in the alpha (8-12 Hz) and high gamma (70-110 Hz) bands at neuroanatomical locations implicated in auditory processing. Specifically, we identified stimulus-related ECoG modulations in the alpha band in areas adjacent to primary auditory cortex, which are known to receive afferent auditory projections from the thalamus (80 of a total of 15,107 tested sites). In contrast, we identified stimulus-related ECoG modulations in the high gamma band not only in areas close to primary auditory cortex but also in other perisylvian areas known to be involved in higher-order auditory processing, and in superior premotor cortex (412/15,107 sites). Across all implicated areas, modulations in the high gamma band preceded those in the alpha band by 280 ms, and activity in the high gamma band causally predicted alpha activity, but not vice versa (Granger causality,  $p < 1e(-8)$ ). Additionally, detailed analyses using Granger causality identified causal relationships of high gamma activity between distinct locations in early auditory pathways within superior temporal gyrus (STG) and posterior STG, between posterior STG and inferior frontal cortex, and between STG and premotor cortex. Evidence suggests that these relationships reflect direct cortico-cortical connections rather than common driving input from subcortical structures such as the thalamus. In summary, our inter-subject analyses defined the spatial and temporal relationships between music-related brain activity in the alpha and high gamma bands. They provide experimental evidence supporting current theories about the putative mechanisms of alpha and gamma activity, i.e., reflections of thalamo-cortical interactions and local cortical neural activity, respectively, and the results are also in agreement with existing functional models of auditory processing.

- [20] Sukhbinder Kumar, William Sedley, Gareth R Barnes, Sundeep Teki, Karl J Friston, and Timothy D Griffiths. A brain basis for musical hallucinations. *Cortex*, 52:86--97, March 2014.
- The physiological basis for musical hallucinations (MH) is not understood. One obstacle to understanding has been the lack of a method to manipulate the intensity of hallucination during the course of experiment. Residual inhibition, transient suppression of a phantom percept after the offset of a masking stimulus, has been used in the study of tinnitus. We report here a human subject whose MH were residually inhibited by short periods of music. Magnetoencephalography (MEG) allowed us to examine variation in the underlying oscillatory brain activity in different states. Source-space analysis capable of single-subject inference defined left-lateralised power increases, associated with stronger hallucinations, in the gamma band in left anterior superior temporal gyrus, and in the beta band in motor cortex and posteromedial cortex. The data indicate that these areas form a crucial network in the generation of MH, and are consistent with a model in which MH are generated by persistent reciprocal communication in a predictive coding hierarchy.
- [21] David A Peterson and Michael H Thaut. Music increases frontal EEG coherence during verbal learning. *Neurosci. Lett.*, 412(3):217--221, 2 February 2007.
- Anecdotal and some empirical evidence suggests that music can enhance learning and memory. However, the mechanisms by which music modulates the neural activity associated with learning and memory remain largely unexplored. We evaluated coherent frontal oscillations in the electroencephalogram (EEG) while subjects were engaged in a modified version of Rey's Auditory Verbal Learning Test (AVLT). Subjects heard either a spoken version of the AVLT or the conventional AVLT word list sung. Learning-related changes in coherence (LRCC) were measured by comparing the EEG during word encoding on correctly recalled trials to the immediately preceding trial on which the same word was not recalled. There were no significant changes in coherence associated with conventional verbal learning. However, musical verbal learning was associated with increased coherence within and between left and right frontal areas in theta, alpha, and gamma frequency bands. It is unlikely that the different patterns of LRCC reflect general performance differences; the groups exhibited similar learning performance. The results suggest that verbal learning with a musical template strengthens coherent oscillations in frontal cortical networks involved in verbal encoding.
- [22] Archi Banerjee, Shankha Sanyal, Anirban Patranabis, Kaushik Banerjee, Tarit Guhathakurta, Ranjan Sengupta, Dipak Ghosh, and Partha Ghose. Study on brain dynamics by non linear analysis of music induced EEG signals. *Physica A: Statistical Mechanics and its Applications*, 444:110--120, 15 February 2016.
- Abstract Music has been proven to be a valuable tool for the understanding of human cognition, human emotion, and their underlying brain mechanisms. The objective of this study is to analyze the effect of Hindustani music on brain activity during normal relaxing conditions using electroencephalography (EEG). Ten male healthy subjects without special musical education participated in the study. EEG

signals were acquired at the frontal (F3/F4) lobes of the brain while listening to music at three experimental conditions (rest, with music and without music). Frequency analysis was done for the alpha, theta and gamma brain rhythms. The finding shows that arousal based activities were enhanced while listening to Hindustani music of contrasting emotions (romantic/sorrow) for all the subjects in case of alpha frequency bands while no significant changes were observed in gamma and theta frequency ranges. It has been observed that when the music stimulus is removed, arousal activities as evident from alpha brain rhythms remain for some time, showing residual arousal. This is analogous to the conventional "Hysteresis" loop where the system retains some "memory" of the former state. This is corroborated in the non linear analysis (Detrended Fluctuation Analysis) of the alpha rhythms as manifested in values of fractal dimension. After an input of music conveying contrast emotions, withdrawal of music shows more retention as evidenced by the values of fractal dimension.

- [23] Paulo Barraza, Mario Chavez, and Eugenio Rodríguez. Ways of making-sense: Local gamma synchronization reveals differences between semantic processing induced by music and language. *Brain Lang.*, 152:44--49, January 2016. Similar to linguistic stimuli, music can also prime the meaning of a subsequent word. However, it is so far unknown what is the brain dynamics underlying the semantic priming effect induced by music, and its relation to language. To elucidate these issues, we compare the brain oscillatory response to visual words that have been semantically primed either by a musical excerpt or by an auditory sentence. We found that semantic violation between music-word pairs triggers a classical ERP N400, and induces a sustained increase of long-distance theta phase synchrony, along with a transient increase of local gamma activity. Similar results were observed after linguistic semantic violation except for gamma activity, which increased after semantic congruence between sentence-word pairs. Our findings indicate that local gamma activity is a neural marker that signals different ways of semantic processing between music and language, revealing the dynamic and self-organized nature of the semantic processing.
- [24] Jean-Philippe Després, Pamela Burnard, Francis Dubé, and Sophie Stévançe. Expert improvisers in western classical music learning pathways. *Thinking Skills and Creativity*, 22:167--179, December 2016. Abstract Despite a growing interest in Western classical improvisation among researchers, educators and musicians in recent decades, research insights on expert improvisers' learning pathways are scarce. In order to further understanding this phenomenon, we formulated the following research question: "What characterizes the learning pathways of Western classical music expert improvisers?" Addressing this question, we designed an exploratory case study, conducting open-ended semi-structured videoconference interviews with a purposeful sampling of N = 8 Western classical music expert improvisers. The participants are international classically trained musicians who are recognized as expert improvisers by their peers and who have improvised on professional albums

and in established concert halls. In-depth analysis of our data revealed two distinct learning pathways among the participants: (1) native improvisers, who have improvised since the very beginning of their instrumental learning; and (2) immigrant improvisers, who started to improvise at a later age, during their graduate studies or at the beginning of their professional career. Native improvisers began to improvise spontaneously, without apparent extrinsic incentive, while immigrant improvisers started to improvise in order to attempt to fill a gap in their musical practice. Various factors motivated the immigrant improvisers interviewed to themselves dedicate to this practice, including seeing improvisation as a means to experience (i) a “getting back” to oneself; (ii) an authentic human encounter; (iii) a sense of immediacy characterizing the creative process; and (iv) an equalitarian musical practice. Lastly, a “learn-unlearn” process appears to underlie improvisational expertise development. Implications of these findings for expertise development and skill acquisition will be discussed.

- [25] Örjan de Manzano and Fredrik Ullén. Goal-independent mechanisms for free response generation: creative and pseudo-random performance share neural substrates. *Neuroimage*, 59(1):772--780, 2 January 2012.
- To what extent free response generation in different tasks uses common and task-specific neurocognitive processes has remained unclear. Here, we investigated overlap and differences in neural activity during musical improvisation and pseudo-random response generation. Brain activity was measured using fMRI in a group of professional classical pianists, who performed musical improvisation of melodies, pseudo-random key-presses and a baseline condition (sight-reading), on either two, six or twelve keys on a piano keyboard. The results revealed an extensive overlap in neural activity between the two generative conditions. Active regions included the dorsolateral and dorsomedial prefrontal cortices, inferior frontal gyrus, anterior cingulate cortex and pre-SMA. No regions showed higher activity in improvisation than in pseudo-random generation. These findings suggest that the activated regions fulfill generic functions that are utilized in different types of free generation tasks, independent of overall goal. In contrast, pseudo-random generation was accompanied by higher activity than improvisation in several regions. This presumably reflects the participants' musical expertise as well as the pseudo-random generation task's high load on attention, working memory, and executive control. The results highlight the significance of using naturalistic tasks to study human behavior and cognition. No brain activity was related to the size of the response set. We discuss that this may reflect that the musicians were able to use specific strategies for improvisation, by which there was no simple relationship between response set size and neural activity.



- [26] Aaron L Berkowitz and Daniel Ansari. Generation of novel motor sequences: the neural correlates of musical improvisation. *Neuroimage*, 41(2):535--543, June 2008.

While some motor behavior is instinctive and stereotyped or learned and re-executed, much action is a spontaneous response to a novel set of environmental conditions. The neural correlates of both pre-learned and cued motor sequences have been previously studied, but novel motor behavior has thus far not been examined through brain imaging. In this paper, we report a study of musical improvisation in trained pianists with functional magnetic resonance imaging (fMRI), using improvisation as a case study of novel action generation. We demonstrate that both rhythmic (temporal) and melodic (ordinal) motor sequence creation modulate activity in a network of brain regions comprised of the dorsal premotor cortex, the rostral cingulate zone of the anterior cingulate cortex, and the inferior frontal gyrus. These findings are consistent with a role for the dorsal premotor cortex in movement coordination, the rostral cingulate zone in voluntary selection, and the inferior frontal gyrus in sequence generation. Thus, the invention of novel motor sequences in musical improvisation recruits a network of brain regions coordinated to generate possible sequences, select among them, and execute the decided-upon sequence.

Keywords: Music and sound;

- [27] Jeff Pressing. Improvisation: methods and models. In J Sloboda, editor, *Generative Processes in Music: the Psychology of Performance, Improvisation, and Composition*. Oxford University Press, 1988.

- [28] Genevieve Beaulieu-Boire, Solange Bourque, Frederic Chagnon, Lucie Chouinard, Nicole Gallo-Payet, and Olivier Lesur. Music and biological stress dampening in mechanically-ventilated patients at the intensive care unit ward---a prospective interventional randomized crossover trial. *J. Crit. Care*, 28(4):442--450, 2013.
- Abstract Purpose To evaluate the impact of slow-tempo music listening periods in mechanically ventilated intensive care unit patients. Methods A randomized crossover study was performed in a 16-bed, adult critical care unit at a tertiary care hospital. Still-sedated patients, mandating at least 3 more days of mechanical ventilation, were included. The intervention consisted in two 1-hour daily periods of music-vs-sham-MP3 listening which were performed on Day 1 or 3 post-inclusion, with a Day 2 wash-out. "Before-after" collection of vital signs, recording of daily sedative drug consumption and measurement of stress and inflammatory blood markers were performed. Results Of 55 randomized patients, 49 were included in the final analyses. Along with music listening, (i) vital signs did not consistently change, whereas narcotic consumption tended to decrease to a similar sedation ( $P = .06$  vs sham-MP3); (ii) cortisol and prolactin blood concentrations decreased, whereas Adreno Cortico Trophic Hormone (ACTH)/cortisol ratio increased ( $P = .02$ ;  $P = .038$ ; and  $P = .015$  vs sham-MP3, respectively), (iii) cortisol responders exhibited reversed associated changes in blood methionine (MET)-enkephalin content ( $P = .01$ ). Conclusions In the present trial, music listening is a more sensitive stress-reliever in terms of biological vs clinical response. The

hypothalamus-pituitary adrenal axis stress axis is a quick sensor of music listening in responding mechanically ventilated intensive care unit patients, through a rapid reduction in blood cortisol.

- [29] Janejira Laohawattanakun, Supornpim Chearskul, Hattaya Dumrongphol, Nuanchan Jutapakdeegul, Juntima Yensukjai, Nipaporn Khumphan, Songwit Niltiean, and Wipawan Thangnipon. Influence of music training on academic examination-induced stress in Thai adolescents. *Neurosci. Lett.*, 487(3):310--312, 10 January 2011.

Several pieces of evidence suggest that academic examinations fulfill the classical requirement of a psychological stressor. Academic examinations represent a stressful challenge to many students, but studies on examination-dependent corticosteroid response, a sensitive physiological indicator of a stress response, are inconsistent. In addition, several studies showed that music can decrease cortisol and adrenocorticotropic hormone (ACTH) levels, and other studies have found that music also may enhance a variety of cognitive functions, such as attention, learning, communication and memory. The present study investigated cortisol response in saliva of Thai adolescents taking academic examinations and analyzed the differences of the stress response between musician and control subjects. Also, we observed whether the academic examination-dependent corticosteroid response affected learning and memory in the test subjects, which comprised 30 musician and 30 control students, age ranging from 15 to 17 years. Mathematical examinations were used as the stressor. Pre- and post-academic examination saliva cortisol levels were measured including self-estimated stress levels. Results showed that the pre-academic examination saliva cortisol concentrations of the musician group are significantly lower than those of the control group, whereas there is no difference in the stress inventory scores. Interestingly, among students with grade point average (GPA) of >3.50, pre-academic examination cortisol levels are significantly lower in the musician compared with control group. This study suggests that under academic examination-induced stress condition, music training can reduce saliva cortisol level in Thai adolescents.

