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Commentary Article

Brain Wave Oscillations as an Objective Neurophysiological Biomarker of Homeopathic Subjective Well-Being

Marcus Zulian Teixeira[1]

[1] Departamento de Psiquiatria, Faculdade de Medicina, Universidade de São Paulo, São Paulo, SP, Brazil

Homeopathy

Address for correspondence Marcus Zulian Teixeira, MD, PhD, Departamento de Psiquiatria, Faculdade de Medicina, Universidade de São Paulo, Rua Dr. Ovídio Pires de Campos, 785, São Paulo, SP 05403-903, Brazil (e-mail: marcus@homeozulian.med.br; mzulian@alumni.usp.br).

Abstract

Background Homeopathy uses the "similitude principle" to arouse a therapeutic reaction in the body against its own disorders. For this to occur optimally, the medicinal pathogenetic effects must present similarity with the totality of the individual's symptoms. To assess if this similarity has been successfully achieved, Hahnemann states that "improvement in the disposition and mind"—i.e., subjective well-being—is the most important parameter to consider.

Aim Our aim was to perform a narrative review of the literature, exploring what is known about subjective well-being as a marker of therapeutic action, and to formulate ways in which subjective well-being might be quantifiable and applied in future homeopathy research.

Results The concept of subjective well-being has been extensively studied in the complementary and conventional medical literature. Improved well-being has been observed in clinical trials, including those in the fields of positive psychology and meditation. Positive subjective outcomes of this nature are supported by objective evidence through associated changes in brain oscillatory activity using electroencephalography and/or "brain mapping" by functional magnetic resonance imaging. Neurophysiological responses in the brain have been identified in subjects after they ingested a homeopathic medicine.

Conclusions The concept of subjective well-being is supported by a body of literature and is a measurable entity. When viewed from the perspective of electrophysiological changes, brain activity is an objective neurophysiological biomarker with a potential to quantify individual well-being in the context of homeopathy research.

Keywords
- homeopathy
- subjective well-being
- positive psychology
- meditation
- brain mapping
- EEG
- drug individualization

Introduction

Homeopathic treatment is based on four heterodox and complementary pillars developed by Samuel Hahnemann in the 19th century, each with several lines of research attesting to its validity[1–3]: the principle of therapeutic similitude, homeopathic pathogenetic trials, prescription of individualized medicines, and use of dynamized or potentiated doses. These central homeopathic principles are supplemented with the philosophical concepts of vitalism and

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miasms to broaden understanding of the human illness process and to infer a possible non-material representation or substrate that justifies the action of ultra-high diluted medicines, often at concentration values beyond the Avogadro limit.

In clinical practice, individualization of a homeopathic medicine according to the symptomatic totality can be a complex and demanding task—one which is not always successfully achieved immediately or in the early stages of treatment. Successfully identifying the true similitude and the best dose for the patient to achieve maximum therapeutic benefit can sometimes require periodic, and medium- to long-term follow-up, during which different causative hypotheses and various selected medicines are tested in search of the correct or closely similar homeopathic therapeutic action. Indeed, for some clinical cases, the homeopathic simillimum is never achieved.

Psycho-emotional manifestations assume great importance and are usually placed high in the hierarchy of the health–disease process in all aspects of the homeopathic clinical-therapeutic approach. Hahnemann highlighted that "the state of disposition and mind" are of central importance for understanding the etio-pathogenesis of disease among the symptomatic totality and choosing the correct therapeutic approach (*Organon of Medicine*, 6th ed., paragraphs 252–255).[4]

In addition, when monitoring the evolution of individualized treatment, case prognosis and assessing whether an adequate dose has been given, Hahnemann also said that "a greater degree of comfort, increased calmness and freedom of the mind, higher spirits may be easily perceived on close observation soon after the medicine". Therefore, in evaluating treatment in daily practice or clinical research, this idea of "homeopathic subjective well-being" may be considered the "most certain and instructive" confirmation of therapeutic benefit consistent with homeopathic principles (*Organon,* paragraphs 252–255).[4]

Aims

Hahnemann's clear focus on the importance of improvements in subjective well-being that appear after the correctly individualized homeopathic medicine (homeopathic therapeutic action) could arguably be considered as one of the forerunners of the psychosomatic conception of contemporary medicine. The aim of this Commentary article was therefore to perform a narrative review of the literature, exploring what is known across disciplines about subjective well-being as a marker of therapeutic action (with particular reference to positive psychology and meditation interventions), and to formulate ways in which subjective well-being might be quantifiable and used to inform clinical research studies in homeopathy.

