

Year : 2016
 Volume : 3
 Issue Number : 2
 Doi Number : 10.5455/JNBS.1465994805

Article history:

Received 15 June 2016
 Received in revised form 01 June 2016
 Accepted 14 July 2016

A SPECULATION ON THE MECHANISM OF ECT, TMS, TDCS and SIMILAR TECHNIQUES

EKT, TMU, TDCS VE BENZER TEKNİKLERİN ALTINDA YATAN MEKANİZMALAR ÜZERİNE BİR SPEKÜLASYON

Levon Antikacıoğlu¹, Nevzat Tarhan²

Abstract

In this paper, we tried to explain, what can eventually be the underlying mechanisms of ECT, TMS, tDCS and similar techniques. And tried to explain how, by making some slight changes in the use of the EMW (electromagnetically induced wave) devices, and by integrating them with psychotherapies and pharmacotherapies, we can either better understand their real effectiveness and, design better therapeutic strategies, and increase their positive results. So far, it seems that because of the implemented insufficient designs, either in evaluating the results or, in planning their applications, their positive effects, do not seem to be fully discovered yet.

Keywords: ECT, TMS, tDCS, electromagnetic wave therapy underlying mechanism, EMW

Özet

Bu çalışmada, EKT, TMU, tDCS ve benzer tekniklerin altında yatan muhtemel mekanizmalarının, ne olabileceklerinin açıklanmasına çalışılmıştır. Ve elektromanyetik dalgaların kullanımına paralel olarak, önerdiğimiz bazı ayrıntıların ilavesi ve bunların, psikoterapi, psikofarmakoterapi ve öğrenme prensipleri ile harmanlanmasıyla, nasıl daha iyi sonuçların elde edilebileceği, ve terapi stratejilerinin yapılandırılabilirliği, tartışılmıştır. Çünkü görüldüğü kadarıyla EMD (Elektromanyetik Dalga) kullanımı ile yapılan; onların uygulanmasını ve/veya etkinlik derecelerini araştıran çalışmaların verimlilik oranları aslında, bazı metodolojik yetersizliklerden kaynaklı olarak, ihtimal ki gözden kaçmış olup, henüz tam anlamıyla keşfedilememişlerdir.

Anahtar Kelimeler: EKT, TMU, tDCS, elektromanyetik dalga terapilerinin mekanizması, EMD

¹ Corresponding author: Prof. Dr., Üsküdar University, Faculty of Humanities and Social Sciences, Department of Psychology. Address for Correspondance: Altunizade Mah. Haluk Türksoy sok. No. 14 E- mail: levon.antikacioglu@uskudar.edu.tr

² Üsküdar University, NP İstanbul Hospital, Department of Psychiatry, İstanbul, Turkey. E-mail: nevzat.tarhan@uskudar.edu.tr

1. Introduction

Since decades varieties of psychopharmacotherapies and psychotherapies, either alone or in combined forms are both administrated on mild or severe psychiatric problems, depending on the diseases or preferences of the practitioners by taking in consideration the needs of the patients.

There is a third agent, the ECT (Electro Convulsive Therapy), which in the course of the history, generally by the layman, has always been considered as a controversial treatment. Nevertheless, by considering its efficiency, it is still implemented particularly in drug-resistant and persistent cases. Additionally, in these last years the variations - variations because after all, are all acting through electromagnetic (EMW) waves - like TMS (Trans Magnetic Stimulation) or tDCS (Transcranial Direct Current Stimulation), are all welcomed, because they are not as brusque as ECT.

In this manuscript we tried to discuss, on the probable "mechanism of action" of ECT, TMS, tDCS, namely the "electromagnetically induced waves" therapies and, re-evaluate some issues concerning the methodological problems, either in studying their effects or in determining strategies to empower their not yet fully discovered, efficiencies.

2. Discussion

2.1. Psychopharmacotherapies

The actual psychopharmacological agents, are primarily acting on the,

- a) pre-synaptic axon terminals' neurotransmitters' production and release and re-up taking,
- b) postsynaptic receptors' reception, or
- c) the biochemical interactions within the synaptic cleft.

These are the actual scientific paradigms for the chemical neurons.