- [30] Hajime Fukui and Kumiko Toyoshima. Music increase altruism through regulating the secretion of steroid hormones and peptides. *Med. Hypotheses*, 83(6):706--708, December 2014.

Music is well known for its effect on human behavior especially of their bonding and empathy towards others. Music provokes one's emotion and activates mirror neurons and reward system. It also regulates social hormones such as steroid hormones or peptides, and increases empathy, pro-sociality and altruism. As a result, it improves one's reproductive success.

- [31] Daisy Fancourt, Adam Ockelford, and Abi Belai. The psychoneuroimmunological effects of music: a systematic review and a new model. *Brain Behav. Immun.*, 36:15--26, February 2014.

There has been a growing interest over the past decade into the health benefits of music, in particular examining its psychological and neurological effects. Yet this is the first attempt to systematically review publications on the psychoneuroimmunology of music. Of the selected sixty-three studies published over the past 22 years, a range of effects of music on neurotransmitters, hormones, cytokines, lymphocytes, vital signs and immunoglobulins as well as psychological assessments are cataloged. Research so far points to the pivotal role of stress pathways in linking music to an immune response. However, several challenges to this research are noted: (1) there is very little discussion on the possible mechanisms by which music is achieving its neurological and immunological impact; (2) the studies tend to examine biomarkers in isolation, without taking into consideration the interaction of the biomarkers in question with other physiological or metabolic activities of the body, leading to an unclear understanding of the impact that music may be having; (3) terms are not being defined clearly enough, such as distinctions not being made between different kinds of stress and 'music' being used to encompass a broad spectrum of activities without determining which aspects of musical engagement are responsible for alterations in biomarkers. In light of this, a new model is presented which provides a framework for developing a taxonomy of musical and stress-related variables in research design, and tracing the broad pathways that are involved in its influence on the body.

- [32] Suat Zengin, Sinem Kabul, Behcet Al, Emine Sarcan, Mehmet Doğan, and Cuma Yildirim. Effects of music therapy on pain and anxiety in patients undergoing port catheter placement procedure. *Complement. Ther. Med.*, 21(6):689--696, December 2013.

**BACKGROUND:** Patients scheduled to invasive medical procedures experience high levels of anxiety, which may lead to increased perceptions of pain and vital sign instability throughout. **AIMS:** To examine the effect of a music intervention (MI) on stress hormones, physiologic parameters, pain, and anxiety state before and during port catheter placement procedures (PCPPs). **METHODS:** We conducted a prospective, randomized, controlled study in 100 oncology patients, who were randomly assigned to an MI group (n=50) or a control group (n=50). The effects of music were assessed by determination of serum cortisol and adrenocorticotrophic hormone (ACTH) levels, heart and respiratory rate (HR, RR) and systolic and diastolic blood pressure (SBP, DBP), on arrival in the surgical intervention room, as well as immediately prior to and immediately after the PCPP, in both groups. Furthermore, pain and anxiety levels were identified using visual analogue scale and state-trait anxiety inventory scales. **RESULTS:** On arrival, there were no differences between the patients in terms of serum cortisol and ACTH levels, HR, RR, SBP, DBP and anxiety levels. There were significant reductions in hormone levels ( $p < 0.05$  for all), HR ( $p < 0.001$ ), RR ( $p < 0.001$ ), SBP ( $p < 0.05$ ) and DBP ( $p < 0.05$ ), immediately prior to and immediately after the PCPP

in participants in the MI group compared to those in the control group. Furthermore, music led to a significant reduction in pain ( $p < 0.05$ ) and anxiety scores ( $p < 0.05$ ) in the MI group compared to control group. CONCLUSION: During invasive medical procedures, MI significantly decreases stress hormone levels, physiological parameters, acute procedural pain and anxiety.

- [33] Pasko Rakic. Neurogenesis in adult primate neocortex: an evaluation of the evidence. *Nat. Rev. Neurosci.*, 3(1):65--71, January 2002.  
Reports of continuous genesis and turnover of neurons in the adult primate association neocortex--the site of the highest cognitive functions--have generated great excitement. Here, I review the available evidence, and question the scientific basis of this claim.
- [34] Matthew E Sachs, Robert J Ellis, Gottfried Schlaug, and Psyche Loui. Brain connectivity reflects human aesthetic responses to music. *Soc. Cogn. Affect. Neurosci.*, 11(6):884--891, June 2016.  
Humans uniquely appreciate aesthetics, experiencing pleasurable responses to complex stimuli that confer no clear intrinsic value for survival. However, substantial variability exists in the frequency and specificity of aesthetic responses. While pleasure from aesthetics is attributed to the neural circuitry for reward, what accounts for individual differences in aesthetic reward sensitivity remains unclear. Using a combination of survey data, behavioral and psychophysiological measures and diffusion tensor imaging, we found that white matter connectivity between sensory processing areas in the superior temporal gyrus and emotional and social processing areas in the insula and medial prefrontal cortex explains individual differences in reward sensitivity to music. Our findings provide the first evidence for a neural basis of individual differences in sensory access to the reward system, and suggest that social-emotional communication through the auditory channel may offer an evolutionary basis for music making as an aesthetically rewarding function in humans.
- [35] Joseph Cichon and Wen-Biao Gan. Branch-specific dendritic  $Ca^{2+}$  spikes cause persistent synaptic plasticity. *Nature*, 520(7546):180--185, 9 April 2015.  
The brain has an extraordinary capacity for memory storage, but how it stores new information without disrupting previously acquired memories remains unknown. Here we show that different motor learning tasks induce dendritic  $Ca^{2+}$  spikes on different apical tuft branches of individual layer V pyramidal neurons in the mouse motor cortex. These task-related, branch-specific  $Ca^{2+}$  spikes cause long-lasting potentiation of postsynaptic dendritic spines active at the time of spike generation. When somatostatin-expressing interneurons are inactivated, different motor tasks frequently induce  $Ca^{2+}$  spikes on the same branches. On those branches, spines potentiated during one task are depotentiated when they are active seconds before  $Ca^{2+}$  spikes induced by another task. Concomitantly, increased neuronal activity and performance improvement after learning one task are disrupted when another task is learned. These findings indicate that dendritic-branch-specific generation of

Ca(2+) spikes is crucial for establishing long-lasting synaptic plasticity, thereby facilitating information storage associated with different learning experiences.

- [36] Assal Habibi, B Rael Cahn, Antonio Damasio, and Hanna Damasio. Neural correlates of accelerated auditory processing in children engaged in music training. *Dev. Cogn. Neurosci.*, 21:1--14, October 2016.

Several studies comparing adult musicians and non-musicians have shown that music training is associated with brain differences. It is unknown, however, whether these differences result from lengthy musical training, from pre-existing biological traits, or from social factors favoring musicality. As part of an ongoing 5-year longitudinal study, we investigated the effects of a music training program on the auditory development of children, over the course of two years, beginning at age 6-7. The training was group-based and inspired by El-Sistema. We compared the children in the music group with two comparison groups of children of the same socio-economic background, one involved in sports training, another not involved in any systematic training. Prior to participating, children who began training in music did not differ from those in the comparison groups in any of the assessed measures. After two years, we now observe that children in the music group, but not in the two comparison groups, show an enhanced ability to detect changes in tonal environment and an accelerated maturity of auditory processing as measured by cortical auditory evoked potentials to musical notes. Our results suggest that music training may result in stimulus specific brain changes in school aged children.

- [37] Jan Kamiński, Shannon Sullivan, Jeffrey M Chung, Ian B Ross, Adam N Mamelak, and Ueli Rutishauser. Persistently active neurons in human medial frontal and medial temporal lobe support working memory. *Nat. Neurosci.*, 20 February 2017.

Persistent neural activity is a putative mechanism for the maintenance of working memories. Persistent activity relies on the activity of a distributed network of areas, but the differential contribution of each area remains unclear. We recorded single neurons in the human medial frontal cortex and medial temporal lobe while subjects held up to three items in memory. We found persistently active neurons in both areas. Persistent activity of hippocampal and amygdala neurons was stimulus-specific, formed stable attractors and was predictive of memory content. Medial frontal cortex persistent activity, on the other hand, was modulated by memory load and task set but was not stimulus-specific. Trial-by-trial variability in persistent activity in both areas was related to memory strength, because it predicted the speed and accuracy by which stimuli were remembered. This work reveals, in humans, direct evidence for a distributed network of persistently active neurons supporting working memory maintenance.

- [38] Danielle S Bassett and Olaf Sporns. Network neuroscience. *Nat. Neurosci.*, 20(3):353--364, 23 February 2017.

Despite substantial recent progress, our understanding of the principles and mechanisms underlying complex brain function and cognition remains incomplete. Network neuroscience proposes to tackle these enduring challenges. Approaching

brain structure and function from an explicitly integrative perspective, network neuroscience pursues new ways to map, record, analyze and model the elements and interactions of neurobiological systems. Two parallel trends drive the approach: the availability of new empirical tools to create comprehensive maps and record dynamic patterns among molecules, neurons, brain areas and social systems; and the theoretical framework and computational tools of modern network science. The convergence of empirical and computational advances opens new frontiers of scientific inquiry, including network dynamics, manipulation and control of brain networks, and integration of network processes across spatiotemporal domains. We review emerging trends in network neuroscience and attempt to chart a path toward a better understanding of the brain as a multiscale networked system.

- [39] Christin Scholz, Elisa C Baek, Matthew Brook O'Donnell, Hyun Suk Kim, Joseph N Cappella, and Emily B Falk. A neural model of valuation and information virality. *Proc. Natl. Acad. Sci. U. S. A.*, 27 February 2017.  
Information sharing is an integral part of human interaction that serves to build social relationships and affects attitudes and behaviors in individuals and large groups. We present a unifying neurocognitive framework of mechanisms underlying information sharing at scale (virality). We argue that expectations regarding self-related and social consequences of sharing (e.g., in the form of potential for self-enhancement or social approval) are integrated into a domain-general value signal that encodes the value of sharing a piece of information. This value signal translates into population-level virality. In two studies ( $n = 41$  and  $39$  participants), we tested these hypotheses using functional neuroimaging. Neural activity in response to 80 New York Times articles was observed in theory-driven regions of interest associated with value, self, and social cognitions. This activity then was linked to objectively logged population-level data encompassing  $n = 117,611$  internet shares of the articles. In both studies, activity in neural regions associated with self-related and social cognition was indirectly related to population-level sharing through increased neural activation in the brain's value system. Neural activity further predicted population-level outcomes over and above the variance explained by article characteristics and commonly used self-report measures of sharing intentions. This parsimonious framework may help advance theory, improve predictive models, and inform new approaches to effective intervention. More broadly, these data shed light on the core functions of sharing-to express ourselves in positive ways and to strengthen our social bonds.
- [40] Daniele Durante and David B Dunson. Bayesian inference and testing of group differences in brain networks. *Bayesian Anal.*, 2016.  
Project Euclid - mathematics and statistics online

- [41] Paul A Howard-Jones. Neuroscience and education: myths and messages. *Nat. Rev. Neurosci.*, 15(12):817--824, December 2014.  
For several decades, myths about the brain - neuromyths - have persisted in schools and colleges, often being used to justify ineffective approaches to teaching. Many of these myths are biased distortions of scientific fact. Cultural conditions, such as differences in terminology and language, have contributed to a 'gap' between neuroscience and education that has shielded these distortions from scrutiny. In recent years, scientific communications across this gap have increased, although the messages are often distorted by the same conditions and biases as those responsible for neuromyths. In the future, the establishment of a new field of inquiry that is dedicated to bridging neuroscience and education may help to inform and to improve these communications.
- [42] Axel Cleeremans. The radical plasticity thesis: How the brain learns to be conscious. *Front. Psychol.*, 2:86, 9 May 2011.  
In this paper, I explore the idea that consciousness is something that the brain learns to do rather than an intrinsic property of certain neural states and not others. Starting from the idea that neural activity is inherently unconscious, the question thus becomes: How does the brain learn to be conscious? I suggest that consciousness arises as a result of the brain's continuous attempts at predicting not only the consequences of its actions on the world and on other agents, but also the consequences of activity in one cerebral region on activity in other regions. By this account, the brain continuously and unconsciously learns to redescribe its own activity to itself, so developing systems of meta-representations that characterize and qualify the target first-order representations. Such learned redescriptions, enriched by the emotional value associated with them, form the basis of conscious experience. Learning and plasticity are thus central to consciousness, to the extent that experiences only occur in experiencers that have learned to know they possess certain first-order states and that have learned to care more about certain states than about others. This is what I call the "Radical Plasticity Thesis." In a sense thus, this is the enactive perspective, but turned both inwards and (further) outwards. Consciousness involves "signal detection on the mind"; the conscious mind is the brain's (non-conceptual, implicit) theory about itself. I illustrate these ideas through neural network models that simulate the relationships between performance and awareness in different tasks.
- [43] Luisa de Vivo, Michele Bellesi, William Marshall, Eric A Bushong, Mark H Ellisman, Giulio Tononi, and Chiara Cirelli. Ultrastructural evidence for synaptic scaling across the wake/sleep cycle. *Science*, 355(6324):507--510, 3 February 2017.  
It is assumed that synaptic strengthening and weakening balance throughout learning to avoid runaway potentiation and memory interference. However, energetic and informational considerations suggest that potentiation should occur primarily during wake, when animals learn, and depression should occur during sleep. We measured 6920 synapses in mouse motor and sensory cortices using three-dimensional electron microscopy. The axon-spine interface (ASI) decreased

18% after sleep compared with wake. This decrease was proportional to ASI size, which is indicative of scaling. Scaling was selective, sparing synapses that were large and lacked recycling endosomes. Similar scaling occurred for spine head volume, suggesting a distinction between weaker, more plastic synapses ( 80%) and stronger, more stable synapses. These results support the hypothesis that a core function of sleep is to renormalize overall synaptic strength increased by wake.