Subjective Well-Being and Homeopathic Therapeutic Action

In paragraph 63 of the *Organon*,[4] Hahnemann suggests a physiological explanation for the therapeutic action of individualized medicines prescribed according to the similitude principle (primary action of the drug followed by secondary and opposite action of the body, or vital reaction):

> "Every agent that acts upon the vitality, every medicine, deranges more or less the vital force, and causes a certain alteration in the health of the individual for a longer or a shorter period. This is termed primary action. […]. To its action, our vital force endeavors to oppose its own energy. This resistant action is a property, is indeed an automatic action of our life-preserving power, which goes by the name of secondary action or counteraction." (*Organon*, paragraph 63).[4]

Thus, the homeopathic healing principle considers the secondary action (i.e., vital reaction) of the body to be the therapeutic aspect of treatment and is akin to the principle of homeostasis in modern physiology. This secondary, vital, homeostatic, or paradoxical reaction of the body might also be described scientifically by means of the rebound effect of modern drugs, which might cause iatrogenic events after discontinuation of antipathic or palliative treatment.[5–8]

Hahnemann attributed great importance to the mental and psychological state of the patient in both the etiopathogenesis of acute and chronic diseases and in the obstacles to their cure. Specifically, Hahnemann referred to the patient's "moral and intellectual character" or "the state of his disposition and mind" (*Organon*, paragraphs 5 and 208).[4] To effect a correct homeopathic treatment, he consequently reiterated that:

> "...in all cases of disease we are called on to cure, the state of the patient's disposition [mind] is to be particularly noted, along with the totality of the symptoms, if we would trace an accurate picture of the disease, in order to be able therefrom to treat it homeopathically with success." (*Organon*, paragraph 210).[4]

Additionally:

> "We shall, therefore, never be able to cure conformably to nature – that is to say, homeopathically – if we do not, in every case of disease, even in such as are acute, observe, along with the other symptoms, those relating to the changes in the state of the mind and disposition, and if we do not select, for the patient's relief, from among the medicines a disease-force which, in addition to the similarity of its other symptoms to those of the disease, is also capable of producing a similar state of the disposition and mind." (*Organon*, paragraph 213).[4]

Furthermore, in a later section of the *Organon*, Hahnemann states:

> "Among the signs that, in all diseases, especially in such as are of an acute nature, inform us of a slight commencement of amelioration or aggravation that is not perceptible to everyone, the state of mind and the whole demeanor of the

patient are the most certain and instructive. In the case of ever so slight an improvement we observe a greater degree of comfort, increased calmness and freedom of the mind, higher spirits – a kind of return of the natural state. In the case of ever so small a commencement of aggravation we have, on the contrary, the exact opposite of this: a constrained helpless, pitiable state of the disposition, of the mind, of the whole demeanor, and of all gestures, postures and actions, which may be easily perceived on close observation, but cannot be described in words.*

*The signs of improvement in the disposition and mind, however, may be expected only soon after the medicine has been taken when the dose has been *sufficiently minute* (i.e. as small as possible), an unnecessary large dose of even the most suitable homeopathic medicine acts too violently, and at first produces too great and too lasting a disturbance of the mind and disposition to allow us to perceive the improvement in them immediately." (*Organon*, paragraph 253).[4]

Not only did Hahnemann consider subjective well-being to be a key indicator of therapeutic response by the vital force, he also considered disruption of well-being to be an essential part of causing disease, especially those of a chronic nature. In his work "The Chronic Diseases, their Peculiar Nature and their Homeopathic Cure",[9] in the chapter "Cure of the chronic diseases", sub-section "Psora", Hahnemann describes a series of external and internal environmental factors (events in human life) that he considered weakened the vital force and contributed to chronic diseases, such as: lifestyle, diet, lack of physical activity or excesses of mental or sexual activity, trauma, acute infectious diseases, use of drugs and alcohol, smoking, inadequate treatments and emotional and psychological disorders. Here, he again emphasizes the importance of the mind and psyche in the etio-pathogenesis of chronic diseases:

"By far the most frequent excitement of the slumbering psora into chronic diseases, and the most frequent aggravation of chronic ailments already existing, are caused by grief and vexation." (p. 113).[9]

Therefore, evaluating the evolution of the homeopathic treatment with his prognostic observations, Hahnemann reiterates that "the state of mind and the whole demeanor of the patient are the most certain and instructive". In the case of a good prognosis as the result of prescribing a correctly individualized medicine and administered in an adequate dose, "a greater degree of comfort, increased calmness and freedom of the mind, higher spirits" (i.e. homeopathic subjective well-being) must be observed at the beginning of the treatment "soon after the medicine has been taken". In the opposite case, the reverse of this evolution will be observed: "a constrained helpless, pitiable state of the disposition, of the mind, of the whole demeanor and of all gestures, postures and actions" (*Organon*, paragraphs 252–255).[4]

Subjective Well-Being: A Working Definition

Confirming Hahnemann's insight in observing and describing the homeopathic phenomenon in human health, studies in recent decades have associated "subjective well-being" or "psychological well-being" with beneficial outcomes, including supportive social relationships, career success, improvement in disease prognosis and healthier and longer lives. Subjective or psychological well-being is a broad concept that encompasses similar definitions and constructs from various traditions, including positive emotions, life satisfaction, purpose in life and optimism. As a principal concept underpinning health and disease, subjective well-being is therefore not limited to homeopathy.