Their commonly shared factor is that all the strategies are organized to facilitate or inhibit the neuronal transmission; thus in a way "to manipulate the learning process" too. In other terms "all is done to loosen up the stabilized ties and/or strengthen the desired ones".

2.2. Psychotherapies of any kind

Since the beginning of the human history, several strategies have been used to persuade, impress and heal people. The first practitioners were the tribe's leaders, priests, shamans, highly prestigious governors, senior wise people etc. Nowadays psychotherapists are nothing more than the institutionalized and trained forms of their archaic predecessors.

Needless to say that all the hundreds of therapeutic strategies, are all targeted to loosen up and/or erase the undesired learned ties and/or strengthen the desired ones, indisputably "are, all targeting the manipulation of learning principles and mechanisms".

2.3. Are the above mentioned treatments working?

The truth is that all the statistical data, reveals that the actually applied psychotherapies or/and pharmacotherapies in some cases-diseases-individuals, are perfectly working. But, in some others instead, are ineffective.

At this point our question should be;

- "Why in similar clinical cases, some of the treatments are effective, instead some others, are not at all"?

And immediately after, another question should be,

- "Why in some patients even only a few psychotherapeutic procedures or small doses of medications are able to obtain satisfactory results, but in some others, even the maximum medications or repetitive therapies do not work"?

2.3.1. Which of our steps are hitching?

Whatever we do either by psychological therapy or/and pharmacotherapy, first of all, the patients must possess a neuro-anatomo-physiologically "somehow, healthy and efficiently functioning" neuronal integrity.

Thus at the background of our mind should always be a judgment like these;

- a) "If we ameliorate % 100 the patient by psychopharmacological agents", it means that the broken segment was "only" the one which we affected; practically, the "pre" or "post" synaptic metabolism or synaptic "cleft's" biochemical or mechanical problems.
- b) "If we ameliorate % 100 the patient by any kind of psychotherapy, training, rehabilitation, education"; it means that there was an "erroneous learning" of some behavior or just "a lack of knowledge" and we helped the patient to correct it.
- c) Or if we ameliorate the patient % 100, by the combination of both of the above mentioned ways, no matter which part, and, up to what extend was not working properly, because at the end of the day, the two problematic aspects of the patient, in a combined form, have been treated.
- d) "If we do not ameliorate the patient in none of the above mentioned ways" or ameliorate only "partially", we inevitably have to suppose that "there is some other problem in the rest of the neuron"; in its "nucleus" or "metabolism" or "dendritic" or "axonal" neuroanatomical "constitution" etc. which, in some way are impeding the "electro conductivity" of the neuron/s.

Thus, at this point, our opinion is that, are exactly the ECTs (and successively TMS, tDCS etc.) or better if we express in general terms, the electromagnetically induced waves, that are acting on the neuron to correct the dysfunctional remnants, mentioned at the above last clause.

2.3.2. ECT – TNS – tDCS and similars

It is still unclear the mechanism of ECT (Fosse, R., & Read, J., 2013). At the beginning has been widely used in wide ranges of clinical cases, but now, considering its some side effects, its use is limited to, especially severe cases of drug or/and therapy-resistant morbidities, like major depression or severe OCD. Nevertheless, in general terms it is accepted that “the efficiency of electroconvulsive therapy in major depression is established, but the importance of the electrical dosage and electrode placement in relation to efficacy and side effects is uncertain” (Sackeim, H.A. at al., 1993). On the other hand, it is an empirically documented fact that, the seizures’ intensity, threshold, duration, ECT’s unilateral or bilateral applications are all variables changing the outcomes (Sackeim, H. A., Devanand, D. P., & Prudic, J., 1991). However, it is since long time accepted and documented even on text books that, ECT at least in many cases, situations and diseases is working, especially in delusional depression and, in comparison to other combined treatments (Kroessler, D., 1985).