- [44] Graham H Diering, Raja S Nirujogi, Richard H Roth, Paul F Worley, Akhilesh Pandey, and Richard L Huganir. Homer1a drives homeostatic scaling-down of excitatory synapses during sleep. *Science*, 355(6324):511--515, 3 February 2017. Sleep is an essential process that supports learning and memory by acting on synapses through poorly understood molecular mechanisms. Using biochemistry, proteomics, and imaging in mice, we find that during sleep, synapses undergo widespread alterations in composition and signaling, including weakening of synapses through removal and dephosphorylation of synaptic AMPA-type glutamate receptors. These changes are driven by the immediate early gene Homer1a and signaling from group I metabotropic glutamate receptors mGluR1/5. Homer1a serves as a molecular integrator of arousal and sleep need via the wake- and sleep-promoting neuromodulators, noradrenaline and adenosine, respectively. Our data suggest that homeostatic scaling-down, a global form of synaptic plasticity, is active during sleep to remodel synapses and participates in the consolidation of contextual memory.
- [45] F Cervantes-De la Torre, J I González-Trejo, C A Real-Ramírez, and L F Hoyos-Reyes. Fractal dimension algorithms and their application to time series associated with natural phenomena. *J. Phys. Conf. Ser.*, 475(2013):012002, 16 December 2013.
- [46] Yoshiaki Makabe and Kenji Muto. Application of fractal dimension to the evaluation of environmental sound. In *43rd International Congress on Noise Control Engineering: Improving the World Through Noise Control, INTERNOISE 2014*, 2014.
- [47] Kazuhisa Shibata, Yuka Sasaki, Ji Won Bang, Edward G Walsh, Maro G Machizawa, Masako Tamaki, Li-Hung Chang, and Takeo Watanabe. Overlearning hyperstabilizes a skill by rapidly making neurochemical processing inhibitory-dominant. *Nat. Neurosci.*, 20(3):470--475, March 2017. Overlearning refers to the continued training of a skill after performance improvement has plateaued. Whether overlearning is beneficial is a question in our daily lives that has never been clearly answered. Here we report a new important role: overlearning in humans abruptly changes neurochemical processing, to hyperstabilize and protect trained perceptual learning from subsequent new learning. Usually, learning immediately after training is so unstable that it can be



disrupted by subsequent new learning until after passive stabilization occurs hours later. However, overlearning so rapidly and strongly stabilizes the learning state that it not only becomes resilient against, but also disrupts, subsequent new learning. Such hyperstabilization is associated with an abrupt shift from glutamate-dominant excitatory to GABA-dominant inhibitory processing in early visual areas. Hyperstabilization contrasts with passive and slower stabilization, which is associated with a mere reduction of excitatory dominance to baseline levels. Using hyperstabilization may lead to efficient learning paradigms.

- [48] Michael A Ferguson, Jared A Nielsen, Jace B King, Li Dai, Danielle M Giangrosso, Rachel Holman, Julie R Korenberg, and Jeffrey S Anderson. Reward, salience, and attentional networks are activated by religious experience in devout mormons. *Soc. Neurosci.*, pages 1--13, 29 November 2016.  
High-level cognitive and emotional experience arises from brain activity, but the specific brain substrates for religious and spiritual euphoria remain unclear. We demonstrate using functional magnetic resonance imaging scans in 19 devout Mormons that a recognizable feeling central to their devotional practice was reproducibly associated with activation in nucleus accumbens, ventromedial prefrontal cortex, and frontal attentional regions. Nucleus accumbens activation preceded peak spiritual feelings by 1-3 s and was replicated in four separate tasks. Attentional activation in the anterior cingulate and frontal eye fields was greater in the right hemisphere. The association of abstract ideas and brain reward circuitry may interact with frontal attentional and emotive salience processing, suggesting a mechanism whereby doctrinal concepts may come to be intrinsically rewarding and motivate behavior in religious individuals.
- [49] Stephen Olex, Andrew Newberg, and Vincent M Figueredo. Meditation: should a cardiologist care? *Int. J. Cardiol.*, 168(3):1805--1810, 3 October 2013.  
Meditation refers to a family of practices that may share many similarities, but can have differences in underlying methods and goals. Religious and spiritual associations are common but are not requisite for meditation practice and it should be recognized that the basis of many if not all practices is the training of the brain and body, a process that appears to have profound effects on both structure and function. In recent decades there has been interest regarding the effects of these ancient practices on the cardiovascular system, as meditation has intuitive appeal for benefit in this area. Though there is a relative shortage of quality data, available evidence suggests that meditation may exert beneficial effects on autonomic tone, autonomic reflexes, and decrease blood pressure acutely and after long term practice. In addition, meditation has the potential to positively influence the cardiovascular system through the mind-heart connection and the anti-inflammatory reflex. There is limited but promising data to suggest that meditation based interventions can have beneficial effects on patients with established cardiovascular disease. More high quality and unbiased studies of meditation practices on relevant endpoints in cardiovascular disease are needed, including the effects of such practices on inflammation, baseline heart rate variability,

arrhythmias, myocardial infarction, and cardiovascular mortality.

- [50] Jonathan R Krygier, James A J Heathers, Sara Shahrestani, Maree Abbott, James J Gross, and Andrew H Kemp. Mindfulness meditation, well-being, and heart rate variability: a preliminary investigation into the impact of intensive vipassana meditation. *Int. J. Psychophysiol.*, 89(3):305--313, September 2013.

Mindfulness meditation has beneficial effects on brain and body, yet the impact of Vipassana, a type of mindfulness meditation, on heart rate variability (HRV) - a psychophysiological marker of mental and physical health - is unknown. We hypothesised increases in measures of well-being and HRV, and decreases in ill-being after training in Vipassana compared to before (time effects), during the meditation task compared to resting baseline (task effects), and a time by task interaction with more pronounced differences between tasks after Vipassana training. HRV (5-minute resting baseline vs. 5-minute meditation) was collected from 36 participants before and after they completed a 10-day intensive Vipassana retreat. Changes in three frequency-domain measures of HRV were analysed using 2 (Time; pre- vs. post-Vipassana) × 2 (Task; resting baseline vs. meditation) within subjects ANOVA. These measures were: normalised high-frequency power (HF n.u.), a widely used biomarker of parasympathetic activity; log-transformed high frequency power (ln HF), a measure of RSA and required to interpret normalised HF; and Traube-Hering-Mayer waves (THM), a component of the low frequency spectrum linked to baroreflex outflow. As expected, participants showed significantly increased well-being, and decreased ill-being. ln HF increased overall during meditation compared to resting baseline, while there was a time × task interaction for THM. Further testing revealed that pre-Vipassana only ln HF increased during meditation (vs. resting baseline), consistent with a change in respiration. Post-Vipassana, the meditation task increased HF n.u. and decreased THM compared to resting baseline, suggesting post-Vipassana task-related changes are characterised by a decrease in absolute LF power, not parasympathetic-mediated increases in HF power. Such baroreflex changes are classically associated with attentional load, and our results are interpreted in light of the concept of 'flow' - a state of positive and full immersion in an activity. These results are also consistent with changes in normalised HRV reported in other meditation studies.

- [51] Katya Rubia. The neurobiology of meditation and its clinical effectiveness in psychiatric disorders. *Biol. Psychol.*, 82(1):1--11, September 2009.
- This paper reviews the evidence for changes of Meditation on body and brain physiology and for clinical effectiveness in disorders of psychiatry. The aim of Meditation is to reduce or eliminate irrelevant thought processes through training of internalised attention, thought to lead to physical and mental relaxation, stress reduction, psycho-emotional stability and enhanced concentration. Physiological evidence shows a reduction with Meditation of stress-related autonomic and endocrine measures, while neuroimaging studies demonstrate the functional up-regulation of brain regions of affect regulation and attention control. Clinical studies

show some evidence for the effectiveness of Meditation in disorders of affect, anxiety and attention. The combined evidence from neurobiological and clinical studies seems promising. However, a more thorough understanding of the neurobiological mechanisms of action and clinical effectiveness of the different Meditative practices is needed before Meditative practices can be leveraged in the prevention and intervention of mental illness.

- [52] Wilfredo Blanco, Catia M Pereira, Vinicius R Cota, Annie C Souza, César Rennó-Costa, Sharlene Santos, Gabriella Dias, Ana M G Guerreiro, Adriano B L Tort, Adrião D Neto, and Sidarta Ribeiro. Synaptic homeostasis and restructuring across the Sleep-Wake cycle. *PLoS Comput. Biol.*, 11(5):e1004241, May 2015. Sleep is critical for hippocampus-dependent memory consolidation. However, the underlying mechanisms of synaptic plasticity are poorly understood. The central controversy is on whether long-term potentiation (LTP) takes a role during sleep and which would be its specific effect on memory. To address this question, we used immunohistochemistry to measure phosphorylation of Ca<sup>2+</sup>/calmodulin-dependent protein kinase II (pCaMKII $\alpha$ ) in the rat hippocampus immediately after specific sleep-wake states were interrupted. Control animals not exposed to novel objects during waking (WK) showed stable pCaMKII $\alpha$  levels across the sleep-wake cycle, but animals exposed to novel objects showed a decrease during subsequent slow-wave sleep (SWS) followed by a rebound during rapid-eye-movement sleep (REM). The levels of pCaMKII $\alpha$  during REM were proportional to cortical spindles near SWS/REM transitions. Based on these results, we modeled sleep-dependent LTP on a network of fully connected excitatory neurons fed with spikes recorded from the rat hippocampus across WK, SWS and REM. Sleep without LTP orderly rescaled synaptic weights to a narrow range of intermediate values. In contrast, LTP triggered near the SWS/REM transition led to marked swaps in synaptic weight ranking. To better understand the interaction between rescaling and restructuring during sleep, we implemented synaptic homeostasis and embossing in a detailed hippocampal-cortical model with both excitatory and inhibitory neurons. Synaptic homeostasis was implemented by weakening potentiation and strengthening depression, while synaptic embossing was simulated by evoking LTP on selected synapses. We observed that synaptic homeostasis facilitates controlled synaptic restructuring. The results imply a mechanism for a cognitive synergy between SWS and REM, and suggest that LTP at the SWS/REM transition critically influences the effect of sleep: Its lack determines synaptic homeostasis, its presence causes synaptic restructuring.
- [53] Nicolas Dumay. Sleep not just protects memories against forgetting, it also makes them more accessible. *Cortex*, 74:289--296, January 2016. Two published datasets (Dumay & Gaskell, 2007, *Psychological Science*; Tamminen, Payne, Stickgold, Wamsley, & Gaskell, 2010, *Journal of Neuroscience*) showing a positive influence of sleep on declarative memory were re-analyzed, focusing on the “fate” of each item at the 0-h test and 12-h retest. In particular, I looked at which items were retrieved at test and “maintained” (i.e., not forgotten) at

retest, and which items were not retrieved at test, but eventually “gained” at retest. This gave me separate estimates of protection against loss and memory enhancement, which the classic approach relying on net recall/recognition levels has remained blind to. In both free recall and recognition, the likelihood of maintaining an item between test and retest, like that of gaining one at retest, was higher when the retention interval was filled with nocturnal sleep, as opposed to day-time (active) wakefulness. And, in both cases, the effect of sleep was stronger on gained than maintained items. Thus, if sleep indeed protects against retroactive, unspecific interference, it also clearly promotes access to those memories initially too weak to be retrieved. These findings call for an integrated approach including both passive (cell-level) and active (systems-level) consolidation, possibly unfolding in an opportunistic fashion.

- [54] Xiaoqing Hu, James W Antony, Jessica D Creery, Iliana M Vargas, Galen V Bodenhausen, and Ken A Paller. Cognitive neuroscience. unlearning implicit social biases during sleep. *Science*, 348(6238):1013--1015, 29 May 2015.

Although people may endorse egalitarianism and tolerance, social biases can remain operative and drive harmful actions in an unconscious manner. Here, we investigated training to reduce implicit racial and gender bias. Forty participants processed counterstereotype information paired with one sound for each type of bias. Biases were reduced immediately after training. During subsequent slow-wave sleep, one sound was unobtrusively presented to each participant, repeatedly, to reactivate one type of training. Corresponding bias reductions were fortified in comparison with the social bias not externally reactivated during sleep. This advantage remained 1 week later, the magnitude of which was associated with time in slow-wave and rapid-eye-movement sleep after training. We conclude that memory reactivation during sleep enhances counterstereotype training and that maintaining a bias reduction is sleep-dependent.

- [55] David M Greenberg, Simon Baron-Cohen, David J Stillwell, Michal Kosinski, and Peter J Rentfrow. Musical preferences are linked to cognitive styles. *PLoS One*, 10(7):e0131151, 22 July 2015.

