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Dynamical Neurofeedback® Neuroptimal®: A New Approach to Improve the Perception of Tinnitus Through Cerebral Self-Regulation.

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ABSTRACT

We provide results of our multi-center research Palermo-Milan which aims to evaluate the effectiveness of NeurOptimal®, a new therapeutic tool useful for patients suffering from tin-nitus. We hypothesize the use of NeurOptimal® can improve perception of tinnitus and psycho-physical symptoms related to it. NeurOptimal® is a form of training that allows the brain to self-regulate its activity by optimizing it. To evaluate its effectiveness, we are subjecting voluntary patients, diagnosed with tinnitus, to a series of Non-Linear NeurOptimal® Neurofeedback Sessions, collecting data from audiometric measurements and self-assessment questionnaires con-cerning the handicap caused by tinnitus, and the level of pathological worry, depression, anxiety and stress. The results that we illustrate, although they need to be verified on a larger sample, are promising and seem to confirm the peculiar characteristic of this unique technique, which is based on the cardinal principles of cerebral activity, self-regulation, neuroplasticity, and learning.

Keywords: Tinnitus; THI; DASS-21; Penn State Worry Questionnaire; Self-regulation; Neuromod-ulation; Brain; Electrical activity; Psychophysical symptoms; Non-Linear Dynamical Neurofeed-back; Self-assessment questionnaires

INTRODUCTION

Our thesis was that Dynamical Neurofeedback® NeurOptimal® Sessions given over a period of four months would result in a decrease of clinician-determined audi-ological tinnitus symptoms and an improvement in the patient's emotional state and tolerance of this disorder. For about five years, a multi-center research project (in

Pa-lermo and Milano) has been underway with the aim of evaluating the effectiveness of NeurOptimal® for patients suffering from tinnitus.

Dynamical Neurofeedback® NeurOptimal® is an alternative approach to traditional neurofeedback: the latter is an extension of biofeedback and has a directive approach which consists in increasing or inhibiting specific brain frequencies related to traumas. Dynamical Neurofeedback® NeurOptimal®, instead, does not identify specific brain waves but is based on the principle that the brain is able to find solutions to its problems on its own. Traditional neurofeedback has as its objective "treatment" of the brain based on a quantified EEG: brain waves are quantified by normalizing them to the reference parameters of an "ideal" brain. Dynamical Neurofeedback® NeurOp-timal®, on the other hand, is a "brain training" approach: it detects and notifies the ongoing change in cortical activity without making any kind of judgment and without needing any type of diagnosis. Dynamical Neurofeedback® NeurOptimal® does not tell the brain what it should or should not do; it detects the variability emerging from EEG and its notification consists in dynamically adapting to that specific brain by no-tidying it in real time of the significance of the emergence of a new behaviour.

Dynamical Neurofeedback® NeurOptimal® takes the form of spontaneous neu-romodulation of the brain's electrical activity, which we hypothesize can improve perception of tinnitus and the related psychophysical symptoms. NeurOptimal® is a sort of training that allows the brain to self-regulate its activity by optimizing it. The hypothesis is that a series of NeurOptimal® Sessions will lead to a decrease in the per-ception of tinnitus, also leading to an improvement in the psychophysical state. It is a non-medical, non-invasive, and painless methodology, which is based on the principles of self-regulation, neuroplasticity, and learning. According to self-regulation, as the body continuously regulates its parameters, so the brain also has its own self-regulation mechanisms; thanks to called neuroplasticity, the brain continuously changes and adapts to the surrounding environment and the plasticity of the brain makes organizational changes possible that will allow it to function better. EEG-based algorithms are operational: when these detect excessive variability or decreased com-plexity, indicating that the Central Nervous System (CNS) has moved out of its current specific optimal range of activity, feedback is activated that helps the brain to "reset" and, over time, to self-regulate. The repetition of these feedbacks determines optimization of the CNS, so that the dysfunctional patterns are abandoned and consequently also the symptoms.