The relatively modern TMS, given its more “human” applicability and, apparently less adverse effects, conceded a more extensive usability in a variety of morbid entities. Also in TMS there are different studies, sometimes contradictory, are documenting its positive effects on cognition, memory and effect’s durability beyond the applied times (Thut, G., & Pascual-Leone, A., 2010). etc. For instance, TMS is used in rehabilitation, brain injuries, and depression with relatively fewer side effects (Nielson, D. M., 2015). There are researches which are dealing with the orientation-positioning of the coils; Opitz, A. at al. (2016) pointed the fact that “Three distinct DLPFC stimulation zones were identified, differing with respect to the network to be affected (default, frontoparietal) and sensitivity to coil orientation (Opitz, A. at al., 2016). Carni, L. at al (2015) by conducting a treatment program by TMS (Deep Cranial Magnetic Stimulation) on OCD, concluded; “lacking the ability to target the CSTC circuit directly, standard TMS treatment protocols for OCD showed diversified results. But concluded that the stimulation of targeted deeper neuronal pathways by dTMS, is a promising therapeutic intervention on OCD” (Carmi, L. at al., 2015).

tDCS seems even safer, hence is used more extensively. A well guided mapping is necessary to be able to target the exact points and is used in perceptual, cognitive, and behavioral functions (Nitsche, M. A. at al., 2008). It is very remarkable the summative opinion made by Li (Li, L. at all. 2015); “With the slew of studies reporting ‘promising results’ for everything from motor recovery after stroke to boosting memory function, one could be easily seduced by the idea of tDCS being the next panacea for all neurological ills. However, huge variability exists in the reported effects of tDCS, with great variability in the effect sizes and even contradictory results reported. In this review, we consider the interindividual factors that may contribute to this variability” (Li, L. M. At al., 2015). Brunoni, A.R. at al. (2016) concluded that tDCS has mixed results, probably caused by heterogeneity of the studied groups (Brunoni, A. R. At al., 2016). Kekic, M. at al (2016)

concluded that in “Overall, data suggested that tDCS interventions comprising multiple sessions can ameliorate symptoms of several major psychiatric disorders, both acutely and in the long-term. Nevertheless, the tDCS field is still in its infancy” (Kekic, M. At al., 2016).

Up to this point, the only exact words we can spell are “all of the above mentioned electromagnetically induced, wave therapies” have “different effects” on “different diseases” and “patients”, in “different degrees”. Nevertheless, the general opinion, though cautiously, is that TMS (Kimiskidis, V. K., 2016; Oliveira, J. at al., 2016) and tDCS (Marriage, A. P., 2016; Nitsche, M. A. at al., 2009; Nitsche, M. A., & Paulus, W., 2000; Gandiga, P. C. At al., 2006; Tortella, G. at al., 2015; Hone-Blanchet, A. at al., 2015; Vanderhasselt, M. A. at al., 2015) are promising tools for the future.

2.4. Aproposal on the probable neuro-anatomo-physiological mechanism of electromagnetically induced, wave therapies

In principle, during any kind of conditioning and/or, operational excitatory and/or inhibitory activity, along the chemical neurons, the electrical currents flow only unidirectionally; “toward the axonal terminal buttons”. By nature, under normal physiological circumstances any electrical flow occurring toward opposite direction of the neuron (from terminal buttons toward dendrites) can’t exist at all. This is all the necessary backbone to keep in mind to base the entire mechanism that we will now propose below.

2.4.1. Facilitated flow

By applying the electromagnetic therapy device’s electrodes to the scalp, we discharge the current from one electrode, toward the other one, across the brain; from a point A, up to a point B.

The same is valid also in TMS; although it does not possess any electrodes, its pulses’ waves are going from a source point A, which is the magnetic source’s center, toward the point B, which is its, virtually unlimited, natural spherical three-dimensional axial distributions.

If we induce to the scalp an “electromagnetic discharge”, headed for instance from the electrode A, toward the electrode B, all those neurons on its course, having the same polarity orientation (“soma→terminal button”) and aligned in a “parallel” or “quasi parallel” or at most “oblique” position, in respect to the orientation of the current, those neurons inevitably will be stimulated-facilitated (Figure 1); for they have the same polarity with the applied EMW.

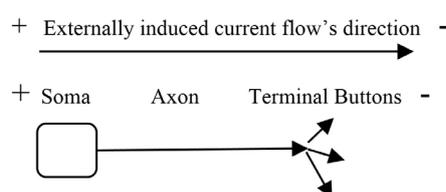


Figure 1: The External current flow, in case of having the same direction, in respect to the neuronal natural current flow.