Why do we like the music we do? Research has shown that musical preferences and personality are linked, yet little is known about other influences on preferences such as cognitive styles. To address this gap, we investigated how individual differences in musical preferences are explained by the empathizing-systemizing (E-S) theory. Study 1 examined the links between empathy and musical preferences across four samples. By reporting their preferential reactions to musical stimuli, samples 1 and 2 (Ns = 2,178 and 891) indicated their preferences for music from 26 different genres, and samples 3 and 4 (Ns = 747 and 320) indicated their preferences for music from only a single genre (rock or jazz). Results across samples showed that empathy levels are linked to preferences even within genres and account for significant proportions of variance in preferences over and above personality traits for various music-preference dimensions. Study 2 (N = 353) replicated and extended these findings by

investigating how musical preferences are differentiated by E-S cognitive styles (i.e., 'brain types'). Those who are type E (bias towards empathizing) preferred music on the Mellow dimension (R&B/soul, adult contemporary, soft rock genres) compared to type S (bias towards systemizing) who preferred music on the Intense dimension (punk, heavy metal, and hard rock). Analyses of fine-grained psychological and sonic attributes in the music revealed that type E individuals preferred music that featured low arousal (gentle, warm, and sensual attributes), negative valence (depressing and sad), and emotional depth (poetic, relaxing, and thoughtful), while type S preferred music that featured high arousal (strong, tense, and thrilling), and aspects of positive valence (animated) and cerebral depth (complexity). The application of these findings for clinicians, interventions, and those on the autism spectrum (largely type S or extreme type S) are discussed.

- [56] Arianna N LaCroix, Alvaro F Diaz, and Corianne Rogalsky. The relationship between the neural computations for speech and music perception is context-dependent: an activation likelihood estimate study. *Front. Psychol.*, 6:1138, 11 August 2015.

The relationship between the neurobiology of speech and music has been investigated for more than a century. There remains no widespread agreement regarding how (or to what extent) music perception utilizes the neural circuitry that is engaged in speech processing, particularly at the cortical level. Prominent models such as Patel's Shared Syntactic Integration Resource Hypothesis (SSIRH) and Koelsch's neurocognitive model of music perception suggest a high degree of overlap, particularly in the frontal lobe, but also perhaps more distinct representations in the temporal lobe with hemispheric asymmetries. The present meta-analysis study used activation likelihood estimate analyses to identify the brain regions consistently activated for music as compared to speech across the functional neuroimaging (fMRI and PET) literature. Eighty music and 91 speech neuroimaging studies of healthy adult control subjects were analyzed. Peak activations reported in the music and speech studies were divided into four paradigm categories: passive listening, discrimination tasks, error/anomaly detection tasks and memory-related tasks. We then compared activation likelihood estimates within each category for music vs. speech, and each music condition with passive listening. We found that listening to music and to speech preferentially activate distinct temporo-parietal bilateral cortical networks. We also found music and speech to have shared resources in the left pars opercularis but speech-specific resources in the left pars triangularis. The extent to which music recruited speech-activated frontal resources was modulated by task. While there are certainly limitations to meta-analysis techniques particularly regarding sensitivity, this work suggests that the extent of shared resources between speech and music may be task-dependent and highlights the need to consider how task effects may be affecting conclusions regarding the neurobiology of speech and music.

- [57] Christopher R Holdgraf, Wendy de Heer, Brian Pasley, Jochem Rieger, Nathan Crone, Jack J Lin, Robert T Knight, and Frédéric E Theunissen. Rapid tuning shifts in human auditory cortex enhance speech intelligibility. *Nat. Commun.*, 7:13654, 20 December 2016.

Experience shapes our perception of the world on a moment-to-moment basis. This robust perceptual effect of experience parallels a change in the neural representation of stimulus features, though the nature of this representation and its plasticity are not well-understood. Spectrotemporal receptive field (STRF) mapping describes the neural response to acoustic features, and has been used to study contextual effects on auditory receptive fields in animal models. We performed a STRF plasticity analysis on electrophysiological data from recordings obtained directly from the human auditory cortex. Here, we report rapid, automatic plasticity of the spectrotemporal response of recorded neural ensembles, driven by previous experience with acoustic and linguistic information, and with a neurophysiological effect in the sub-second range. This plasticity reflects increased sensitivity to spectrotemporal features, enhancing the extraction of more speech-like features from a degraded stimulus and providing the physiological basis for the observed 'perceptual enhancement' in understanding speech.

- [58] Jayne M Standley. A meta-analysis of the efficacy of music therapy for premature infants. *J. Pediatr. Nurs.*, 17(2):107--113, April 2002.

This meta-analysis on music research with premature infants in neonatal intensive care units (NICU) showed an overall large, significant, consistent effect size of almost a standard deviation ( $d = .83$ ) (Cohen, 1998). Effects were not mediated by infants' gestational age at the time of study, birthweight, or type of music delivery nor by physiologic, behavioral, or developmental measures of benefit. The homogeneity of findings suggests that music has statistically significant and clinically important benefits for premature infants in the NICU. The unique acoustic properties that differentiate music from all other sounds are discussed and clinical implications for research-based music therapy procedures cited.

- [59] Hong Kim, Myoung-Hwa Lee, Hyun-Kyung Chang, Taeck-Hyun Lee, Hee-Hyuk Lee, Min-Chul Shin, Mal-Soon Shin, Ran Won, Hye-Sook Shin, and Chang-Ju Kim. Influence of prenatal noise and music on the spatial memory and neurogenesis in the hippocampus of developing rats. *Brain Dev.*, 28(2):109--114, March 2006.

During the prenatal period, the development of individual is influenced by the environmental factors. In the present study, the influence of prenatal noise and music on the spatial memory and neurogenesis in the hippocampus of developing rats was investigated. The exposure to the noise during pregnancy caused growth retardation, decreased neurogenesis in the hippocampus, and impaired spatial learning ability in pups. The exposure to music during pregnancy, on the other hand, caused increased neurogenesis in the hippocampus and enhanced spatial learning ability in pups. The present study has shown the importance of the prenatal environmental conditions for the cognition and brain development.

- [60] Amy L Anderson and Moriah E Thomason. Functional plasticity before the cradle: a review of neural functional imaging in the human fetus. *Neurosci. Biobehav. Rev.*, 37(9 Pt B):2220--2232, November 2013.

The organization of the brain is highly plastic in fetal life. Establishment of healthy neural functional systems during the fetal period is essential to normal growth and development. Across the last several decades, remarkable progress has been made in understanding the development of human fetal functional brain systems. This is largely due to advances in imaging methodologies. Fetal neuroimaging began in the 1950-1970's with fetal electroencephalography (EEG) applied during labor. Later, in the 1980's, magnetoencephalography (MEG) emerged as an effective approach for investigating fetal brain function. Most recently, functional magnetic resonance imaging (fMRI) has arisen as an additional powerful approach for examining fetal brain function. This review will discuss major developmental findings from fetal imaging studies such as the maturation of prenatal sensory system functions, functional hemispheric asymmetry, and sensory-driven neurodevelopment. We describe how with improved imaging and analysis techniques, functional imaging of the fetus has the potential to assess the earliest point of neural maturation and provide insight into the patterning and sequence of normal and abnormal brain development.

- [61] Tania Sanyal, Pradeep Palanisamy, T C Nag, T S Roy, and Shashi Wadhwa. Effect of prenatal loud music and noise on total number of neurons and glia, neuronal nuclear area and volume of chick brainstem auditory nuclei, field L and hippocampus: a stereological investigation. *Int. J. Dev. Neurosci.*, 31(4):234--244, June 2013.

The present study explores whether prenatal patterned and unpatterned sound of high sound pressure level (110 dB) has any differential effect on the morphology of brainstem auditory nuclei, field L (auditory cortex analog) and hippocampus in chicks (*Gallus domesticus*). The total number of neurons and glia, mean neuronal nuclear area and total volume of the brainstem auditory nuclei, field L and hippocampus of post-hatch day 1 chicks were determined in serial, cresyl violet-stained sections, using stereology software. All regions studied showed a significantly increased total volume with increase in total neuron number and mean neuronal nuclear area in the patterned music stimulated group as compared to control. Contrastingly the unpatterned noise stimulated group showed an attenuated volume with reduction in the total neuron number. The mean neuronal nuclear area was significantly reduced in the auditory nuclei and hippocampus but increased in the field L. Glial cell number was significantly increased in both experimental groups, being highest in the noise group. The brainstem auditory nuclei and field L showed an increase in glia to neuron ratio in the experimental groups as compared to control. In the hippocampus the ratio remained unaltered between control and music groups, but was higher in the noise group. It is thus evident that though the sound pressure level in both experimental groups was the same there were differential changes in the morphological parameters of the brain regions studied, indicating that the characteristics of the sound had a role in mediating these effects.

- [62] Bo Meng, Shujia Zhu, Shijia Li, Qingwen Zeng, and Bing Mei. Global view of the mechanisms of improved learning and memory capability in mice with music-exposure by microarray. *Brain Res. Bull.*, 80(1-2):36--44, 28 August 2009. Music has been proved beneficial to improve learning and memory in many species including human in previous research work. Although some genes have been identified to contribute to the mechanisms, it is believed that the effect of music is manifold, behind which must concern a complex regulation network. To further understand the mechanisms, we exposed the mice to classical music for one month. The subsequent behavioral experiments showed improvement of spatial learning capability and elevation of fear-motivated memory in the mice with music-exposure as compared to the naïve mice. Meanwhile, we applied the microarray to compare the gene expression profiles of the hippocampus and cortex between the mice with music-exposure and the naïve mice. The results showed approximately 454 genes in cortex (200 genes up-regulated and 254 genes down-regulated) and 437 genes in hippocampus (256 genes up-regulated and 181 genes down-regulated) were significantly affected in music-exposing mice, which mainly involved in ion channel activity and/or synaptic transmission, cytoskeleton, development, transcription, hormone activity. Our work may provide some hints for better understanding the effects of music on learning and memory.
- [63] Norbert Jaušovec, Ksenija Jaušovec, and Ivan Gerlič. The influence of Mozart's music on brain activity in the process of learning. *Clin. Neurophysiol.*, 117(12):2703--2714, December 2006. Objective The study investigated the influence Mozart's music has on brain activity in the process of learning. A second objective was to test Rauscher et al.'s (1993) priming explanation of the Mozart effect. Methods In Experiment 1 individuals were first trained in how to solve spatial rotation tasks, and then solved similar tasks. Fifty-six students were divided into 4 groups: a control one -- CG who prior to and after training relaxed, and three experimental groups: MM -- who prior to and after training listened to music; MS -- who prior to training listened to music and subsequently relaxed; and SM -- who prior to training relaxed and afterward listened to music. The music used was the first movement of Mozart's sonata (K. 448). In Experiment 2, thirty-six respondents were divided into three groups: CG, MM (same procedure as in Experiment 1), and BM -- who prior to and after training listened to Brahms' Hungarian dance No. 5. In both experiments the EEG data collected during problem solving were analyzed using the methods of event-related desynchronization/synchronization (ERD/ERS) and approximated entropy (ApEn). Results In the first experiment the respondents of the MM, MS, and SM groups showed a better task-performance than did the respondents of the CG group. Individuals of the MM group displayed less complex EEG patterns and more  $\alpha$  band synchronization than did respondents of the other three groups. In Experiment 2 individuals who listened to Mozart showed a better task performance than did the respondents of the CG and BM groups. They displayed less complex EEG patterns and more lower-1  $\alpha$  and  $\gamma$  band synchronization than did the respondents of the BM group. Conclusions Mozart's music, by activating task-relevant brain areas, enhances the learning of spatio-temporal rotation tasks.



Significance The results support Rauscher et al.'s (1993) priming explanation of the Mozart effect.

- [64] Stanley N Graven and Joy V Browne. Auditory development in the fetus and infant. *Newborn Infant Nurs. Rev.*, 8(4):187--193, December 2008.

Auditory development in the fetus and infant entails the structural parts of the ears that develop in the first 20 weeks of gestation, and the neurosensory part of the auditory system develops primarily after 20 weeks' gestational age. The auditory system becomes functional at around 25 weeks' gestation. The cochlea of the middle ear and the auditory cortex in the temporal lobe are most important in the development of the auditory system. They are both easily affected by the environment and care practices in the newborn intensive care unit (NICU). The period from 25 weeks' gestation to 5 to 6 months of age is most critical to the development of the neurosensory part of the auditory system. This is the time when the hair cells of the cochlea, the axons of the auditory nerve, and the neurons of the temporal lobe auditory cortex are tuned to receive signals of specific frequencies and intensities. Unlike the visual system, the auditory system requires outside auditory stimulation. This needs to include speech, music, and meaningful sounds from the environment. The preterm as well as the term infant cannot recognize or discriminate meaningful sounds with background noise levels greater than 60 dB. The more intense the background noise, especially low frequency, the fewer specific frequencies (pitch) can be heard and used to tune the hair cells of the cochlea. Continuous exposure to loud background noise in the NICU or home will interfere with auditory development and especially frequency discrimination. The initial stimulation of the auditory system (speech and music) needs to occur in utero or in the NICU to develop tonotopic columns in the auditory cortex and to have the critical tuning of the hair cells of the cochlea occur. The control of outside noise, the exposure to meaningful speech sounds and music, and the protection of sleep and sleep cycles, especially rapid eye movement sleep, are essential for healthy auditory development. The environment and care practices for the fetus in utero or the infant in the NICU are critical factors in the development of the auditory system.

- [65] Alix Zorrillo Pallavicino. Sound and silence, rhythm and harmony as the basis for prenatal education through music musical pedagogical experiences with expectant parents. *Procedia - Social and Behavioral Sciences*, 191:2136--2139, 2 June 2015.