Subjective well-being is influenced by a combination of individual characteristics, such as genetics, personality traits and age, with psychosocial factors, such as having a reasonable income or satisfactory affective or social relationships, as well as by lifestyle-related factors such as exercise, meditation and other health promotion practices.

Although a large amount of evidence has advanced our understanding of the roles of these factors in the experience of subjective well-being, several essential issues remain unclear. Among these, a key question refers to whether brain mechanisms support well-being; if so, this could help clarify why some people experience greater well-being than others, what might go wrong in affective disturbances and how different types of interventions can enhance brain function and well-being. Recent associations among neurotransmitters, hormones, brain networks and cognitive functions, enabling the investigation of neurophysiological correlates of positive emotions and overall well-being, have provided essential contributions to answering these fundamental questions.[10,11]

Since individuals, groups, literature and cultures conceptualize "subjective well-being" differently, it is frequently defined according to qualitative conceptuals and quantitative constituents. For the purpose of this article, we define "*homeopathic* subjective well-being" in accordance with Hahnemann's conception (*Organon*, paragraph 253)[4]: that is "the signs of improvement in the disposition and mind characterized by an increase of comfort, disposition, calmness/tranquility, freedom of the mind and higher spirits".

Measuring Subjective Well-Being: Positive Emotions and Brain Structures

In seeking a functional understanding of the phenomenon of subjective well-being, neuroscientific approaches have described the brain structures and neurophysiological processes involved. An abundance of evidence indicates that the subjective experience of happiness, pleasure, rewards and general well-being depends on overlapping networks of sub-cortical and cortical regions of the brain. These networks include subcortical structures (amygdala, ventral tegmental area, nucleus accumbens and ventral pallidum) and pre-frontal cortex regions (medial pre-frontal cortex, orbitofrontal cortex, anterior cingulate cortex and insula). At the neurochemical level,

Table 1 Brain structures and affective (emotional) processes

Brain structures		Affective (emotional) processes
PFC	Left PFC	Positive affective processes
	Right PFC	Negative affective processes
OFC		Motivation, liking and experiencing pleasure
Rostral ACC		Via its intricate connectivity with cortical and limbic regions, may facilitate the healthy experience of positive emotions via guiding attention toward positive stimuli
AIC	Left AIC	Positive affective processes
	Right AIC	Negative affective processes
Amygdala	Left amygdala	Positive affective processes
	Right amygdala	Negative affective processes

Abbreviations: ACC, anterior cingulate cortex; AIC, anterior insular cortex; OFC, orbito-frontal cortex; PFC, pre-frontal cortex.

neurotransmitters (dopamine and endorphin), neuropeptides (oxytocin) and hormones (androgens and estrogens) have been implicated in these subjective experiences too.[10,11]

In the context that flexible brain networks implement positive affective or emotional processes (well-being), some brain structures assume important participation, such as the general pre-frontal cortex (PFC), orbito-frontal cortex (OFC), anterior cingulate cortex (ACC), anterior insular cortex (AIC) and amygdala[10,11] (summarized in ►**Table 1**).

While distinct cortical and sub-cortical brain structures are associated with processing positive stimuli and emotions, it is theorized that these brain regions work in conjunction as part of flexible networks that respond to perpetually shifting contextual task demands. The default mode network (DMN), which represents a brain network of cortical regions (left PFC, medial PFC, ACC, OFC, pre-cuneus and posterior parietal cortex) implicated in affective processing, internal thought processes and representations of the self, may perform a critical function in supporting well-being, positive emotions and possibly happiness.[10,12]

Measuring Subjective Well-Being: Brain Oscillations

Objectively, brain (or mental)[13] states and functions are the result of brain oscillations (waves or frequencies) emitted by the various brain structures, which can be identified by functional magnetic resonance imaging (fMRI) and electroencephalography (EEG), among other methods. Integrating physiology and neuroscience, psychophysiology uses these methods to investigate and understand brain functions and brain states, analyzing cognitive, emotional and consciousness processes, as well as normal and pathological conditions. In the last three decades, brain oscillation analysis—also referred to as "brain mapping"—has been one of the most important areas of developing research in the neuroscience literature.[14]

By way of clarification, EEG is the measurement of electrical patterns at the surface of the scalp which reflect cortical activity and are referred to as brain oscillations, waves, or frequencies. Quantitative electroencephalography (qEEG) is a procedure that processes the recorded EEG activity from a multi-electrode recording using a computer. The digital data are statistically analyzed, sometimes comparing values with normative database reference values. The processed EEG is commonly converted into color maps of brain functioning called "brain maps". fMRI measures the small changes in blood flow that occur with brain activity and is a class of imaging methods developed to demonstrate regional, time-varying, changes in brain metabolism. These metabolic changes can be consequent on task-induced cognitive state changes or the result of unregulated processes in the resting brain.