Let's assume that this "pushed neuronal current", or in other terms, "the current, dragged from the direction of the soma and, dropped toward the axonal terminal button" (from the "+" pole, to the "-one), by this externally induced stronger wave/energy, in addition to the fact that will promote-facilitate an stimulus, will not do any considerable harm to the neurons, provided it remains within the safe power and duration limits. At most, they will be activated-facilitated.

2.4.2. Obstructed flow

If along the course of the externally applied electrical discharges, there are neurons lined-up toward "opposite directions – polarities", inevitably those neurons, will get some "nano-scale electric shock" and will be obstructed and, (Oppositely oriented currents will clash with each other's.) will be hurt; because the externally applied stronger current, will force the neurons to carry the current toward opposite direction, which is contrary to their innate morpho-physiology (Figure 2).

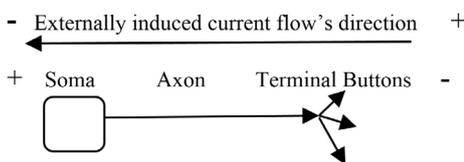


Figure 2: The External current flow, in case of having an opposite direction, in respect to the neuronal natural current flow.

Not only, but, after all, the clusters of neurons are wet environments; and if remained in between two electrodes, they will serve as just conductors. As a natural consequence, either the neuronal soma, or its nuclear functions, or the pre-post synaptic functions or cleft's physiologic bio-mechanisms, all will be stunned; vesicles, receptors, neurotransmitters and every micro or nano system in them, will suffer and their functions will be diverted, overstimulated or over inhibited.

But as long as the implemented currents remain within safe biological limits, obviously, these adverse effects will be reversible. We will get permanent side effects only if the externally induced waves are higher than the biologically tolerable threshold, or, the durations are longer, up to the point of creating structural damage on the neurons and/or on their synaptic connections. These damages don't need to be necessarily at visible scales; changes at nano-scales also, can perfectly be sufficient to spoil the integrity of the neuro-anatomo-physiological functionality. As a consequence, after the sessions, the patient will express some "side effects-negative feelings and experiences" etc.

2.4.3. Neurons and their connections are not aligned along a straight-line

The brain is a mess of anatomical (hard wired) connections and plus, with unlimited fCs (functional connectomes-connections created by personal experiences), oriented virtually toward any direction, depending on the individuals' own brainprint. And it is almost impossible to

meet any functional or anatomical connection overlapping with the externally induced, quasi straight-line current trajectory; for the neuronal connections quite likely, are in form of labyrinths, zigzags and curves.

Thus any externally induced current along its course will "contemporarily" encounter neurons, either of the same or, opposite polarity.

As a final sum, the externally induced waves eventually, along their own trajectory (from "+" toward "-". Figure 3), will encounter the curved and zigzagged continuations of the same neurons too; of which, some of the segments having the same polarity will be facilitated, but instead the parts having the opposite polarity, will be obstructed (Figure 3). Needless to say, the final outcome will be a micro-shock and consequentially will result in an obstruction.

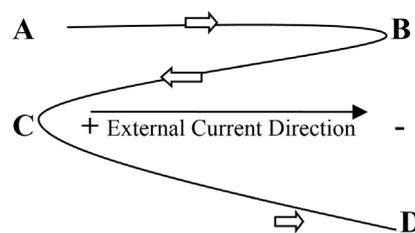


Figure 3: The External current flow which on its way, along the same neuronal axon, encounters, some segments with the same and, some other segments, with oppositely oriented neuronal current flows, just because the axon is not a straight line, instead, has some snake-like shape.

A→B segment is facilitated, B←C segment is obstructed, and C→D segment is facilitated.

2.4.4. Nano-Neurophysiotherapy and/or Neuroplasticity?

We know that in any cerebral location related to, overused organs or faculties, becomes more developed. Conversely, lessened functions are sign of diminished brain volume in the respective areas.

There is no reason to not accept that TMS application also, creates similar consequences; In fact, Bohning (Bohning, D. E. at all. 2000) reported that "Single TMS pulses applied over the motor cortex with sufficient intensity to induce thumb movement produced BOLD-fMRI responses detectable in both the ipsilateral motor cortex" (Bohning, D. E. at al., 2000). In other words, they detected an augmentation of blood flow; hence we would propose that this data gives us a possibility to conclude; that probably its repetitive applications can create a massage-like effect to the neurons and then, an upcoming neuroplasticity.