Art begins with life: the construction of primary sounds begins in the womb. The voices of mother and father join in this "gestational symphony", influencing its harmony with their interactions. The scientific community recognizes the key role of the prenatal period: international researches confirm the importance of a harmonious primary relationship. My own musical pedagogical work over the past several years has confirmed to me that the optimum medium for educating to listen and to live in harmony with the self and others, is provided by experiences based on the individual's personal sensibility and fostering immediate reflection.

- [66] Hajime Fukui and Kumiko Toyoshima. Music facilitate the neurogenesis, regeneration and repair of neurons. *Med. Hypotheses*, 71(5):765--769, November 2008.

Experience has shown that therapy using music for therapeutic purposes has certain effects on neuropsychiatric disorders (both functional and organic disorders). However, the mechanisms of action underlying music therapy remain unknown, and scientific clarification has not advanced. While that study disproved the Mozart effect, the effects of music on the human body and mind were not disproved. In fact, more scientific studies on music have been conducted in recent years, mainly in the field of neuroscience, and the level of interest among researchers is increasing. The results of past studies have clarified that music influences and affects cranial nerves in humans from fetus to adult. The effects of music at a cellular level have not been clarified, and the mechanisms of action for the effects of music on the brain have not been elucidated. We propose that listening to music facilitates the neurogenesis, the regeneration and repair of cerebral nerves by adjusting the secretion of steroid hormones, ultimately leading to cerebral plasticity. Music affects levels of such steroids as cortisol (C), testosterone (T) and estrogen (E), and we believe that music also affects the receptor genes related to these substances, and related proteins. In the prevention of Alzheimer's disease and dementia, hormone replacement therapy has been shown to be effective, but at the same time, side effects have been documented, and the clinical application of hormone replacement therapy is facing a serious challenge. Conversely, music is noninvasive, and its existence is universal and mundane. Thus, if music can be used in medical care, the application of such a safe and inexpensive therapeutic option is limitless.

- [67] Hsing-Chi Chang, Chen-Hsiang Yu, Shu-Yueh Chen, and Chung-Hey Chen. The effects of music listening on psychosocial stress and maternal-fetal attachment during pregnancy. *Complement. Ther. Med.*, 23(4):509--515, August 2015. OBJECTIVE: While music listening has been studied as an intervention to help reduce anxiety in pregnant women, few studies have explored the effect of music listening on pregnancy-specific stress relief. This study examines the effects of music listening on psychosocial stress and maternal-fetal attachment during pregnancy. DESIGN: A randomized controlled trial was implemented. A valid sample of 296 pregnant women in their second or third trimester was randomly distributed into an experimental group (n=145) and a control group (n=151). INTERVENTIONS: The experimental group received routine prenatal care and music listening. The control group received routine prenatal care only. MAIN OUTCOME MEASURES: Data were collected using a demographic form, Pregnancy Stress Rating Scale (PSRS), Perceived Stress Scale (PSS), and Maternal-Fetal Attachment Scale (MFAS). RESULTS: The post-test results identified a significantly lower level of psychosocial stress in the experimental group than in the control group, particularly in terms of the stresses related to baby care and changing family relationships and to maternal role identification. However, no statistically significant differences in terms of perceived stress and maternal-fetal attachment were found between the post-test results of the two groups. CONCLUSION: This study provides evidence in support of using of music

in interventions designed to relieve psychosocial stress in prenatal women. IRB approval number: ER98223.

- [68] Caroline J Hollins Martin. A narrative literature review of the therapeutic effects of music upon childbearing women and neonates. *Complement. Ther. Clin. Pract.*, 20(4):262--267, November 2014.

Therapeutic effects of music are well recognised within the literature, with benefits for a variety of health problems documented. This narrative review summarises benefits in terms of reducing stress, anxiety, labour pain and depression in childbearing women. For neonates, music has been shown to reduce number of days to discharge, reduce pain response behaviours, increase weight gain, improve Brazelton scores, improve parent/infant intimacy, improve oxygen saturation, increase formula intake, stabilize vital signs and increase parental reports of calmed infants. The main criticism of the studies reviewed is lack of categorisation of the particulars of the variables within the music that directly influenced outcome variables. A recommendation is made that a music package be developed and relationships with variables rigorously evaluated. The validated product may then be made available for use. Since evidence supports advantages from listening to music, it is suggested that maternity professionals use it in more creative ways.

- [69] H Poikonen, V Alluri, E Brattico, O Lartillot, M Tervaniemi, and M Huotilainen. Event-related brain responses while listening to entire pieces of music. *Neuroscience*, 312:58--73, 15 January 2016.

Brain responses to discrete short sounds have been studied intensively using the event-related potential (ERP) method, in which the electroencephalogram (EEG) signal is divided into epochs time-locked to stimuli of interest. Here we introduce and apply a novel technique which enables one to isolate ERPs in human elicited by continuous music. The ERPs were recorded during listening to a Tango Nuevo piece, a deep techno track and an acoustic lullaby. Acoustic features related to timbre, harmony, and dynamics of the audio signal were computationally extracted from the musical pieces. Negative deflation occurring around 100 milliseconds after the stimulus onset (N100) and positive deflation occurring around 200 milliseconds after the stimulus onset (P200) ERP responses to peak changes in the acoustic features were distinguishable and were often largest for Tango Nuevo. In addition to large changes in these musical features, long phases of low values that precede a rapid increase - and that we will call Preceding Low-Feature Phases - followed by a rapid increase enhanced the amplitudes of N100 and P200 responses. These ERP responses resembled those to simpler sounds, making it possible to utilize the tradition of ERP research with naturalistic paradigms.

- [70] Francesco Angelucci, Enzo Ricci, Luca Padua, Andrea Sabino, and Pietro Attilio Tonali. Music exposure differentially alters the levels of brain-derived neurotrophic factor and nerve growth factor in the mouse hypothalamus. *Neurosci. Lett.*, 429(2-3):152--155, 18 December 2007.

It has been reported that music may have physiological effects on blood pressure, cardiac heartbeat, respiration, and improve mood state in people affected by anxiety, depression and other psychiatric disorders. However, the physiological bases of these phenomena are not clear. Hypothalamus is a brain region involved in the regulation of body homeostasis and in the pathophysiology of anxiety and depression through the modulation of hypothalamic-pituitary-adrenal (HPA) axis. Hypothalamic functions are also influenced by the presence of the neurotrophins brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF), which are proteins involved in the growth, survival and function of neurons in the central nervous system. The aim of this study was to investigate the effect of music exposure in mice on hypothalamic levels of BDNF and NGF. We exposed young adult mice to slow rhythm music (6h per day; mild sound pressure levels, between 50 and 60 dB) for 21 consecutive days. At the end of the treatment mice were sacrificed and BDNF and NGF levels in the hypothalamus were measured by enzyme-linked immunosorbent assay (ELISA). We found that music exposure significantly enhanced BDNF levels in the hypothalamus. Furthermore, we observed that music-exposed mice had decreased NGF hypothalamic levels. Our results demonstrate that exposure to music in mice can influence neurotrophin production in the hypothalamus. Our findings also suggest that physiological effects of music might be in part mediated by modulation of neurotrophins.

- [71] Sachiko Chikahisa, Hiroyoshi Sei, Masaki Morishima, Atsuko Sano, Kazuyoshi Kitaoka, Yutaka Nakaya, and Yusuke Morita. Exposure to music in the perinatal period enhances learning performance and alters BDNF/TrkB signaling in mice as adults. *Behav. Brain Res.*, 169(2):312--319, 15 May 2006.

Music has been suggested to have a beneficial effect on various types of performance in humans. However, the physiological and molecular mechanism of this effect remains unclear. We examined the effect of music exposure during the perinatal period on learning behavior in adult mice, and measured the levels of brain-derived neurotrophic factor (BDNF) and its receptor, tyrosine kinase receptor B (TrkB), which play critical roles in synaptic plasticity. In addition, we measured the levels of 3-phosphoinositide-dependent protein kinase-1 (PDK1) and mitogen-activated protein kinase (MAPK), downstream targets of two main pathways in BDNF/TrkB signaling. Music-exposed mice completed a maze learning task with fewer errors than the white noise-exposed mice and had lower levels of BDNF and higher levels of TrkB and PDK1 in the cortex. MAPK levels were unchanged. Furthermore, TrkB and PDK1 protein levels in the cortex showed a significant negative correlation with the number of errors on the maze. These results suggest that perinatal exposure of mice to music has an influence on BDNF/TrkB signaling and its intracellular signaling pathway targets, including PDK1, and thus may induce improved learning and memory functions.

- [72] Yingshou Xing, Wenxi Chen, Yanran Wang, Wei Jing, Shan Gao, Daqing Guo, Yang Xia, and Dezhong Yao. Music exposure improves spatial cognition by enhancing the BDNF level of dorsal hippocampal subregions in the developing rats. *Brain Res. Bull.*, 121:131--137, March 2016.
- Previous research has shown that dorsal hippocampus plays an important role in spatial memory process. Music exposure can enhance brain-derived neurotrophic factor (BDNF) expression level in dorsal hippocampus (DH) and thus enhance spatial cognition ability. But whether music experience may affect different subregions of DH in the same degree remains unclear. Here, we studied the effects of exposure to Mozart K.448 on learning behavior in developing rats using the classical Morris water maze task. The results showed that early music exposure could enhance significantly learning performance of the rats in the water maze test. Meanwhile, the BDNF/TrkB level of dorsal hippocampus CA3 (dCA3) and dentate gyrus (dDG) was significantly enhanced in rats exposed to Mozart music as compared to those without music exposure. In contrast, the BDNF/TrkB level of dorsal hippocampus CA1 (dCA1) was not affected. The results suggest that the spatial memory improvement by music exposure in rats may be associated with the enhanced BDNF/TrkB level of dCA3 and dDG.
- [73] Serap Simavli, Ikbal Kaygusuz, Ilknur Gumus, Betul Usluogullari, Melahat Yildirim, and Hasan Kafali. Effect of music therapy during vaginal delivery on postpartum pain relief and mental health. *J. Affect. Disord.*, 156:194--199, March 2014.
- BACKGROUND: Childbirth is an important experience in a woman's life, and unfavorable birth experiences have been shown to negatively impact postpartum maternal health. Aim of this study was to evaluate the effects of music therapy on postpartum pain, anxiety level, satisfaction and early postpartum depression rate. METHODS: Totally 161 primiparous women were recruited and randomized either music group (n=80) or a control group (n=81). Women in the music group listened to self-selected music during labor. Postpartum pain intensity, anxiety level and satisfaction rate were measured using the visual analog scale (VAS), postpartum depression rate was assessed with Edinburg Postpartum Depression Scale (EPDS) at postpartum day one and day eight. RESULTS: Mothers in the music therapy group had a lower level of postpartum pain and anxiety than the control group and it was statistically significant at all time intervals (1, 4, 8, 16 and 24h,  $p < 0.001$ ). A significant difference was observed between the two groups in terms of satisfaction rate ( $p < 0.001$ ) and postpartum depression rate at postpartum day one and day eight ( $p < 0.05$ ). LIMITATIONS: We only measured the effect of music therapy on early postpartum depression rate. Effect of music on late postpartum depression rate should be investigated in future. CONCLUSIONS: Using music therapy during labor decreased postpartum anxiety and pain, increased the satisfaction with childbirth and reduced early postpartum depression rate. Music therapy can be clinically recommended as an alternative, safe, easy and enjoyable nonpharmacological method for postpartum well-being.

- [74] Faranak Safdari Dehcheshmeh and Hossein Rafiei. Complementary and alternative therapies to relieve labor pain: A comparative study between music therapy and hoku point ice massage. *Complement. Ther. Clin. Pract.*, 21(4):229--232, November 2015.
- BACKGROUND & AIM: Pain is a common experience for women during labor. In the present study, we compared the effect of two types of non-pharmacological pain relief methods "music therapy" and "Hoku point ice massage" on the severity of labor pain. METHODS: This prospective, randomized, controlled trial was conducted in Shahrekord, Iran, from September 2013 to June 2014. We randomly assigned 90 primiparous women who expected a normal childbirth into three groups: group "A" received music therapy, group "B" received Hoku point ice massage, and group "C" received usual labor care. At the beginning of the active phase (4 cm cervical dilation) and before and after each intervention (at dilations 4, 6, and 8 cm), the intensities of labor pain were measured using Visual Analogue Scale (VAS). RESULTS: At the beginning of the active phase, the mean VAS scores were 5.58 1.29, 5.42 1.31, and 6.13 1.37 in the women in groups "A," "B," and "C," respectively ( $P > 0.05$ ). After the intervention, the mean pain scores were significantly lower at all of the time points in groups "A" and "B" than in group "C" women ( $P 0.05$ ). CONCLUSIONS: Music therapy and Hoku point ice massage are easily available and inexpensive methods and have a similar effect in relieving labor pain.
- [75] Maryléa Elizabeth Ramos Vargas. Music as a resource to develop cognition. *Procedia - Social and Behavioral Sciences*, 174:2989--2994, 12 February 2015. The paper focuses on cognition as an element for human development and application of musical language resources in order to stimulate and strengthen neural connections favorable for learning. The study relies on research and analysis of current researches in neuroscience on scientific evidences dealing with the effects of music on the brain and the reflection on human behavior.
- [76] Holger Mohr, Uta Wolfensteller, Richard F Betzel, Bratislav Mišić, Olaf Sporns, Jonas Richiardi, and Hannes Ruge. Integration and segregation of large-scale brain networks during short-term task automatization. *Nat. Commun.*, 7:13217, 3 November 2016.
- The human brain is organized into large-scale functional networks that can flexibly reconfigure their connectivity patterns, supporting both rapid adaptive control and long-term learning processes. However, it has remained unclear how short-term network dynamics support the rapid transformation of instructions into fluent behaviour. Comparing fMRI data of a learning sample ( $N=70$ ) with a control sample ( $N=67$ ), we find that increasingly efficient task processing during short-term practice is associated with a reorganization of large-scale network interactions. Practice-related efficiency gains are facilitated by enhanced coupling between the cingulo-opercular network and the dorsal attention network. Simultaneously, short-term task automatization is accompanied by decreasing activation of the fronto-parietal network, indicating a release of high-level cognitive control, and a

segregation of the default mode network from task-related networks. These findings suggest that short-term task automatization is enabled by the brain's ability to rapidly reconfigure its large-scale network organization involving complementary integration and segregation processes.