The brain should behave dynamically, it should be able to manage each event in a unique, creative, original way, but often proposes repetitive, redundant, predictable behaviors. The "feedback" notifications allow an orientation response and subsequent synchronization which triggers a self-regulation process. The mathematical algorithm underlying NeurOptimal® draws inspiration from the holonomic or holographic mod-el of the brain (David Joseph Bohm and Karl Harry Pribram) according to which the brain has a diffuse memory as well as a localized memory. Every single part of the brain reproduces the whole: the brain is able to recover the lost information locally in a sufficiently large portion of the dendritic tree that reproduces the whole.

MATERIALS AND METHODS

We collect data from self-assessment questionnaires about the handicap level provoked by tinnitus (THI Tinnitus Handicap Inventory Questionnaire), tendency to pathological preoccupation (Penn State Worry

Questionnaire or PSWQ) and depression, anxiety and stress (DASS-21 Questionnaire), at these times: T0 (before training) and T3 (after 30 sessions).

Tests in clinical psychology are used to evaluate quantitatively and qualitatively momentary or lasting conditions of normal or pathological psychic functioning, or in-dividual functions, and to detect personality traits [1]. They therefore provide very important data for diagnosis and for the treatment of the pa-tient, and not only in the psychological field. They can be profitably employed in stud-ies of an epidemiological, social and even medical type. To use them correctly and ex-tract the greatest amount of significant information, thorough knowledge of the char-acteristics and potential of the tests is required. The usefulness of psychological tests depends on certain basic conditions and is linked to technical problems: the relational dimension, observation of the ways in which the subject copes with the test situation, the strategies through which the proposed task is carried out, and verbal and non-verbal behavior during the session are equally important sources of information [2].

In choosing the psycho-diagnostic tools to use, it is appropriate to take many variables into account: the characteristics of the tool itself, with its particular limitations and advantages; the age of the subject and the type of disorder, as well as the goal of the administration: it is essential to choose tests based on the information that we in-tend to obtain from them, in a sort of procedure of consecutive hypotheses. Also, we must not forget that any psycho-diagnostic process is a complex operation that re-quires necessary activity of integration of the information collected, in order to reach a picture that is as complete and organized as possible about the psychic functioning of the subject examined [3]. In any case, it must be kept in mind that a single test cannot give a complete picture of the individual examined and is unlikely to provide comprehensive information on a limited aspect. For these reasons, it is vital to resort to a battery of tests, in order to integrate data relating to different areas of the psychic reality of the subject.

The most widely used measurements in clinical psychology and in the psychiat-ric-medical field are self-assessment scales [4]. These questionnaires are objective measurements, as they provide application methods, modalities of response and interpretation of objective and standardized results, and above all are self-descriptive, as it is the patient himself or herself who provides a self-description with respect to the variables emerging in the questionnaire itself.

In reality it is not so true that so-called objective tests are entirely objective: often the items of a self-report questionnaire imply some subjectivity with respect to the way the person examined can interpret them. An example is found in the frequency of a behavior: alternative answers such as “often”, "sometimes" etc. imply a choice on the part of the subject which does not necessarily correspond to that of another subject [5].

These measurements typically include various elements which are designed to sample specific aspects of a particular function. They consist of quite long lists of symptoms or behaviors to be evaluated for presence/absence or more often severity (for example, scales ranging from 0 to 4), whose application requires adequate time.

In a medical context such as the otoneurological one [6], self-report scales are widely used. Self-assessment measurements of disorders are emerging as useful clinical tools in the otoneurological field for two main reasons. Firstly, they help quantify hearing and balance symptoms of patients that are not easily detectable using audiometric and vestibulometric tests. Secondly, handicap self-assessment scales serve as outcome