There are other researches that sustain; "Despite the fact that different studies have been performed using transcranial direct current stimulation (tDCS) in aphasia, so far, to what extend the stimulation of a cerebral region may affect the activity of anatomically connected regions remain unclear" (Cipollari, S. at al., 2015). But this interpretation pertains to the specific condition of aphasia. For other conditions can perfectly be invalid.

In short, we would propose that externally induced EMWs, eventually are acting like a nano-physiotherapy and, at least promoting blood circulation or, revitalizing for some reason the grown lazy neurons or, mobilizing inert neuronal clusters and giving some form of push or, making a massage-like stimulation or, something else and "making the neurons participate to the integrity of the cerebral functionality".

2.5. Reinterpretation of the literature and proposal of a different model

If we sum up all of the abovementioned facts, the somehow conflicting results, of researches done by "electromagnetic wave therapies", became clearer and understandable; it seems highly probable that in reality they are not conflicting at all, and are working better than we think.

The problem stands only in the fact that, in clinical researches it is very difficult to control the variables as much as in the experimental conditions. We need, to find new methodological strategies, to adequately split conditions, to keep under strict control the independent variables and, to better understand the EMWs' therapy effects.

We know that old memories are more deeply rooted; our ancestors probably new it since the beginning of the human history but since some decades ago, we also have scientifically documented, thanks to Ebbinghouse's colossal and ingenious experiments (Ebbinghaus, H., 1913).

Needless to mention that either our everyday experiences or clinical (for instance in senile dementia or alzheimer), psychopathological observations, confirm that the old personal memories, having strong ties with each other's, are the best conserved and, last deteriorated ones. It seems that the old memories have the same resistance against ECT sessions too. In fact, Squire et al. (Squire, L.R. et al., 1981) documented that after ECT, older memories have been more easily recovered (Squire, L. R. at al., 1981).

But how can we know which patient's which memory, we mean psychopathological symptom or syndrome, is deeper or shallower than the other's one? It is impossible to arrive to a healthy conclusion, within the limited methodological designs and conditions of clinical applications. As a consequence, we can neither understand what a patient's older/newer memory is, or compare the patients, with each other's psychopathological conditions and, arrive to results. This is more than enough to see conflicting results after EMW applications.

On the other hand, it is a very well-known reality that the older diseases are difficultly cured. So how it is possible to say 1-year-old OCD is an old or new one, and, standardize a group by such a criterion? Will not it depend of course on the patients' age? Another problem is that not only the durations, but also the severities, intensities, undoubtedly are important dimensions, variables and cannot be easily measured. It is hypothesized that the "strength or weakness of a learned material is directly proportional to the quantity, quality and intensity of the ties made within the entire Central Nervous System Network" (Antikacioglu, L., 2015).

All the above mentioned facts can perfectly explain why, "the efficiency of electroconvulsive therapy in major depression is established, but the importance of the electrical dosage and electrode placement, in relation to efficacy and side effects, is uncertain" (Sackeim, H. A. at al.,1993). Or why ECT seizures' intensity, threshold, duration, ECT's unilateral or bilateral applications are all variables changing the outcomes (Sackeim, H. A. at al.,1991). Why there are researches which are dealing with the orientation-positioning of the coils; Opitz, A. at al. (2016) pointed the fact that "Three distinct DLPFC stimulation zones were identified, differing with respect to the network to be affected (default, frontoparietal) and sensitivity to coil orientation (Opitz, A. at al., 2016). Why Carni, L. at al. (2015) by conducting a treatment program by TMS (Deep Cranial Magnetic Stimulation) on OCD, concluded; "lacking the ability to target the CSTC circuit directly, standard TMS treatment protocols for OCD showed diversified results. But concluded that the stimulation of targeted deeper neuronal pathways by dTMS, is a promising therapeutic intervention on OCD (Carmi, L. at al., 2015). Why Nitsche, M. A. at al. (2008) proposes that a well guided mapping is necessary to be able to target the exact points and is used in perceptual, cognitive, and behavioral functions (Nitsche, M. A. at al., 2008). Why Brunoni, A.R. at al. (2016) concluded that tDCS has mixed results, probably caused by heterogeneity of the studied groups. Why Kekic, M. at al (2016) concluded that in "Overall, data suggested that tDCS interventions comprising multiple sessions can ameliorate symptoms of several major psychiatric disorders, both acutely and in the long-term. Nevertheless, the tDCS field is still in its infancy".