Since the first report (1929) on the discovery of the electroencephalogram by Hans Berger, most sensory and cognitive processes have been linked to at least one of five natural brain frequency bands: delta (<4 Hz), theta (4–8 Hz), α (8–12 Hz), β (12–30 Hz) and gamma (>30 Hz). Modulation of neuronal frequencies demonstrates causal links between brain oscillations and brain states (cognitive, emotional and consciousness processes), revealing important information about human brain function. Some associations among the many studies that address the correlation of EEG oscillations with sensory and cognitive processes are widely accepted. In general terms, slow frequency signals, such as delta, theta and α, have been related to sleep, rest and relaxation (well-being state), whereas faster brain oscillations, such as β and gamma, are related to alertness, concentration and higher-order cognitive tasks[15,16] (summarized in ►**Table 2**).

The combined application of several analytical methods (analysis of spontaneous electroencephalogram spectra, evoked oscillations, event-related oscillations and coherences in both spontaneous EEG and event-related oscillations, among others) is the best form for analyzing brain oscillations. EEG power can be measured in either absolute or relative terms by qEEG, where absolute power is amplitude squared for each frequency, and relative power is each frequency's power as a proportion of the total.[15,17]

Contributing to neural homeostasis, the brain's ability to become flexible through various brain wave frequencies plays an important role in successfully managing stress, focusing on tasks and getting a good night's sleep. If one of the five types of brain waves is produced in excess and/or in short supply, it can cause disturbances. Therefore, it is important to understand that there is no single brain wave that is better or more important than the others. Each brain oscillation serves a purpose in handling different situations, both to aid in processing and in learning new information and to calm down after a stressful situation.[18]

Table 2 Brain oscillations, brain structures, and brain states (cognitive, emotional and consciousness processes)

Brain oscillations	Brain structures and brain states
Delta (<4 Hz)	Delta oscillations are emitted by thalamus and cortex (frontal and cingulate). In line with their low frequency, these frequencies span a rather wide region of neural networks, possibly in an inhibitory manner. This assumption is in line with a role in cognitive processes such as attention, since attending to one stimulus or location can be achieved by inhibiting other stimuli or locations. Abnormal delta activity may occur when the person has learning disabilities or has difficulties maintaining conscious awareness (such as in cases of brain injuries or coma). Brain state: sleep.
Theta (4–8 Hz)	Theta oscillations are emitted by cortical and sub-cortical structures. Increased cortical theta activity is described during a variety of learning tasks, including memory, recognition, recall and virtual spatial navigation. Theta frequency occurs in the PFC and ACC during wakefulness, and is associated with internalized attention and activation of the parasympathetic system. In addition to local oscillatory activity, theta rhythms are synchronized across multiple brain regions during complex cognitive tasks. Theta oscillations are involved in sleep or day-dreaming, and can indicate intuition or automatic tasks. Brain state: deeply relaxed and inward focused.
Alpha (8–12 Hz)	Alpha oscillations are most commonly emitted in the parieto-occipital brain region. Alpha activity is modulated during sensory stimulation and is most notably seen in various sleep stages. In addition, they reflect memory and attentional processes. Alpha oscillations exhibit an inverse correlation with cognitive performance, thus suggesting an inhibition of task-irrelevant cortical structures. Alpha waves connect the gap between our conscious thinking and subconscious mind. It helps us to calm down or it promotes a feeling of relaxation. Brain state: very relaxed and passive attention.
Beta (12–30 Hz)	Beta oscillations are emitted by the sensorimotor cortex and basal ganglia structures. In addition to somatosensory processing, β activity is modulated during various motor and cognitive tasks. This frequency is visible in logical-analytical reasoning (problem solving). Brain state: vigilant and active attention.
Gamma (>30 Hz)	Gamma oscillations are emitted by many cortical regions. Gamma rhythms are involved in several sensory and cognitive responses. While many of the low-frequency waves have been associated with functional inhibition, faster gamma-band waves are believed to reflect cortical activation. Depending on the cortical region, gamma oscillations are closely related to attentive processing of information, active maintenance of memory contents and conscious perception. The gamma frequency is important for linking our senses to perception and is involved in learning new activities. Brain state: concentration and conscious perception.