measurements when used in paradigms that include a pre- and post-treatment phase, with reduction of the perceived handicap as the desired positive result. In this sense, self-assessment measurements have been used to document the benefits of hearing aid provision, rehabilitation-based hearing counseling, and balance and vestibular rehabilitation. In addition to hearing and balance measurements, self-assessment of subjectively perceived disability because of tinnitus is being recog-nized as useful in quantifying the impact of tinnitus on everyday life [7]. The THI is a self-assessment questionnaire which is easy to administer and offers a psychometrically robust measurement of the impact of tinnitus on daily life [7]. It consists of 25 questions, each of which has three possible answers quantifiable with a score (yes = 4, sometimes = 2, no = 0). The final total score makes it possible to quantify for each individual at that moment the degree of suffering from tinnitus (grade 1 = 0-16; grade 2 = 18-36; grade 3 = 38-56; grade 4 = 58-76; grade 5 = 78-100) (Davis, & El Refaie, 2000).

Grade 1 (0-16, minimum). Tinnitus is only perceived in a quiet environment and is very easily disguised. It does not interfere with sleep or daily activities.

Grade 2 (18-36, mild). Tinnitus is easily masked by ambient noise and easily for-gotten during daily activities. It can occasionally disturb sleep but does not interfere with the performance of daily activities.

Grade 3 (38-56, moderate). Tinnitus can even be perceived in the presence of background or ambient noise, although daily activities can be carried out normally. It is perceived less during tasks that require concentration. It often hinders sleep and activities performed in silence. Most people with pathology from tinnitus should fall into grades 2 and 3.

Grade 4 (58-76, severe). Tinnitus is almost always heard, and can rarely be masked. It causes sleep disturbances and can interfere with a person's ability to per-form normal daily activities. Activities performed in silence are negatively affected. Hearing loss may be present but its presence is not fundamental. According to epide-miological data it should be difficult to find subjects with this degree of suffering from tinnitus.

Grade 5 (78-100, catastrophic). All symptoms of pathology from tinnitus are at the highest levels of severity. It is likely hearing loss is also present but it is not essential in determining symptoms. Psychological problems are often present that are already known to the general practitioner or registered in previous hospitalizations. According to epidemiological data it is an extremely limited group [8].

The THI evaluates reactive responses of a functional, emotional and catastrophic type to tinnitus, has major reliability for the total scale and sufficient for the functional and emotional subscales; it is insufficient for the catastrophic scale but nonetheless useful for Identifying individuals with severe reactions to tinnitus such as to require the intervention of a psychologist or psychiatrist [9]. Future investigations should be planned to evaluate the stability of the instrument over a period of months to evaluate the long-term treatment results.

DASS-21 is a psychometric test devised by Peter F. Lovibond 10 of the University of New South Wales. The test consists of 21 questions and has no diagnostic function, but is rather an indication regarding the levels of anxiety, depression and stress that must be integrated with the data obtained from the clinical interview. The test typically lasts 3 to 5 minutes. The examiner advises the patient to answer each item, considering what he or she has experienced in the last week, and to choose the answer that comes to mind first. For each item it is possible to provide one answer:

- A= never
- B= sometimes
- C= often
- D= always

DASS-21 assesses the severity of behavioral and emotional symptoms correlated with depression, anxiety and stress and provides a mild, moderate and severe result. Questions related to each axis are:

- Items relating to symptoms of depression: 3, 5, 10, 13, 16, 17, 21.
- Items relating to symptoms linked to anxiety disorder: 2, 4, 7, 9,15, 19, 20.
- Stress-related symptom items: 1, 6, 8, 11, 12, 14, 18.

Each of the answers is evaluated from 0 to 3. Therefore, each of the axes has partial scores from 0 to 18-24 depending on the number of questions assigned (Henry & Crawford, 2005, 11).

The DASS-21 test does not claim to offer a diagnosis by itself; it is simply a self-assessment scheme and it should be followed by a complete psychological or psychiatric evaluation.