In short, the above outcomes are endlessly diversified, because in our opinion, along the course of the externally applied waves, are paved neurons either of the same (and can be facilitated) or, opposite (and can be obstructed) polarity. As a natural consequence at the end, all of them will be shocked. These clashing currents cause what we call "side effects", that are consequences of the "neuro-anatomophysiological traumatic micro-shocks". And in turn are also effects of the loosening memory ties.

Probably, "simultaneously and paradoxically" the so called "side effects" generated by flutterings created by the shocks, which manifest themselves in form of attention difficulty, memory loss, concentration impossibilities, dizziness or other similar problems, "will also be the initiator of the awakening, revitalization, blood supply, neurophysiological reanimation, activation and neuroplastic changes of the inert neurons" (along with the facilitation or obstruction effects which they have got) provided they, genetically or neuro-anatomically are not totally handicapped.

Which of the above agents to what extend will be effective, depends on the individuals' brainprints. And in order to achieve improvements, we need both; slacking off the old memories and promoting new connections too, through psychotherapies and pharmacotherapies.

Now let's us concentrate on some preliminary factors which can be useful either in "designing researches to measure the effectiveness of the EMW treatments" or/ and, in "designing the treatments" themselves.

2.6 Better strategies for research and therapy purposes

2.6.1 Early intervention

Probably the first step to take in consideration should be an "early intervention".

As the main principle of the EMW therapies is to loosen the memories connections and if possible to erase them, our primary goal must urgently be, an early intervention. Old memories are the least forgotten. The sooner the intervention the better is the result.

2.6.2. Duration of sessions

After all, EMW therapies are unnatural interventions. Just to prevent any predictable or unpredictable permanent side effects, we should suggest personalized durations. Hypothetically every individual has his own resistance threshold. The best length is, neither a longer nor a shorter than the "necessary" duration. Unnecessarily long durations can make more harm than benefit. Shorter than the optimum degree, cannot do any good. To adequately tailor flexible and optimum session durations, the patient need to be carefully and continuously observed.

2.6.3. Intensity of EMWs

Perhaps to standardize the wave intensities we should better create some kind of "resistance index" in base of body weight or some other criteria. If we exceed the necessary threshold of the individual, probably it augments the loosening process of the memories (or symptoms, syndromes etc.) but then, renders difficult to build up new ones or, harms in some other form.

2.6.4. Direction of waves

We have to continuously change the position of the electrodes. Probably the more parts are multidirectionally affected and stimulated, the better are the results.

Probably in affecting the brain throughout multiple EMW axial orientations, TMS has a remarkably superior manageability, in respect tDCSs. But by continuously changing electrodes' positions, and systematically moving them, tDCS also, can have the advantage of reaching to sufficiently remote brain points.

2.6.5. Multi-Device Intervention

Every device, has its own advantages and limits. Thus perhaps, instead of being stuck to one device only, it is better to intervene to the patient with different EMW devices.

2.6.6. Unilateral versus Bilateral

Undoubtedly both unilateral and bilateral sessions should be made. As our end goal is, nothing more than massaging and revitalizing the "entirety" of the brain, and make it function in "integrity", we have to reach every deep cerebral locality as far as the technology permits.

2.6.7. Whatever the intervention is for, in order to relocate desired habits, practices are a must

The mission of loosening the old ties and revitalizing the lazy neurons is just the half of the job. We still need to teach and solidify the adaptive behavioral patterns. Between the sessions, we must achieve, an intense and multidimensional psychotherapeutic approach, tailored to the individual. This last rule, in our opinion, should be our primary importance.

Just EMWs alone, cannot work to any full extend. Or at least, cannot have a lasting effect.

The total absence or, a weak support of psychotherapies and psychopharmacotherapies explains perfectly, why EMWs' constructive effects become disputable. The overwhelming majority of researches and treatments done by using EMWs, are concentrated solely on variables like ages, strokes' localities, morbidities, sessions' frequencies, intensities and durations. Of course by default they are all necessary, but are not enough. The primary target must be, to intensively plan the patient's life, between his/her EMW therapy sessions. In other words, the EMW applications, should not be our final target, but just an "intermediary tool" in reassessing, the mental-physical rehabilitation.