Spontaneous brain activity (resting EEG power) in the absence of controlled stimulus input or an explicit active task is topologically organized in multiple functional networks maintaining a high degree of connectivity. There is accumulating evidence that this oscillatory activity plays a significant role in regulating brain function. Beyond emotional and consciousness processes, rhythmic phenomena are routinely observed during perceptive, motor and cognitive tasks and have been implicated in altered functions across a broad range of health disorders (Parkinson's disease, Alzheimer's disease, autism, addiction, attention-deficit hyperactivity disorder, bipolar disorder, depression, stroke, epilepsy, dementia, anxiety, insomnia and post-traumatic stress, among others). In turn, these signals of abnormal network activity normalize with usual treatment and/or predict disease progression or recovery.[17,19–23]

In a recent systematic review of the neural correlates of well-being, 11 studies used qEEG (measuring the EEG power) to link well-being to regional brain activation, suggesting that a larger α asymmetry (more activation on the brain's left side than on the right) is related to greater well-being, according to the neuropsychological theory of lateralized affective function.[24]

With the aim of using EEG profiles as a biomarker of well-being, Chilver et al[25] examined the association between mental well-being and EEG power (delta, theta, α and β) in 422 healthy adults using linear mixed models. A significant association between well-being and an interaction of α, β and delta power was found, whereby a resting EEG profile characterized by low β power and high α and delta was associated with greater well-being. The results indicate that resting measures of brain activity may be an electrophysiological biomarker of mental well-being.

Assessing Subjective Well-Being in Clinical Homeopathy Research

In homeopathy, changes in subjective well-being are generally considered to be a non-specific but clinically important outcome of treatment. While Hahnemann made his claims based on first-hand experience, empirical evidence now exists to support his observations. That is, subjective well-being is often used as an outcome measure in observational and experimental clinical studies, usually through instruments, scales, or questionnaires that assess the different components of this construct.[26–29]

Seeking to measure the vital force strength in classical homeopathy, Bell et al[30] explored associations between an overall rating for the classical homeopathic construct of vital force and clinician/patient ratings on previously validated bio-psycho-social-spiritual questionnaires. Beyond the absence of disease, homeopathic vital force ratings reflected better perceived mental function, energy and positive dimensions of the individual: that is, "higher vigor" and "greater positive states of

mind" as related by the patients, and "lesser fatigue" and "increased emotional well-being" as related by the conventional medical provider. Similarly, Steinsbekk and Lüdtke[31] developed a prospective uncontrolled observational multicenter outcome study with 654 patients to evaluate the patient-reported effects of homeopathic care 6 months after first consultations, finding an improvement in general well-being in 51% of the patients.

With the aim of evaluating whether homeopathy influenced overall health status and subjective well-being when used as an adjunct to conventional cancer therapy, Frass et al[32] conducted a pragmatically designed randomized controlled trial (RCT) with 410 patients treated by standard anti-neoplastic therapy. Patients were randomized to receive or not receive classical homeopathic adjunctive therapy in addition to standard treatment, and the main outcome measures were overall health status and subjective well-being as assessed by the patients. The results suggested that the overall health status and subjective well-being of these cancer patients significantly improved when classical homeopathic treatment was administered in addition to conventional therapy.

Homeopathy, Subjective Well-Being and the Placebo Effect

It is worth mentioning that a change in subjective well-being is one of the main components of the placebo effect, as a result of the consultation/rapport effect and/or the positive expectation for improvement arising from any treatment (pharmacological or not), which alters the activity of certain brain regions and promotes the release of specific neurotransmitters. Therefore, the placebo effect must be part of the set of variables analyzed in the subjective well-being observed after a therapeutic intervention, but it is not the only part. Thus, RCTs should be performed to study subjective well-being to minimize the placebo effect and the consequent bias in the interpretation of clinical results.[33–36]

Neurophysiological Effects of Homeopathic Treatment

Given the advances in neurophysiology and the availability of methods to quantitatively assess changes in brain activity (functional or electrical), what is known about the ability of homeopathic medicines to modify brain activity? Here, we present a brief review of the literature.

In a series of three pre-clinical studies,[37–39] Ruiz-Vega et al investigated the homeopathic therapeutic effect of *Coffea cruda* on the sleep patterns of rats via EEG from the parietal region. The first study[37] suggested that *Coffea cruda* 30c enhanced slow delta activity in the treatment group. The second experiment[38] showed that *Coffea cruda* 30c increased the delta-band power of slow wave sleep (stages 3 and 4) compared with placebo. In a third experiment,[39] which studied a subset of rats pre-treated with caffeine, *Coffea cruda* 30c produced different patterns of change in parietal EEG delta power when comparing the later with the earlier period of sleep. Another similar experimental RCT investigated the effect of *Histamine* 30c on arousal through changes in the sleep patterns of rats, finding that the mean delta band spectral density was lower in the treatment groups than the placebo group.[40] Thus, a change in brain frequencies in accordance with the recognized principle of therapeutic similitude (drug biphasic action)[5–8] was seen, since the known therapeutic effects on the sleep pattern of the homeopathic medicines *Coffea cruda* (drowsiness) and *Histaminum* (sleeplessness) were observed in the increase and decrease of the delta EEG frequency respectively.