- [77] Harnam Singh and Michael W O'Boyle. Interhemispheric interaction during global-local processing in mathematically gifted adolescents, average-ability youth, and college students. *Neuropsychology*, 18(2):371--377, April 2004.  
Interhemispheric interaction in mathematically gifted (MG) adolescents, average-ability (AA) youth, and college students (CS) was examined by presenting hierarchical letter pairs in 3 viewing conditions: (a) unilaterally to the right hemisphere (RH), (b) unilaterally to the left hemisphere (LH), or (c) bilaterally, with 1 member of the pair presented to each hemisphere simultaneously. Participants made global-local, match-no-match judgments. For the AA and CS, the LH was faster for local matches and the RH for global matches. The MG showed no hemispheric differences. Also, AA and CS were slower on cooperative compared with unilateral trials, whereas the MG showed the opposite pattern. These results suggest that enhanced interhemispheric interaction is a unique functional characteristic of the MG brain.
- [78] M H Thaut. Neurologic music therapy in cognitive rehabilitation. *Music Perception: An Interdisciplinary Journal*, 27(4):281--285, 2010.  
Abstract NEUROLOGIC MUSIC THERAPY LAST CAME INTO research and clinical focus via cognitive rehabilitation. New imaging techniques studying higher cognitive functions in the human brain'in vivo'and theoretical advancements in music and brain function have facilitated this development. There are shared cognitive and perceptual mechanisms and shared neural systems between musical cognition and parallel nonmusical cognitive ...
- [79] Shantala Hegde. Music-based cognitive remediation therapy for patients with traumatic brain injury. *Front. Neurol.*, 5:34, 24 March 2014.  
Traumatic brain injury (TBI) is one of the common causes of disability in physical, psychological, and social domains of functioning leading to poor quality of life. TBI leads to impairment in sensory, motor, language, and emotional processing, and also in cognitive functions such as attention, information processing, executive functions, and memory. Cognitive impairment plays a central role in functional recovery in TBI. Innovative methods such as music therapy to alleviate cognitive impairments have been investigated recently. The role of music in cognitive rehabilitation is evolving, based on newer findings emerging from the fields of neuromusicology and music cognition. Research findings from these fields have contributed significantly to our understanding of music perception and cognition, and its neural underpinnings. From a neuroscientific perspective, indulging in music is considered as one of the best cognitive exercises. With "plasticity" as its veritable nature, brain engages in producing music indulging an array of cognitive functions and the product, the music, in turn permits restoration and alters brain

functions. With scientific findings as its basis, “neurologic music therapy” (NMT) has been developed as a systematic treatment method to improve sensorimotor, language, and cognitive domains of functioning via music. A preliminary study examining the effect of NMT in cognitive rehabilitation has reported promising results in improving executive functions along with improvement in emotional adjustment and decreasing depression and anxiety following TBI. The potential usage of music-based cognitive rehabilitation therapy in various clinical conditions including TBI is yet to be fully explored. There is a need for systematic research studies to bridge the gap between increasing theoretical understanding of usage of music in cognitive rehabilitation and application of the same in a heterogeneous condition such as TBI.

- [80] Michael H Thaut, David A Peterson, and Gerald C McIntosh. Temporal entrainment of cognitive functions: musical mnemonics induce brain plasticity and oscillatory synchrony in neural networks underlying memory. *Ann. N. Y. Acad. Sci.*, 1060:243--254, December 2005.

In a series of experiments, we have begun to investigate the effect of music as a mnemonic device on learning and memory and the underlying plasticity of oscillatory neural networks. We used verbal learning and memory tests (standardized word lists, AVLT) in conjunction with electroencephalographic analysis to determine differences between verbal learning in either a spoken or musical (verbal materials as song lyrics) modality. In healthy adults, learning in both the spoken and music condition was associated with significant increases in oscillatory synchrony across all frequency bands. A significant difference between the spoken and music condition emerged in the cortical topography of the learning-related synchronization. When using EEG measures as predictors during learning for subsequent successful memory recall, significantly increased coherence (phase-locked synchronization) within and between oscillatory brain networks emerged for music in alpha and gamma bands. In a similar study with multiple sclerosis patients, superior learning and memory was shown in the music condition when controlled for word order recall, and subjects were instructed to sing back the word lists. Also, the music condition was associated with a significant power increase in the low-alpha band in bilateral frontal networks, indicating increased neuronal synchronization. Musical learning may access compensatory pathways for memory functions during compromised PFC functions associated with learning and recall. Music learning may also confer a neurophysiological advantage through the stronger synchronization of the neuronal cell assemblies underlying verbal learning and memory. Collectively our data provide evidence that melodic-rhythmic templates as temporal structures in music may drive internal rhythm formation in recurrent cortical networks involved in learning and memory.



- [81] Wiebke Trost and Patrik Vuilleumier. Rhythmic entrainment as a mechanism for emotion induction by music. In *The Emotional Power of Music*, pages 213--225. 11 July 2013.  
Official Full-Text Publication: Rhythmic entrainment as a mechanism for emotion induction by music on ResearchGate, the professional network for scientists.
- [82] Bruno Gingras, Gerald Pohler, and W Tecumseh Fitch. Exploring shamanic journeying: repetitive drumming with shamanic instructions induces specific subjective experiences but no larger cortisol decrease than instrumental meditation music. *PLoS One*, 9(7):e102103, 7 July 2014.  
Exposure to repetitive drumming combined with instructions for shamanic journeying has been associated with physiological and therapeutic effects, such as an increase in salivary immunoglobulin A. In order to assess whether the combination of repetitive drumming and shamanic instructions is specifically associated with these effects, we compared the effect of listening to either repetitive drumming or instrumental meditation music for 15 minutes on salivary cortisol concentration and on self-reported physiological and psychological states. For each musical style, two groups of participants were exposed to two conditions: instructions for shamanic journeying or relaxation instructions. A total of 39 participants (24 females) inexperienced in shamanic journeying completed the experiment. Salivary cortisol concentrations were measured before and after exposure to music. In addition, participants filled out a mood questionnaire before and after the experiment and completed a post experiment questionnaire on their experiences. A significant decrease in the concentration in salivary cortisol was observed across all musical styles and instructions, indicating that exposure to 15 minutes of either repetitive drumming or instrumental meditation music, while lying down, was sufficient to induce a decrease in cortisol levels. However, no differences were observed across conditions. Significant differences in reported emotional states and subjective experiences were observed between the groups. Notably, participants exposed to repetitive drumming combined with shamanic instructions reported experiencing heaviness, decreased heart rate, and dreamlike experiences significantly more often than participants exposed to repetitive drumming combined with relaxation instructions. Our findings suggest that the subjective effects specifically attributed to repetitive drumming and shamanic journeying may not be reflected in differential endocrine responses.
- [83] N G Karthick, V I T Ahamed, and J K Paul. Music and the EEG: A study using nonlinear methods. In *2006 International Conference on Biomedical and Pharmaceutical Engineering*, pages 424--427, December 2006.  
The effect of two types of music on the electroencephalogram (EEG) activity is examined, namely Indian Carnatic classical and rock music. About 300 seconds worth of EEG data is used to study the effect of each type of music. The analysis is carried out using two different methods based on nonlinear theory. The scaling properties of the EEG are studied using the detrended fluctuation analysis (DFA) algorithm, and the complexity of the electroencephalogram signal is quantified by

the multiscale entropy (MSE) method. It is found that both methods show significant difference in the values of the estimated parameters for the electroencephalogram with and without music. The MSE method shows higher values of entropy for both types of music, indicating that the complexity of the electroencephalogram increases when the brain processes music.

- [84] Satoshi Nakamura, Norihiro Sadato, Tsutomu Oohashi, Emi Nishina, Yoshitaka Fuwamoto, and Yoshiharu Yonekura. Analysis of music--brain interaction with simultaneous measurement of regional cerebral blood flow and electroencephalogram beta rhythm in human subjects. *Neurosci. Lett.*, 275(3):222-226, 19 November 1999.

To elucidate the neural substrates of the receptive aspect of music, we measured regional cerebral blood flow (rCBF) with positron emission tomography (PET) and simultaneously recorded the electroencephalogram (EEG) in eight normal volunteers. Compared with the rest condition, listening to music caused a significant increase in EEG beta power spectrum (13--30 Hz) averaged over the posterior two third of the scalp. The averaged beta power spectrum was positively correlated with rCBF in the premotor cortex and adjacent prefrontal cortices bilaterally, the anterior portion of the precuneus and the anterior cingulate cortex in both the rest and the music conditions. Listening to music newly recruited the posterior portion of the precuneus bilaterally. This may reflect the interaction of the music with the cognitive processes, such as music-evoked memory recall or visual imagery.

- [85] S Ogata. Human EEG responses to classical music and simulated white noise: effects of a musical loudness component on consciousness. *Percept. Mot. Skills*, 80(3 Pt 1):779--790, June 1995.

The main purpose of the present study was to investigate the psychophysiological effects of music on human EEG. For this purpose, a sound modulator was developed which simulates the sound-pressure variations of a given piece of music by white noise (sim-music). Using this apparatus, the author tested the psychophysiological effects of music on human EEG. The electroencephalograms (EEG), electrocardiograms (ECG), and electrooculograms (EOG) of eight normal volunteers were recorded for a total of 21 min., 5 sec. per session for each subject under three sound conditions: silence for 5 min., two types of music (music) or two types of simulated noise (sim-music) for 11 min., 5 sec., followed by silence for another 5 min. Each subject was exposed to a total of 10 music and 10 sim-music conditions. At the low consciousness level (drowsiness, Stage S1), higher delta component power densities were observed with sim-music than with music. Thus, even in the same Stage S1, entire physiological consciousness levels may be higher when listening to music than to sim-music. While listening to music, many subjects reported that they felt pleasantly relaxed or comfortable. However, with the sim-music, they reported feeling unpleasantly weary and sleepy. It seems that the mental set toward two sound conditions differed greatly for many subjects. In Stage S1, the differences in EEG slow components showed that the differences in

consciousness had a physiological aspect and indicated differences in mental set toward both sound conditions and mental activity during the listening conditions.

- [86] F Fikejz. Influence of music on human electroencephalogram. In *2011 International Conference on Applied Electronics*, pages 1--4, 2011.

This paper deals with a research of an influence of listening to sound sequence on changing of brain activity. Differences of human electroencephalogram (EEG) monitored by a four channel device on silent conditions and while listening to a sound sequence are described. Sound sequence consisted of fourteen tracks separated by five seconds of silence. This experiment was performed on four subjects sitting on a chair with closed eyes inside an audiology room. The average of four channels was used for additional processing. Signal of each subject was edited to fifteen parts representing EEG signals during listening to each track. All parts of EEG signal were filtered to delta, theta, alpha, beta and gamma activities. Energy of all these activities was calculated. For each activity the changeability of EEG during listening to the tracks was analyzed by analysis of variance.

- [87] Patrick A McConnell, Brett Froeliger, Eric L Garland, Jeffrey C Ives, and Gary A Sforzo. Auditory driving of the autonomic nervous system: Listening to theta-frequency binaural beats post-exercise increases parasympathetic activation and sympathetic withdrawal. *Front. Psychol.*, 5:1248, 14 November 2014.
- Binaural beats are an auditory illusion perceived when two or more pure tones of similar frequencies are presented dichotically through stereo headphones. Although this phenomenon is thought to facilitate state changes (e.g., relaxation), few empirical studies have reported on whether binaural beats produce changes in autonomic arousal. Therefore, the present study investigated the effects of binaural beating on autonomic dynamics [heart rate variability (HRV)] during post-exercise relaxation. Subjects ( $n = 21$ ; 18-29 years old) participated in a double-blind, placebo-controlled study during which binaural beats and placebo were administered over two randomized and counterbalanced sessions (within-subjects repeated-measures design). At the onset of each visit, subjects exercised for 20-min; post-exercise, subjects listened to either binaural beats ('wide-band' theta-frequency binaural beats) or placebo (carrier tones) for 20-min while relaxing alone in a quiet, low-light environment. Dependent variables consisted of high-frequency (HF, reflecting parasympathetic activity), low-frequency (LF, reflecting sympathetic and parasympathetic activity), and LF/HF normalized powers, as well as self-reported relaxation. As compared to the placebo visit, the binaural-beat visit resulted in greater self-reported relaxation, increased parasympathetic activation and increased sympathetic withdrawal. By the end of the 20-min relaxation period there were no observable differences in HRV between binaural-beat and placebo visits, although binaural-beat associated HRV significantly predicted subsequent reported relaxation. Findings suggest that listening to binaural beats may exert an acute influence on both LF and HF components of HRV and may increase subjective feelings of relaxation.