The PSWQ is a questionnaire of 16 items that aims to measure the worry trait, using the Likert Scale, with 1 indicating “not at all typical of me” and 5 “very typical of me." The completion time is 5-6 minutes. Eleven items explore pathological worry, so that a higher score in these items is symptomatic of a pathological level of concern (e.g., “Once I start to worry, I can't stop"), while the remaining five items are formulated to indicate that the concern is not a totally disabling problem (e.g. "I never worry about anything"). The total score is calculated by adding the scores of the first 11 items and the scores of the last 5 items in a negative form, which therefore need a correction grid. Higher PSWQ scores reflect greater levels of pathological concern, and hence re-search suggests that the tool has a strong capacity to differentiate patients with Generalized Anxiety Disorder (GAD) from other anxiety disorders, since the worry that the instrument detects is considered to be the dominant feature of GAD compared to other anxiety disorder groups or non-anxious controls, and is often used as an indicator of treatment change (Stöber and Bittencout, 1998, 12). Since its development in 1990, the PSWQ has grown into a widely used self-report tool that attempts to measure excess, pervasiveness and uncontrollable dimensions of worry. The PSWQ has demonstrated a high level of internal consistency and good test-retest reliability (Meyer et al., 1990, 13).

We recruited a sample of 209 patients, with a medical history of tinnitus, for the period from September 2017 to April 2022, in the two sites Milan and Palermo, with these demographic features Table 1 and Table 2.

Table 1: Demographic features: sex.

Sex	100% = patients at time T0
Male	64%
Female	36%

Table 2: Demographic features: age.

Age	100% = patients at time T0
19-24 years	4%
25-34 years	7%
35-44 years	13%
45-54 years	30%

55-64 years	30%
65-74 years	13%
75-84 years	3%

For recruitment we considered the following inclusion criteria

- Tinnitus for a minimum of 1 year
- Absence of psychiatric or neurological diseases
- Absence of any disease that accounts for the tinnitus
- Noise-induced hearing loss
- Cochlear and retrocochlear damage and the following exclusion criteria
- Conductive hearing loss
- Mixed hearing loss
- Meniere's disease
- Systemic vascular disease
- Diabetic disease
- Vestibular Schwannoma
- Tumors of the cerebello-pontine angle
- Pulsatile tinnitus
- Pregnancy
- Other tinnitus treatments in the 6 months prior to the NeurOptimal® Neu-rofeedback Sessions or during the training.

RESULTS

Before starting the NeurOptimal® training, the recruited patients underwent an Audiometric Test (the audiometric evaluation is until 8.000 Hz): 64% were Normoacusic, see Table 3.

Table 3: Audiometric Types at time T0.

Audiometric Type	**100% = patients at time T0**
Normoacusia	64%
Mild Perceptive Hypoacusia	22%
Severe Perceptive Hypoacusia	14%

Overlapping the previous audiometric classifications is the cluster of tinnitus, including hyperacusic, which are 15% of the sample.

Before starting the Neuroptimal training, we performed an ABR (Auditory Brain-stem Response) test on all patients to assess retrocochlearity, to establish whether or not there is an acoustic neuroma as the cause of tinnitus: 4% of the sample presented retrocochlearity and then underwent a brain rnm + pontocerebellar corners + internal auditory ducts with contrast media which excluded neuromas or other compressive pathologies on the auditory nerves.

To produce the analysis of the results, we assigned the corresponding scores to all the answers of the THI, PSWQ and DASS-21. The socio-demographic and audiometric findings were analyzed with a frequency analysis, i.e. evaluations of each question-naire with an analysis of the frequency and the average.

By assigning each response the degree of severity (class), we developed an average profile for each of the self-assessments level of THI, PSWQ and DASS-21.

The average profile was evaluated both for the total sample and for each corresponding class or degree of severity.

On the total sample, for THI, PSWQ and DASS-21, the distances of the average scores between time T3 (after 30 training sessions) and time T0 (before training) were evaluated: for each pair of values the statistical significance was verified with the t-test for dependent samples. The basic hypothesis that there is a significant difference between time T3 and time T0 was verified, showing that NeurOptimal® was effective in reducing the perception of symptoms related to tinnitus.