With the primary aim of verifying the short-term modulatory effect of *Coffea cruda* 30c and *Nux vomica* 30c on stage 3 and 4 slow wave sleep EEG (characterized by delta frequency) via computed multiscale entropy (MSE), Bell et al[41] conducted an RCT with 54 young adult college students who had a history of coffee-induced insomnia. Consistent with the rat study findings, the MSE results indicated robust and significant *Coffea cruda* biphasic effects, especially later in the night during the rapid eye movement (REM) cycle: an initial increase in insomnia with a subsequent decrease, in accordance with the MSE results at multiple sites for both stages 3 and 4 in both REM cycles.

With the innovative proposal of studying neurophysiological changes related to the homeopathic therapeutic action, Bell et al conducted a series of RCTs[42–47] using different EEG parameters and analyses capable of identifying an early homeopathic response. In a first RCT on patients with fibromyalgia (FM),[43] pre-frontal EEG α frequency cordance (EEG-C, an algorithm-based derivative of absolute and relative spectral EEG data used as a correlate of functional brain activity) was characterized for all patients. Interestingly, patients that were considered to be "exceptional responders" to individualized homeopathic medicines exhibited significantly more negative initial EEG-C difference scores at pre-frontal sites compared with other patients. These findings suggest that pre-frontal EEG-C can act as an early neurophysiological biomarker of simillimum homeopathic medicines in patients with FM. Or, in other words, EEG-C might be an early indicator of the "correctness" of the chosen homeopathic medicine per patient.

A second study with FM patients[44] evaluated possible sensitization-related changes in EEG relative α magnitude during a 4-month RCT of daily, orally administered, individualized homeopathic medicines (simillimum homeopathic medicines, previously identified in another study)[48] or placebo in 48 patients, with an additional 2-month optional crossover phase, and including three EEG laboratory sessions (0, 3 and 6 months). A total of 19 EEG relative α magnitude leads at rest and during olfactory administration of treatment and placebo solutions were evaluated in each session (that is, olfactory doses were used to test whether patients responded to individualized homeopathic medicines previously administered orally). As a result, individuals receiving active treatment showed significantly increased α-1 (8–10 Hz) and α-2 (10–12 Hz) at all evaluation times during bottle sniffs over sessions, while the placebo group showed a decrease.[44] These findings suggest an increase in EEG relative α magnitude had been caused by the individualized homeopathic medicines.

Another RCT using EEG-C as an outcome[46] evaluated the effects of homeopathic remedies (*Sulfur* or *Pulsatilla nigricans*) after an olfactory activation protocol on 97 healthy young adults screened for a matching homeopathic symptomatic profile. The subjects underwent a series of three once-weekly double-blinded sessions during which they repeatedly sniffed the remedy matched to them and solvent controls. Each remedy was given in 6c, 12c and 30c potency, one potency per week, in a randomly assigned order. Prefrontal resting EEG-C values in the pre-sniffing and post-sniffing rest periods showed significant two-way oscillatory interactions of remedy and time for β, α, theta and delta cordance.

When taken together, these studies indicate that EEG (according to different analysis parameters) is able to detect a short-term, or almost immediate, physiological response to an olfactory homeopathic stimulus through changes in the respective brain oscillations. Indeed, the authors felt able to conclude that "EEG alpha offers an objective biomarker of remedy effects for future studies and potential method for distinguishing time-dependent effects of specific remedies and remedy potencies from one another".[45]

Subjective Well-Being in Other Fields: Positive Psychology and Meditation

Consistent with the ideal of homeopathic cure and the health–disease conception of Hahnemannian vitalism, the understanding and promotion of factors which contribute to developing "improvement in the disposition and mind" has been the aim of a burgeoning "human flourishing movement" in the context of "positive psychology". Positive psychology helps to foster happiness and emotional wellness, reflecting the biological, behavioral and psychosocial correlations between psychological well-being and human health. It does this by helping people capitalize on their strengths, heighten their gratitude and awareness, connect to others and develop the wisdom needed to live a more meaningful and fulfilling life.[49–51]

According to Martin Seligman, exponent of positive psychology, "psychological well-being has been defined in various ways and encompasses the positive thoughts and feelings that individuals use to evaluate their lives favorably", suggesting that "individual-level interventions, such as mindfulness-based programs and positive psychological interventions, have shown promise for modifying psychological well-being".[52]

In considering the protective role of positive psychological well-being in the evolution of health disorders, the most robust evidence comes from cardiovascular diseases, which is the leading cause of death worldwide and includes diagnoses such as coronary heart disease and stroke. Research in this area has caught the attention of the American Heart Association, which identified well-being as "an important frontier of knowledge" in its 2030 goal to promote healthier lives for all members of the population.[51,53–57]

One accessible method of improving psychological well-being is through meditation. Meditation practices are grounded in contemporary affective science theories and are postulated to enhance the capacity for and experience of, positive emotions, as well as promoting subjective well-being. Despite its newness, the burgeoning neuroscience research on meditation, theoretical and experimental models already exist to map the processes via which meditation specifically enhances the experience of positive emotions. Among these, changes in neurophysiological activity have been observed during and following the meditative state, via qEEG (brain oscillations) and/or fMRI (brain activity).[58–62] Meditation practice is also associated with improved concentration and reduced symptoms of stress, anxiety and depression. Additionally, different forms of meditation training are used as interventions for a variety of psychological and somatic disorders.[10,59–62]