- [88] Shotaro Karino, Masato Yumoto, Kenji Itoh, Akira Uno, Keiko Yamakawa, Sotaro Sekimoto, and Kimitaka Kaga. Neuromagnetic responses to binaural beat in human cerebral cortex. *J. Neurophysiol.*, 96(4):1927--1938, October 2006. The dichotic presentation of two sinusoids with a slight difference in frequency elicits subjective fluctuations called binaural beat (BB). BBs provide a classic example of binaural interaction considered to result from neural interaction in the central auditory pathway that receives input from both ears. To explore the cortical representation of the fluctuation of BB, we recorded magnetic fields evoked by slow BB of 4.00 or 6.66 Hz in nine normal subjects. The fields showed small amplitudes; however, they were strong enough to be distinguished from the noise accompanying the recordings. Spectral analyses of the magnetic fields recorded on single channels revealed that the responses evoked by BBs contained a specific spectral component of BB frequency, and the magnetic fields were confirmed to represent an auditory steady-state response (ASSR) to BB. The analyses of spatial distribution of BB-synchronized responses and minimum-norm current estimates revealed multiple BB ASSR sources in the parietal and frontal cortices in addition to the temporal areas, including auditory cortices. The phase of synchronized waveforms showed great variability, suggesting that BB ASSR does not represent changing interaural phase differences (IPD) per se, but instead it reflects a higher-order cognitive process corresponding to subjective fluctuations of BB. Our findings confirm that the activity of the human cerebral cortex can be synchronized with slow BB by using information on the IPD.
- [89] Hillel Pratt, Arnold Starr, Henry J Michalewski, Andrew Dimitrijevic, Naomi Bleich, and Nomi Mittelman. Cortical evoked potentials to an auditory illusion: binaural beats. *Clin. Neurophysiol.*, 120(8):1514--1524, August 2009. OBJECTIVE: To define brain activity corresponding to an auditory illusion of 3 and 6Hz binaural beats in 250Hz or 1000Hz base frequencies, and compare it to the sound onset response. METHODS: Event-Related Potentials (ERPs) were recorded in response to unmodulated tones of 250 or 1000Hz to one ear and 3 or 6Hz higher to the other, creating an illusion of amplitude modulations (beats) of 3Hz and 6Hz, in base frequencies of 250Hz and 1000Hz. Tones were 2000ms in duration and presented with approximately 1s intervals. Latency, amplitude and source current density estimates of ERP components to tone onset and subsequent beats-evoked oscillations were determined and compared across beat frequencies with both base frequencies. RESULTS: All stimuli evoked tone-onset P(50), N(100) and P(200) components followed by oscillations corresponding to the beat frequency, and a subsequent tone-offset complex. Beats-evoked oscillations were higher in amplitude with the low base frequency and to the low beat frequency. Sources of the beats-evoked oscillations across all stimulus conditions located mostly to left lateral and inferior temporal lobe areas in all stimulus conditions. Onset-evoked components were not different across stimulus conditions; P(50) had significantly different sources than the beats-evoked oscillations; and N(100) and P(200) sources located to the same temporal lobe regions as beats-evoked oscillations, but were bilateral and also included frontal and parietal contributions. CONCLUSIONS: Neural activity with slightly different

volley frequencies from left and right ear converges and interacts in the central auditory brainstem pathways to generate beats of neural activity to modulate activities in the left temporal lobe, giving rise to the illusion of binaural beats. Cortical potentials recorded to binaural beats are distinct from onset responses. SIGNIFICANCE: Brain activity corresponding to an auditory illusion of low frequency beats can be recorded from the scalp.

- [90] Ann-Katrin Becher, Marlene Höhne, Nikolai Axmacher, Leila Chaieb, Christian E Elger, and Juergen Fell. Intracranial electroencephalography power and phase synchronization changes during monaural and binaural beat stimulation. *Eur. J. Neurosci.*, 41(2):254--263, January 2015.
- Auditory stimulation with monaural or binaural auditory beats (i.e. sine waves with nearby frequencies presented either to both ears or to each ear separately) represents a non-invasive approach to influence electrical brain activity. It is still unclear exactly which brain sites are affected by beat stimulation. In particular, an impact of beat stimulation on mediotemporal brain areas could possibly provide new options for memory enhancement or seizure control. Therefore, we examined how electroencephalography (EEG) power and phase synchronization are modulated by auditory stimulation with beat frequencies corresponding to dominant EEG rhythms based on intracranial recordings in presurgical epilepsy patients. Monaural and binaural beat stimuli with beat frequencies of 5, 10, 40 and 80 Hz and non-superposed control signals were administered with low amplitudes (60 dB SPL) and for short durations (5 s). EEG power was intracranially recorded from mediotemporal, temporo-basal and temporo-lateral and surface sites. Evoked and total EEG power and phase synchronization during beat vs. control stimulation were compared by the use of Bonferroni-corrected non-parametric label-permutation tests. We found that power and phase synchronization were significantly modulated by beat stimulation not only at temporo-basal, temporo-lateral and surface sites, but also at mediotemporal sites. Generally, more significant decreases than increases were observed. The most prominent power increases were seen after stimulation with monaural 40-Hz beats. The most pronounced power and synchronization decreases resulted from stimulation with monaural 5-Hz and binaural 80-Hz beats. Our results suggest that beat stimulation offers a non-invasive approach for the modulation of intracranial EEG characteristics.
- [91] Wiebke Trost, Sascha Frühholz, Daniele Schön, Carolina Labbé, Swann Pichon, Didier Grandjean, and Patrik Vuilleumier. Getting the beat: entrainment of brain activity by musical rhythm and pleasantness. *Neuroimage*, 103:55--64, December 2014.
- Rhythmic entrainment is an important component of emotion induction by music, but brain circuits recruited during spontaneous entrainment of attention by music and the influence of the subjective emotional feelings evoked by music remain still largely unresolved. In this study we used fMRI to test whether the metric structure of music entrains brain activity and how music pleasantness influences such

entrainment. Participants listened to piano music while performing a speeded visuomotor detection task in which targets appeared time-locked to either strong or weak beats. Each musical piece was presented in both a consonant/pleasant and dissonant/unpleasant version. Consonant music facilitated target detection and targets presented synchronously with strong beats were detected faster. fMRI showed increased activation of bilateral caudate nucleus when responding on strong beats, whereas consonance enhanced activity in attentional networks. Meter and consonance selectively interacted in the caudate nucleus, with greater meter effects during dissonant than consonant music. These results reveal that the basal ganglia, involved both in emotion and rhythm processing, critically contribute to rhythmic entrainment of subcortical brain circuits by music.

- [92] Stefan N Oline, Go Ashida, and R Michael Burger. Tonotopic optimization for temporal processing in the cochlear nucleus. *J. Neurosci.*, 36(32):8500--8515, 10 August 2016.

UNLABELLED: In the auditory system, sounds are processed in parallel frequency-tuned circuits, beginning in the cochlea. Auditory nerve fibers reflect this tonotopy and encode temporal properties of acoustic stimuli by “locking” discharges to a particular stimulus phase. However, physiological constraints on phase-locking depend on stimulus frequency. Interestingly, low characteristic frequency (LCF) neurons in the cochlear nucleus improve phase-locking precision relative to their auditory nerve inputs. This is proposed to arise through synaptic integration, but the postsynaptic membrane's selectivity for varying levels of synaptic convergence is poorly understood. The chick cochlear nucleus, nucleus magnocellularis (NM), exhibits tonotopic distribution of both input and membrane properties. LCF neurons receive many small inputs and have low input thresholds, whereas high characteristic frequency (HCF) neurons receive few, large synapses and require larger currents to spike. NM therefore presents an opportunity to study how small membrane variations interact with a systematic topographic gradient of synaptic inputs. We investigated membrane input selectivity and observed that HCF neurons preferentially select faster input than their LCF counterparts, and that this preference is tolerant of changes to membrane voltage. We then used computational models to probe which properties are crucial to phase-locking. The model predicted that the optimal arrangement of synaptic and membrane properties for phase-locking is specific to stimulus frequency and that the tonotopic distribution of input number and membrane excitability in NM closely tracks a stimulus-defined optimum. These findings were then confirmed physiologically with dynamic-clamp simulations of inputs to NM neurons. SIGNIFICANCE STATEMENT: One way that neurons represent temporal information is by phase-locking, which is discharging in response to a particular phase of the stimulus waveform. In the auditory system, central neurons are optimized to retain or improve phase-locking precision compared with input from the auditory nerve. However, the difficulty of this computation varies systematically with stimulus frequency. We examined properties that contribute to temporal processing both physiologically and in a computational model. Neurons processing low-frequency input benefit from integration of many weak inputs, whereas those processing higher frequencies progressively lose precision by integration of multiple inputs.

Here, we reveal general features of input-output optimization that apply to all neurons that process time varying input.

- [93] Padmini Rangamani, Michael G Levy, Shahid Khan, and George Oster. Paradoxical signaling regulates structural plasticity in dendritic spines. *Proc. Natl. Acad. Sci. U. S. A.*, 113(36):E5298--307, 6 September 2016. Transient spine enlargement (3- to 5-min timescale) is an important event associated with the structural plasticity of dendritic spines. Many of the molecular mechanisms associated with transient spine enlargement have been identified experimentally. Here, we use a systems biology approach to construct a mathematical model of biochemical signaling and actin-mediated transient spine expansion in response to calcium influx caused by NMDA receptor activation. We have identified that a key feature of this signaling network is the paradoxical signaling loop. Paradoxical components act bifunctionally in signaling networks, and their role is to control both the activation and the inhibition of a desired response function (protein activity or spine volume). Using ordinary differential equation (ODE)-based modeling, we show that the dynamics of different regulators of transient spine expansion, including calmodulin-dependent protein kinase II (CaMKII), RhoA, and Cdc42, and the spine volume can be described using paradoxical signaling loops. Our model is able to capture the experimentally observed dynamics of transient spine volume. Furthermore, we show that actin remodeling events provide a robustness to spine volume dynamics. We also generate experimentally testable predictions about the role of different components and parameters of the network on spine dynamics.
- [94] Antonios Garas, Frank Schweitzer, and Shlomo Havlin. A k-shell decomposition method for weighted networks. 16 May 2012. [ bib | [arXiv](#) ] We present a generalized method for calculating the k-shell structure of weighted networks. The method takes into account both the weight and the degree of a network, in such a way that in the absence of weights we resume the shell structure obtained by the classic k-shell decomposition. In the presence of weights, we show that the method is able to partition the network in a more refined way, without the need of any arbitrary threshold on the weight values. Furthermore, by simulating spreading processes using the susceptible-infectious-recovered model in four different weighted real-world networks, we show that the weighted k-shell decomposition method ranks the nodes more accurately, by placing nodes with higher spreading potential into shells closer to the core. In addition, we demonstrate our new method on a real economic network and show that the core calculated using the weighted k-shell method is more meaningful from an economic perspective when compared with the unweighted one.

- [95] Nir Lahav, Baruch Ksherim, Eti Ben-Simon, Adi Maron-Katz, Reuven Cohen, and Shlomo Havlin. K-shell decomposition reveals hierarchical cortical organization of the human brain. *New J. Phys.*, 18(8):083013, 2 August 2016.

In recent years numerous attempts to understand the human brain were undertaken from a network point of view. A network framework takes into account the relationships between the different parts of the system and enables to examine how global and complex functions might emerge from network topology. Previous work revealed that the human brain features “small world” characteristics and that cortical hubs tend to interconnect among themselves. However, in order to fully understand the topological structure of hubs, and how their profile reflect the brain’s global functional organization, one needs to go beyond the properties of a specific hub and examine the various structural layers that make up the network. To address this topic further, we applied an analysis known in statistical physics and network theory as k-shell decomposition analysis. The analysis was applied on a human cortical network, derived from MRI data of six participants. Such analysis enables us to portray a detailed account of cortical connectivity focusing on different neighborhoods of inter-connected layers across the cortex. Our findings reveal that the human cortex is highly connected and efficient, and unlike the internet network contains no isolated nodes. The cortical network is comprised of a nucleus alongside shells of increasing connectivity that formed one connected giant component, revealing the human brain’s global functional organization. All these components were further categorized into three hierarchies in accordance with their connectivity profile, with each hierarchy reflecting different functional roles. Such a model may explain an efficient flow of information from the lowest hierarchy to the highest one, with each step enabling increased data integration. At the top, the highest hierarchy (the nucleus) serves as a global interconnected collective and demonstrates high correlation with consciousness related regions, suggesting that the nucleus might serve as a platform for consciousness to emerge.

- [96] Ann Sizemore, Chad Giusti, Ari Kahn, Richard F Betzel, and Danielle S Bassett. Cliques and cavities in the human connectome. 11 August 2016. [ bib | [arXiv](#) ] Encoding brain regions and their connections as a network of nodes and edges captures many of the possible paths along which information can be transmitted as humans process and perform complex behaviors. Because cognitive processes involve large and distributed networks of brain areas, examinations of multi-node routes within larger connection patterns can offer fundamental insights into the complexities of brain function. Here, we investigate both densely connected groups of nodes that could perform local computations as well as larger patterns of interactions that would allow for parallel processing. Finding such structures necessitates we move from considering pairwise interactions to capturing higher order relations, concepts naturally expressed in the language of algebraic topology. These tools can be used to study mesoscale structures arising from the arrangement of densely connected substructures called cliques in otherwise sparsely connected brain networks. We detect cliques (all-to-all connected sets of brain regions) in the average structural connectomes of 8 healthy adults and



discover the presence of more large cliques than expected in null networks constructed via wiring minimization, providing architecture through which brain network can perform rapid, local processing. We then locate topological cavities of different dimensions, around which information may flow in either diverging or converging patterns. These cavities exist consistently across subjects, differ from those observed in null model networks, and link regions of early and late evolutionary origin in long loops, underscoring their unique role in controlling brain function. These results offer a first demonstration that techniques from algebraic topology offer a novel perspective on structural connectomics, highlighting loop-like paths as crucial features in the human brain's structural architecture.