For 55% of the patients in the sample, tinnitus originates from auditory differentiation, while in the remaining 45% the cause is of the cross-modal type.

In most cases (73%), patients have had tinnitus for less than 2 years Table 4.

Table 4: How long have they had tinnitus.

How long	100% = patients at time T0
From 0 months to 2 years	73%
From 2 years and 1 day to 5 years	11%
From 5 years and 1 day to 10 years	5%
Over 10 years	11%

The greatest incidence is for unilateral tinnitus, of the 'whistle' type and persistent: see Table 5, Table 6 and Table 7.

Table 5: Tinnitus Site at time T0.

Site	100% = patients at time T0
Unilateral Left	42%
Unilateral Right	26%
Bilateral	23%
Bilateral to the Right	3%
Bilateral to the Left	3%
Center of the brain or nuchal	3%

Table 6: Tinnitus Type at time T0.

Site	100% = patients at time T0
Whistle	50%
Buzz	13%
Rustle	7%
Whistle and Buzz or Buzz and Rustle	17%
Dull sound	13%

Table 7: Tinnitus Performance at time T0.

Performance	100% = patients at time T0
Persistent	68%
Intermittent throughout the day	19%
Occasional	13%

Our Tinnitus recruits displayed, on average baseline scores, moderate THI (score = 49.9) (Table 8) and moderate PSWQ (score = 46.8) Table 9.

Table 8: THI on a sample of 209 patients at time T0.

THI class	100% = patients at time T0
Minimum	9%
Mild	20%
Moderate	37%
Severe	20%
Catastrophic	14%

Table 9: PSWQ on a sample of 209 patients at time T0.

PSWQ class	100% = patients at time T0
Very low	0%
Low	24%
Moderate	62%
High	14%

In addition, our Tinnitus recruits displayed, on average baseline scores, mild depression (Score = 5.9) (Table 10), moderate anxiety (Score = 4.7) Table 11 and mild stress (Score = 8.1) Table 12.

Table 10: DASS-21 Depression on sample of 209 patients at time T0.

DASS-21 Depression class	100% = patients at time T0
Normal	47%
Mild	14%
Moderate	19%
Severe	10%
Extremely Severe	10%

Table 11: DASS-21 Anxiety on sample of 209 patients at time T0.

DASS-21 Anxiety class	100% = patients at time T0
Normal	46%
Mild	19%
Moderate	13%
Severe	8%
Extremely Severe	14%

Table 12: DASS-21 Stress on sample of 209 patients at time T0.

DASS-21 Stress class	100% = patients at time T0
Normal	52%
Mild	12%
Moderate	14%
Severe	15%
Extremely Severe	7%

In the preliminary phase, before proceeding with the observational study whose results we are going to describe, we implemented a test-control system to verify the applicability of Neuroptimal on tinnitus.

We selected two samples of 20 patients who were very similar in terms of age, gender, audiometric and tinnitus characteristics; each patient did not know in which group he or she would be included. We gave 10-15 weeks (30 sessions) of standard training to the test group and 10-15 weeks (30 sessions) of control training to the control group.

The control training consisted in positioning the sensors but not activating the assisted software procedure that generates the training, and rather sending the piece of music on the headphones with the false feedback inserted not generated by any brain frequency of the specific patient. In the control group, therefore, each patient listens to music through headphones with the same sequence of interruptions, since the interruptions are false, i.e. they are in no way connected to the electroencephalogram signals read by the software.

For the test and control group we collected data from THI, PSWQ and DASS-21 Questionnaire at time T0 (before start with standard or control training) and time T3 (after 30 standard or control sessions).

The results suggested continuing with the observational study (Table 13).

Table 13: Average score after 30 sessions Variation % vs. T0 - Test Training vs. Control Training.

Score	Test Training Variation % vs. T0	Control Training Variation % vs. T0
Thi	-16%	-11%
PSWQ	-3%	-2%
Depression	-65%	-15%
Anxiety	-68%	-19%
Stress	-32%	-9%

We therefore observed and analyzed only patients who received the standard training of 10-15 weeks (30 sessions).