In a comprehensive systematic review and meta-analysis that evaluated the psychological effects of different meditation practices, Sedlmeier et al[63] investigated the action on psychological variables that can be extracted from 163 empirical studies, concentrating on the effects of meditation on healthy adults. The largest effects of meditation were obtained for variables that referred to positive changes in relationships (inter-personal), state anxiety, negative emotions and trait anxiety. The least effects were for measures of learning and memory, negative personality traits and emotion regulation. Overall, it seems that the more cognitive measures were less influenced by meditation than emotional measures, especially negative ones. Measures that refer to focused and open attention yielded medium effects (attention and mindfulness), close to the average effect for all articles included in the review. Specific findings varied across different approaches to meditation. Comparatively strong effects for transcendental meditation were found in reducing negative emotions, trait anxiety and neuroticism, and being helpful in learning, memory and self-realization. For mindfulness meditation, strong effects were identified in reducing negative personality traits, reducing stress and improving attention and mindfulness.[63]

Despite the wide-ranging nature of the different meditation techniques, experimental studies have shown that meditation practice can improve PFC functions like cognition, self-awareness, attention and memory, and reduce negative psychological symptoms. Rathore et al[64] suggested a positive theoretical correlation between meditation and the functional connectivity of the PFC and reviewed various neuroimaging interventions of functional connectivity associated with the PFC and different brain areas during distinct meditation practices on healthy meditators compared with non-meditators. fMRI findings showed that meditation practices are associated with increased neural function and processing, gray matter volume and functional coupling in brain areas related to different regions of PFC: dorsolateral (dl) PFC, dorsomedial (dm) PFC, ventromedial (vm) PFC and OFC. The PFC's functional connectivity is associated with increased attention, working memory, cognitive and executive control, emotion regulation, self-awareness, self-perception and self-compassion, as well as decreased anxiety, depression, perceived stress, negative emotion and hyperarousal symptoms.[10,16]

In a general review, Fell et al[65] described the results of qEEG studies in meditation practices, seeking to correlate them to the distinct states of consciousness of its practitioners. In most studies, independent from meditation technique and degree of experience, the most dominant described effect was a state-related slowing of the α rhythm, in combination with an increase in the left-sided anterior frontal region's α power (internal attention and positive emotions). Similarly, a general increase of theta activity has been reported in a large number of meditation studies, unrelated to a specific practice or the practioner's experience level. Many of these studies described increasing theta activity in the form of sharp-burst or theta trains, which are preceded and followed by α rhythm (distinguishing deep meditation state of sleep stage I). A few other studies reported high-amplitude gamma-band oscillations during meditation practices, correlating the largest amplitude increases of gamma band activity with long-term practitioners. The authors interpreted these findings as evidence that altered states of consciousness are associated with distinguishable patterns of brain activation.

Aiming to correlate different meditative states with brain oscillations, DeLosAngeles et al[66] studied EEG correlates of five concentrative meditation states (levels), comparing effects between meditators and meditation-naive participants. The alpha activity was increased over all meditative states, not depth related. Decreases in β and gamma power were identified during the deeper absorption state and increases in theta power. These results are consistent with increased theta correlating with tightness of focus and reduced β/gamma with the desynchronization associated with enhanced alertness.

In a systematic review of the brain oscillations underlying meditation, Lee et al[16] compared the neural oscillatory patterns during the most commonly practiced meditation techniques. Despite the distinct differences in oscillatory neural activity between different techniques, the authors described the general role of brain frequencies in meditative states: (1) the function of delta frequency is not well described in the context of meditation; increased delta activity during deep sleep and meditation suggests that changes during meditative state promote an enhanced state of wakefulness; (2) increased theta activity has been observed during all meditation practices, suggesting improvements in cognition (attention, concentration and memory); increased theta power was positively correlated with the amount of training and experience in each meditation practice, explaining the improvements in memory and attention; (3) α activity has been observed during all meditation practices, with increased and stable α power observed in pre-frontal, frontal, parietal and/or occipital regions, being positively correlated with the amount of meditation training; (4) the role of β rhythm is conflicting in meditation, with evidence suggesting that β activity may increase, decrease, or remain unchanged, according to the various practices; (5) gamma oscillations appear to be involved in a range of sensory and cognitive responses, including consciousness processes; similar to theta and α frequencies, there is evidence of increased gamma activity in advanced practitioners of various meditation practices.