- [97] Yuan-Pin Lin, Yi-Hsuan Yang, and Tzyy-Ping Jung. Fusion of electroencephalographic dynamics and musical contents for estimating emotional responses in music listening. *Front. Neurosci.*, 8:94, 1 May 2014.
- Electroencephalography (EEG)-based emotion classification during music listening has gained increasing attention nowadays due to its promise of potential applications such as musical affective brain-computer interface (ABCI), neuromarketing, music therapy, and implicit multimedia tagging and triggering. However, music is an ecologically valid and complex stimulus that conveys certain emotions to listeners through compositions of musical elements. Using solely EEG signals to distinguish emotions remained challenging. This study aimed to assess the applicability of a multimodal approach by leveraging the EEG dynamics and acoustic characteristics of musical contents for the classification of emotional valence and arousal. To this end, this study adopted machine-learning methods to systematically elucidate the roles of the EEG and music modalities in the emotion modeling. The empirical results suggested that when whole-head EEG signals were available, the inclusion of musical contents did not improve the classification performance. The obtained performance of 74.76% using solely EEG modality was statistically comparable to that using the multimodality approach. However, if EEG dynamics were only available from a small set of electrodes (likely the case in real-life applications), the music modality would play a complementary role and augment the EEG results from around 61-67% in valence classification and from around 58-67% in arousal classification. The musical timber appeared to replace less-discriminative EEG features and led to improvements in both valence and arousal classification, whereas musical loudness was contributed specifically to the arousal classification. The present study not only provided principles for constructing an EEG-based multimodal approach, but also revealed the fundamental insights into the interplay of the brain activity and musical contents in emotion modeling.

- [98] Cesare V Parise and Marc O Ernst. Correlation detection as a general mechanism for multisensory integration. *Nat. Commun.*, 7:11543, 6 June 2016.  
The brain efficiently processes multisensory information by selectively combining related signals across the continuous stream of multisensory inputs. To do so, it needs to detect correlation, lag and synchrony across the senses; optimally integrate related information; and dynamically adapt to spatiotemporal conflicts across the senses. Here we show that all these aspects of multisensory perception can be jointly explained by postulating an elementary processing unit akin to the Hassenstein-Reichardt detector—a model originally developed for visual motion perception. This unit, termed the multisensory correlation detector (MCD), integrates related multisensory signals through a set of temporal filters followed by linear combination. Our model can tightly replicate human perception as measured in a series of empirical studies, both novel and previously published. MCDs provide a unified general theory of multisensory processing, which simultaneously explains a wide spectrum of phenomena with a simple, yet physiologically plausible model.
- [99] Richard Boyce, Stephen D Glasgow, Sylvain Williams, and Antoine Adamantidis. Causal evidence for the role of REM sleep theta rhythm in contextual memory consolidation. *Science*, 352(6287):812--816, 13 May 2016.  
Rapid eye movement sleep (REMS) has been linked with spatial and emotional memory consolidation. However, establishing direct causality between neural activity during REMS and memory consolidation has proven difficult because of the transient nature of REMS and significant caveats associated with REMS deprivation techniques. In mice, we optogenetically silenced medial septum  $\gamma$ -aminobutyric acid-releasing (MS(GABA)) neurons, allowing for temporally precise attenuation of the memory-associated theta rhythm during REMS without disturbing sleeping behavior. REMS-specific optogenetic silencing of MS(GABA) neurons selectively during a REMS critical window after learning erased subsequent novel object place recognition and impaired fear-conditioned contextual memory. Silencing MS(GABA) neurons for similar durations outside REMS episodes had no effect on memory. These results demonstrate that MS(GABA) neuronal activity specifically during REMS is required for normal memory consolidation.
- [100] Samira Anderson and Nina Kraus. Auditory training: Evidence for neural plasticity in older adults. *Perspect Hear Hear Disord Res Res Diagn*, 17:37--57, May 2013.  
Improvements in digital amplification, cochlear implants, and other innovations have extended the potential for improving hearing function; yet, there remains a need for further hearing improvement in challenging listening situations, such as when trying to understand speech in noise or when listening to music. Here, we review evidence from animal and human models of plasticity in the brain's ability to process speech and other meaningful stimuli. We considered studies targeting populations of younger through older adults, emphasizing studies that have employed randomized controlled designs and have made connections between neural and behavioral changes. Overall results indicate that the brain remains

malleable through older adulthood, provided that treatment algorithms have been modified to allow for changes in learning with age. Improvements in speech-in-noise perception and cognition function accompany neural changes in auditory processing. The training-related improvements noted across studies support the need to consider auditory training strategies in the management of individuals who express concerns about hearing in difficult listening situations. Given evidence from studies engaging the brain's reward centers, future research should consider how these centers can be naturally activated during training.

- [101] Max Wolotsky, Mohammad Husain, and Elisha Choe. Chill-Pass: Using Neuro-Physiological responses to chill music to defeat coercion attacks. 3 May 2016. [ bib | [arXiv](#) ]

Current alphanumeric and biometric authentication systems cannot withstand situations where a user is coerced into releasing their authentication materials under hostile circumstances. Existing approaches of coercion resistant authentication systems (CRAS) propose authentication factors such as implicit learning tasks, which are non-transferable, but still have the drawback that an attacker can force the victim (causing stress) to perform the task in order to gain unauthorized access. Alternatively, there could be cases where the user could claim that they were coerced into giving up the authentication materials, whereas in reality they acted as an insider attacker. Therefore, being able to detect stress during authentication also helps to achieve non-repudiation in such cases. To address these concerns, we need CRAS that have both the non-transferable property as well as a mechanism to detect stress related to coercion. In this paper, we study the feasibility of using Chill (intensely pleasurable) music as a stimulus to elicit unique neuro-physiological responses that can be used as an authenticating factor for CRAS. Chill music and stress are both stimuli for a neuro-chemical called Dopamine. However, they release the Dopamine at different parts of the brain, resulting in different neuro-physiological responses, which gives us both the non-transferable and stress-detection properties necessary for CRAS. We have experimentally validated our proposed Chill music based CRAS using human subjects and measuring their neuro-physiological responses on our prototype system. Based on the 100 samples collected from the subjects, we were able to successfully authenticate the subjects with an accuracy of over 90%. Our work not only demonstrates the potential of Chill music as a unique stimulus for CRAS, but also paves the path of wider adoption of CRAS in general.

- [102] Masako Tamaki, Ji Won Bang, Takeo Watanabe, and Yuka Sasaki. Night watch in one brain hemisphere during sleep associated with the First-Night effect in humans. *Curr. Biol.*, 26(9):1190--1194, 9 May 2016.

We often experience troubled sleep in a novel environment [1]. This is called the first-night effect (FNE) in human sleep research and has been regarded as a typical sleep disturbance [2-4]. Here, we show that the FNE is a manifestation of one hemisphere being more vigilant than the other as a night watch to monitor unfamiliar surroundings during sleep [5, 6]. Using advanced neuroimaging techniques [7, 8] as well as polysomnography, we found that the temporary sleep

disturbance in the first sleep experimental session involves regional interhemispheric asymmetry of sleep depth [9]. The interhemispheric asymmetry of sleep depth associated with the FNE was found in the default-mode network (DMN) involved with spontaneous internal thoughts during wakeful rest [10, 11]. The degree of asymmetry was significantly correlated with the sleep-onset latency, which reflects the degree of difficulty of falling asleep and is a critical measure for the FNE. Furthermore, the hemisphere with reduced sleep depth showed enhanced evoked brain response to deviant external stimuli. Deviant external stimuli detected by the less-sleeping hemisphere caused more arousals and faster behavioral responses than those detected by the other hemisphere. None of these asymmetries were evident during subsequent sleep sessions. These lines of evidence are in accord with the hypothesis that troubled sleep in an unfamiliar environment is an act for survival over an unfamiliar and potentially dangerous environment by keeping one hemisphere partially more vigilant than the other hemisphere as a night watch, which wakes the sleeper up when unfamiliar external signals are detected.

- [103] Erika Nyhus and Tim Curran. Functional role of gamma and theta oscillations in episodic memory. *Neurosci. Biobehav. Rev.*, 34(7):1023--1035, June 2010. The primary aim of this review is to examine evidence for a functional role of gamma and theta oscillations in human episodic memory. It is proposed here that gamma and theta oscillations allow for the transient interaction between cortical structures and the hippocampus for the encoding and retrieval of episodic memories as described by the hippocampal memory indexing theory (Teyler and DiScenna, 1986). Gamma rhythms can act in the cortex to bind perceptual features and in the hippocampus to bind the rich perceptual and contextual information from diverse brain regions into episodic representations. Theta oscillations act to temporally order these individual episodic memory representations. Through feedback projections from the hippocampus to the cortex these gamma and theta patterns could cause the reinstatement of the entire episodic memory representation in the cortex. In addition, theta oscillations could allow for top-down control from the frontal cortex to the hippocampus modulating the encoding and retrieval of episodic memories.
- [104] Selen Atasoy, Isaac Donnelly, and Joel Pearson. Human brain networks function in connectome-specific harmonic waves. *Nat. Commun.*, 7:10340, 21 January 2016. A key characteristic of human brain activity is coherent, spatially distributed oscillations forming behaviour-dependent brain networks. However, a fundamental principle underlying these networks remains unknown. Here we report that functional networks of the human brain are predicted by harmonic patterns, ubiquitous throughout nature, steered by the anatomy of the human cerebral cortex, the human connectome. We introduce a new technique extending the Fourier basis to the human connectome. In this new frequency-specific representation of cortical activity, that we call 'connectome harmonics', oscillatory networks of the human brain at rest match harmonic wave patterns of certain

frequencies. We demonstrate a neural mechanism behind the self-organization of connectome harmonics with a continuous neural field model of excitatory-inhibitory interactions on the connectome. Remarkably, the critical relation between the neural field patterns and the delicate excitation-inhibition balance fits the neurophysiological changes observed during the loss and recovery of consciousness.

- [105] Johannes Friedrich and Máté Lengyel. Goal-Directed decision making with spiking neurons. *J. Neurosci.*, 36(5):1529--1546, 3 February 2016.
- UNLABELLED: Behavioral and neuroscientific data on reward-based decision making point to a fundamental distinction between habitual and goal-directed action selection. The formation of habits, which requires simple updating of cached values, has been studied in great detail, and the reward prediction error theory of dopamine function has enjoyed prominent success in accounting for its neural bases. In contrast, the neural circuit mechanisms of goal-directed decision making, requiring extended iterative computations to estimate values online, are still unknown. Here we present a spiking neural network that provably solves the difficult online value estimation problem underlying goal-directed decision making in a near-optimal way and reproduces behavioral as well as neurophysiological experimental data on tasks ranging from simple binary choice to sequential decision making. Our model uses local plasticity rules to learn the synaptic weights of a simple neural network to achieve optimal performance and solves one-step decision-making tasks, commonly considered in neuroeconomics, as well as more challenging sequential decision-making tasks within 1 s. These decision times, and their parametric dependence on task parameters, as well as the final choice probabilities match behavioral data, whereas the evolution of neural activities in the network closely mimics neural responses recorded in frontal cortices during the execution of such tasks. Our theory provides a principled framework to understand the neural underpinning of goal-directed decision making and makes novel predictions for sequential decision-making tasks with multiple rewards.
- SIGNIFICANCE STATEMENT: Goal-directed actions requiring prospective planning pervade decision making, but their circuit-level mechanisms remain elusive. We show how a model circuit of biologically realistic spiking neurons can solve this computationally challenging problem in a novel way. The synaptic weights of our network can be learned using local plasticity rules such that its dynamics devise a near-optimal plan of action. By systematically comparing our model results to experimental data, we show that it reproduces behavioral decision times and choice probabilities as well as neural responses in a rich set of tasks. Our results thus offer the first biologically realistic account for complex goal-directed decision making at a computational, algorithmic, and implementational level.

- [106] Joseph Cichon and Wen-Biao Gan. Branch-specific dendritic  $Ca^{2+}$  spikes cause persistent synaptic plasticity. *Nature*, 520(7546):180--185, 9 April 2015.
- The brain has an extraordinary capacity for memory storage, but how it stores new information without disrupting previously acquired memories remains unknown. Here we show that different motor learning tasks induce dendritic  $Ca^{2+}$  spikes on different apical tuft branches of individual layer V pyramidal neurons in the mouse motor cortex. These task-related, branch-specific  $Ca^{2+}$  spikes cause long-lasting potentiation of postsynaptic dendritic spines active at the time of spike generation. When somatostatin-expressing interneurons are inactivated, different motor tasks frequently induce  $Ca^{2+}$  spikes on the same branches. On those branches, spines potentiated during one task are depotentiated when they are active seconds before  $Ca^{2+}$  spikes induced by another task. Concomitantly, increased neuronal activity and performance improvement after learning one task are disrupted when another task is learned. These findings indicate that dendritic-branch-specific generation of  $Ca^{2+}$  spikes is crucial for establishing long-lasting synaptic plasticity, thereby facilitating information storage associated with different learning experiences.
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