2.6.8. How to implement our proposal either in designing researches or intervening sessions?

We would propose that probably, by taking in consideration the above mentioned few simple rules and by using them as independent variables, we can both "design, better experimental and research models, to prove the efficacy of EMV therapies", and to obtain better results during treatments.

Our opinion about the controversy of the researches' results is that, with a very high probability, the ones which obtained better results are the ones which willingly / unwillingly or knowingly / unknowingly, have met the abovementioned criteria. Or vice versa, the ones who didn't obtain desirable results, are the ones that didn't met the above simple rules.

3. Conclusion

Our opinion simply is, that applying EMWs to the scalp; giving them micro-shocks, stunning the neurons' functions and, by this way loosening neural old ties-memories and, simultaneously revitalizing the lazy ones, are all, simply a preparation to a new mind-state and, are only half of the way.

In order to obtain curative results instead, between the sessions of the EMW therapies, by taking advantage of learning mechanisms, we must plan adequately personalized, extensive and intensive psychotherapies supported by pharmacotherapies. For the final target is the rehabilitation. Using only EMW does not rehabilitate but, it can be used as a preparative therapeutic milieu, in other words all the EMW therapy devices, can only be an intermediary tool.

Not just, but by planning efficient psychopharmacotherapies between the EMW therapy sessions, by taking in better control the EMWs' timings, durations, intensities, directions and laterality as above discussed, and by tailoring all of them in relation to the patients'/subjects' personal conditions, it is very highly probable that we will obtain better evaluative research designs, therapeutic outcomes and, the apparent controversies will fade.

