The role of technologies of nonlinear stimulation in the treatment of brain diseases and potential of their applications in healthy individuals

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The theory justified in 2015 set that the complexity of a structure of neuronal networks and activity in the healthy brain depend on the complexity of dynamics of visual and other environmental signals and habitat of the person - the acquired by him the experience of nonlinear stimulation.

The simplification of the dynamics of environmental signals is associated with abnormal development and aging of the CNS.

The use of fractal visual and audio–stimulation, and other incentives may enhance the effectiveness of strategies for recovery of the anatomical and functional connectivity of the brain via the reactivation of neuroplasticity.

Even the temporal opening of the window of an enhanced plasticity in the adult brain can be an attractive therapeutic strategy aimed to rewire damaged neural circuits.

An enrichment of habitat by complex nonlinear stimuli of various modalities (the fractality of sensations) is expected to be efficient strategy.
The evolution of man and his adaptation to the natural conditions is occurring in a noisy, nonlinear world. The hallmark of healthy physiological processes is their fractal, complex dynamics with a power spectrum corresponding to $1/f$.

Pink noise is dominant in nature

Nonlinear fluctuations of parameters of physiological processes refer to noise and are classified by their power spectrum density.

White noise - $1/f^0$

Brownian (brown) noise - $1/f^2$

Pink (fractal or ‘flicker’) noise - $1/f$

The natural noises with different dynamics affect the adaptation of living systems to environmental conditions.

The Norm is characterized by the fractal pattern of variability with long-term correlations.

With aging and pathology, the fractal structure of physiological processes is lost and a highly ordered or random dynamics develops.

The simplification of the structure of neural networks and the activity of the brain were found in aging and many brain disorders.
The normally functioning brain operates in a state of ‘self–organized criticality’
Bak, Tang, Wiesenfeld, 1987; Kitzbichler et al., 2009; Bilder, Knudsen, 2014

Phase synchronization between pairs of processes in the signals of functional MRI and MEG

**Self–organized criticality** is a physiological state, in which the system is spontaneously self-organized to be ready to operate at a critical zone between order and randomness.

Critical systems were associated with a fractal scaling and the presence of long-range correlations in space and time.

Kitzbichler et al. (2009) proved the scale invariant behavior for two models of the critical dynamics of neural networks and human functional systems of the brain oscillating at low (below 0.5 Hz) and higher frequencies (1-125 Hz).

Timme et al (2016) demonstrated that the neural systems operate at the critical point where their complexity is optimized.

In the recent work, several methods were used to analyze neuronal avalanches in the 435 records of cell activity in dissociated rat hippocampal cultures, and in the cortical models of branching of neuronal avalanches.

Application of nonlinear brain stimulation technology is promising in the treatment of neurological disorders and injuries to increase the effectiveness of restoration of the anatomic and functional structure of the brain, cognitive functions and behavior.

We substantiate the potential use of non-linear stimulation technologies in a healthy person in a variety of situations that can lead to a simplification of the neural circuits and pattern of brain activity.
Visual stimuli seem to play a greater role in comparing to other sensory modalities in therapeutic stimulation.

In our earlier work, we for the first time drew attention to the importance of the fractal structure of light flashes in the electrophysiological diagnosis and treatment of neurodegenerative diseases of the retina and the brain.


The impact of fractal flicker stimulation on the rabbit’s retina

We have created the LED flicker generator, in which the time-invariant (self-similar) sequence of flashes was programmed with the adjustable complexity of dynamics [Zueva M, Spiridonov I, Semenova N, Rezvykh S. Patent RU 2549150, 25.03.15 (priority from 27 Feb 2014)].

In healthy rabbits, the fractal flicker stimulation enhanced the magnitude of scotopic responses of the retina while reducing their latency, pointing to an increase in the efficiency of synaptic transmission from the photoreceptors to bipolar cells [Zueva et al., 2015].

Electroretinogram (ISCEV Standard)

![Graph](image)

Scotopic Flicker ERGs

![Graph](image)

The dynamic “sweep” fractal
Applications of Nonlinear Technologies

The nonlinear stimuli of the complex structure should be regarded as a physiologically adequate technology promoting the normalization of neuronal activity and cognitive function. These technologies can also be useful in healthy individuals in a variety of situations where they can also promote the social impact and a significant economic effect.

**Gerontology:** Under normal physiological human aging, the loss of the memory and some other cognitive functions occurs. Nonlinear stimulation techniques may be useful for maintaining a high level of criticality and long-term preservation of healthy cognitive functions of older people, promoting mental longevity.

**Sport:** Nonlinear stimulation techniques may be helpful for increasing and rapid recovery of mental and physical performance in severe physical or psychological stress in athletes.

**Work and living in the extreme environment:**
Nonlinear stimulation techniques may be useful for the restoration and enhancement of cognitive function, preservation of critical thinking in the extreme conditions of work and stress situations, including for support of the population in the conflict zones and the crew in the long-term space missions and scientific expeditions.

Nonlinear technologies may contribute the recovery of the complex dynamics by maintaining a high level of criticality and improving the adaptive brain reserve. In the spectrum of nonlinear stimulation therapy techniques, different variants of mono- and multimodal fractal stimulation should be considered as well as their combinations with white noise, music therapy and other treatment options.