In summary, most meditation practices have shown an increase in PFC, ACC and insula activity, as well as increased activity of theta and α frequency bands (increased gamma activity in advanced practitioners). These neurophysiological effects of meditation are associated with increased attention function, working memory, cognitive and executive control, emotion regulation, countering negative effects, self-awareness and compassion. The overall increase in functional connectivity and activity of the PFC in meditators may explain the decrease in anxiety, depression, perceived stress, negative emotions and hyper-arousal symptoms. As such, these correlations reiterate the findings of positive psychology research, in which flexible brain networks implement positive emotions and foster improved subjective well-being.[10,64]

Proposals for Future Studies of Homeopathic Subjective Well-Being and Neurophysiological Biomarkers of Homeopathy's Therapeutic Action

In view of the importance of these vital and subjective sensations in the overall assessment of therapeutic intervention in homeopathy, positive psychology and meditation, subjective well-being is used as a variable for analyzing the intervention's effectiveness, usually through questionnaires that assess the different components of this construct.

In recent decades, by valuing the same non-specific aspects employed by homeopathy as an important goal of therapy and factor of analysis for intervention response, positive psychology has associated subjective well-being with personal and social beneficial outcomes, relating it to positive emotions, life satisfaction, purpose in life and optimism. To study the role of positive psychological interventions in subjective well-being and the consequent effects on the health–disease binomial, neurophysiological investigations of positive emotions and overall well-being have provided essential contributions to answering these fundamental questions.

Cortical and sub-cortical brain structures in MRI studies have been shown to be associated with processing positive emotions and working in conjunction as part of flexible networks (the DMN) that respond to perpetually shifting contextual task demands.[10] Using qEEG to link well-being to regional brain activation, studies have related greater well-being to more activation on the left side of the brain and to an EEG power profile characterized by low β and high α and delta frequencies.[25]

Analogous to positive psychology, meditation practices have an association with emotion regulation in opposition to negative effects, characterized by a decrease in anxiety, depression, perceived stress, negative emotions and hyper-arousal symptoms (increase of positive emotions and subjective well-being). Increased PFC, ACC and insula activity, deactivated DMN and increased activity of theta and α frequency bands have been found in the neurophysiological correlates.[10,64]

Consequent to this assembled body of evidence, we propose the novel concept that these same neurophysiological parameters (fMRI and qEEG, but mainly qEEG for the low cost) may be useful in quantifying variables of the homeopathic response that include changes in subjective well-being. Reiterating the indications of the homeopathic researchers who have suggested using the increase of EEG α as an objective biomarker of remedy effects, we therefore add the proposal that brain activity might also be an index of subjective well-being and could be used as an additional indicator of homeopathic therapeutic action. In line with the studies of positive psychology and meditation, this subjective well-being could be measured through characteristic changes in the activity of distinct brain oscillations, such as a decrease in β, and an increase in delta, α and theta brain waves.

In seeking characteristic EEG patterns associated with the subjective well-being response to homeopathic treatment, studies with exceptional responders to individualized homeopathic medicines in several different diseases could be performed to observe any common changes in the activity of various types of brain frequencies.

Although qEEG is a relatively inexpensive and simple method, as long as equipment with recommended technical specifications and specific analyses are employed, fMRI could potentially be used later to corroborate qEEG results and expand understanding of the homeopathic effect on subjective well-being, mapping the activity on different regions and brain networks.

Using subjective well-being as a biomarker of homeopathic therapeutic action in clinical research, it may be possible to apply various qualitative and/or quantitative experimental methods according to an ascending evidence hierarchy of study designs. For example, after an experimenter/patient has reported an initial subjective perception of improved well-being (according to self-qualitative analysis or through validated instruments or questionnaires), a series of qEEG laboratory sessions (comparing the pattern of brain oscillations with and without therapeutic intervention) could suggest homeopathic action.

Seeking to achieve a higher level of evidence, these initial results could then be tested in a series of single-subject (N-of-1) trials,[67,68] for example.

Conclusions

Employing the principle of therapeutic similarity, a homeopathic simillimum medicine stimulates a vital reaction of the body against its own disorders. Consequent improvements in the disposition and mind that can be observed as a subjective outcome may correlate with measurable and characteristic changes of electrical activity in higher-order brain structures. Brain oscillatory activity is thus an objective neurophysiological biomarker that has promise in quantifying individual well-being in the context of clinical homeopathy research. The concept would be testable by studying EEG (and possibly also fMRI) patterns in suitably designed N-of-1 studies of individualized homeopathic treatment.

Highlights

- Homeopathy uses the similitude therapeutic principle to arouse the body's reaction against its own disorders.
- For this body's reaction to occur, it is necessary that medicinal pathogenetic effects present similarity with the patient's symptomatic totality.
- In this complex task, Hahnemann points out that "the improvement in the disposition and mind" is the most important parameter to identify the correct treatment.
- This subjective well-being awakened by individualized homeopathic medicine can be identified through objective neurophysiological parameters (brain frequencies).
- In this proposal, we are suggesting to employ homeopathic subjective well-being according to a pattern of EEG frequency changes as an objective biomarker of the simillimum homeopathic medicine.

Conflict of Interest

None declared.

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