Resources

- Antikacioglu, L. (2015). The More Brain Parts Are Involved The Better Is Learned and Performed. *The Journal of Neurobehavioral Sciences*, 2(3), 114-116.
- Armstrong, B. C., Ruiz-Blondet, M. V., Khalifian, N., Kurtz, K. J., Jin, Z., & Laszlo, S. (2015). Brainprint: Assessing the uniqueness, collectability, and permanence of a novel method for ERP biometrics. *Neurocomputing*, 166, 59-67.
- Bohning, D. E., Shastri, A., Wassermann, E. M., Ziemann, U., Lorberbaum, J. P., Nahas, Z., ... & George, M. S. (2000). BOLD-fMRI response to single-pulse transcranial magnetic stimulation (TMS). *Journal of Magnetic Resonance Imaging*, 11(6), 569-574.
- Brunoni, A. R., Moffa, A. H., Fregni, F., Palm, U., Padberg, F., Blumberger, D. M., ... & Loo, C. K. (2016). Transcranial direct current stimulation for acute major depressive episodes: meta-analysis of individual patient data. *The British Journal of Psychiatry*, bjp-bp.
- Carmi, L., Dar, R., Zohar, J., & Zangen, A. (2015). Deep Transcranial Magnetic Stimulation (Tms) in Obsessive Compulsive Disorder (Ocd) Patients. *European Psychiatry*, 30, 794.
- Cipollari, S., Veniero, D., Razzano, C., Caltagirone, C., Koch, G., & Marangolo, P. (2015). Combining TMS-EEG with transcranial direct current stimulation language treatment in aphasia. *Expert review of neurotherapeutics*, 15(7), 833-845.
- Ebbinghaus, H. (1913).. (H. Ruger, & C. Bussenius, Trans.) New York, NY: Teachers College.
- Fosse, R., & Read, J. (2013). Electroconvulsive treatment: hypotheses about mechanisms of action. *Frontiers in psychiatry*, 4, 94.
- Gandiga, P. C., Hummel, F. C., & Cohen, L. G. (2006). Transcranial DC stimulation (tDCS): a tool for double-blind sham-controlled clinical studies in brain stimulation. *Clinical Neurophysiology*, 117(4), 845-850.
- Hone-Blanchet, A., Edden, R. A., & Fecteau, S. (2015). Online effects of transcranial direct current stimulation in real time on human prefrontal and striatal metabolites. *Biological Psychiatry*.
- Kekic, M., Boysen, E., Campbell, I. C., & Schmidt, U. (2016). A systematic review of the clinical efficacy of transcranial direct current stimulation (tDCS) in psychiatric disorders. *Journal of psychiatric research*, 74, 70-86.
- Kimiskidis, V. K. (2016). Transcranial magnetic stimulation (TMS) coupled with electroencephalography (EEG): Biomarker of the future. *Revue neurologique*, 172(2), 123-126.
- Kroessler, D. (1985). Relative efficacy rates for therapies of delusional depression. *The Journal of ECT*, 1(3), 173-182.
- Li, L. M., Uehara, K., & Hanakawa, T. (2015). The contribution of interindividual factors to variability of response in transcranial direct current stimulation studies. *Frontiers in cellular neuroscience*, 9.
- Marriage, A. P. (2016). Social Psychology and Noninvasive Electrical Stimulation. *European Psychologist*, 21(1), 30-40.
- Nielson, D. M., McKnight, C. A., Patel, R. N., Kalnin, A. J., & Mysiw, W. J. (2015). Preliminary guidelines for safe and effective use of repetitive transcranial magnetic stimulation in moderate to severe traumatic brain injury. *Archives of physical medicine and rehabilitation*, 96(4), S138-S144.
- Nitsche, M. A., & Paulus, W. (2000). Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *The Journal of physiology*, 527(3), 633-639.
- Nitsche, M. A., Boggio, P. S., Fregni, F., & Pascual-Leone, A. (2009). Treatment of depression with transcranial direct current stimulation (tDCS): a review. *Experimental neurology*, 219(1), 14-19.
- Nitsche, M. A., Cohen, L. G., Wassermann, E. M., Priori, A., Lang, N., Antal, A., ... & Pascual-Leone, A. (2008). Transcranial direct current stimulation: state of the art 2008. *Brain stimulation*, 1(3), 206-223.
- Oliveira, J., Sobreira, G., Moreira, C. A., Aleixo, M. A., & Brissos, S. (2016). A review of transcranial magnetic stimulation for treating negative symptoms of schizophrenia. *European Psychiatry*, 33, S554-S555.
- Opitz, A., Fox, M. D., Craddock, R. C., Colcombe, S., & Milham, M. P. (2016). An integrated framework for targeting functional networks via transcranial magnetic stimulation. *NeuroImage*, 127, 86-96.
- Sackeim, H. A., Devanand, D. P., & Prudic, J. (1991). Stimulus intensity, seizure threshold and seizure duration: Impact on the efficacy and safety of electroconvulsive therapy. *Psychiatric Clinics of North America*.
- Sackeim, H. A., Prudic, J., Devanand, D. P., Kiersky, J. E., Fitzsimons, L., Moody, B. J., ... & Settembrino, J. M. (1993). Effects of stimulus intensity and electrode placement on the efficacy and cognitive effects of electroconvulsive therapy. *New England Journal of Medicine*, 328(12), 839-846.
- Squire, L. R., Slater, P. C., & Miller, P. L. (1981). Retrograde amnesia and bilateral electroconvulsive therapy: long-term follow-up. *Archives of General Psychiatry*, 38(1), 89-95.
- Thut, G., & Pascual-Leone, A. (2010). A review of combined TMS-EEG studies to characterize lasting effects of repetitive TMS and assess their usefulness in cognitive and clinical neuroscience. *Brain topography*, 22(4), 219-232.
- Tortella, G., Casati, R., Aparicio, L. V., Mantovani, A., Senço, N., D'Urso, G., ... & Junior, B. D. S. P. (2015). Transcranial direct current stimulation in psychiatric disorders. *World journal of psychiatry*, 5(1), 88.
- Vanderhasselt, M. A., De Raedt, R., Namur, V., Lotufo, P. A., Bensenor, I. M., Boggio, P. S., & Brunoni, A. R. (2015). Transcranial electric stimulation and neurocognitive training in clinically depressed patients: A pilot study of the effects on rumination. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, 57, 93-99.
- Wachinger, C., Golland, P., & Reuter, M. (2014). BrainPrint: identifying subjects by their brain. In *Medical Image Computing and Computer-Assisted Intervention-MICCAI 2014* (pp. 41-48). Springer International Publishing.