On a sample of 115 tinnitus patients who completed the training up to time T3 (30 sessions), we used dependent group t-test to evaluate if there are significant differences between Tinnitus Patient Profile (scores) at time T3 and T0 Table 14.

Table 14: Tinnitus Patient Profile (scores) at time T3 and T0 on a sample of 115 tinnitus patients who completed the training up to time T3.

Score	T0 mean	T3 mean	Variation % T3 vs. T0	alpha level	p value
Thi	48.9	38.3	-22%	1%	<0,0001
PSWQ	49	46.1	-6%	-	-
Depression	6.7	4.7	-29%	1%	<0,0004
Anxiety	4.7	3.3	-29%	1%	<0,0010
Stress	8.3	6.5	-22%	1%	0,0004

The means for the Thi score at time T3 (38.3) and at time T0 (48.9) are statistically significantly different from one another, with a significance level (alpha level) equal to 1% (p-value <0.0001). The % variation for the Thi score at time T3 vs. T0 is -22%.

The catastrophic class goes from 15% at time T0 to 7% at time T3 and the Nil class goes from 7% at time T0 to 24% at time T3 Figure 1.

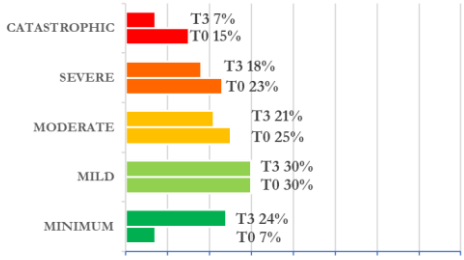

Figure 1: Tinnitus Patient Profile after NeurOptimal® Training: T0 before start of training and T3 after standard 30 sessions – THI Questionnaire class % on sample of 115 tinnitus patients who completed the training up to time T3.

For each THI class declared at time T0, at least 40% of the subjects, at the end of the NeurOptimal® Training, passed to one of the less serious Tinnitus Classes Figure 2.

T0 before start of training	T3 after standard 30 sessions					SWITCH TO LOWER SEVERITY
	MINIMUM	MILD	MODERATE	SEVERE	CATASTROPHIC	
MINIMUM	100%					
MILD	40%	44%	16%	0%	0%	40%
MODERATE	14%	43%	29%	10%	5%	57%
SEVERE	0%	21%	26%	47%	5%	47%
CATASTROPHIC	8%	8%	23%	31%	31%	69%

Figure 2: Tinnitus Patient Profile after NeurOptimal® Training: T0 before start of training and T3 after standard 30 sessions – THI Questionnaire switched to lower severity.

The means for depression score at time T3 (4.7) and at time T0 (6.7) are statistically significantly different from one another, with a significance level (alpha level) equal to 1% (p-value <0.0004). The % variation for the depression score at time T3 vs. T0 is -29%.

The Extremely Severe class went from 12% at time T0 to 2% at time T3, the Mod-erate class from 20% at time T0 to 15% at time T3 and the Normal class from 42% at time T0 to 56% at time T3 Figure 3.

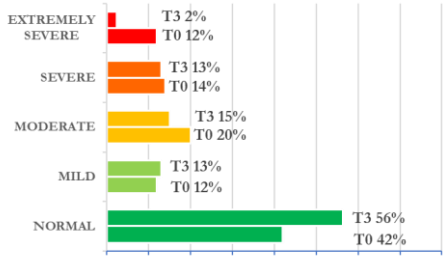

Figure 3: Tinnitus Patient Profile after NeurOptimal® Training: T0 before start of training and T3 after standard 30 sessions – DASS-21 Depression Questionnaire class % on a sample of 115 tinni-tus patients who completed the training up to time T3.

For each DASS-21 class declared at time T0, at least 50% of the subjects, at the end of the NeurOptimal® training, passed to one of the lower severity classes of Depression (Figure 4).

T0 before start of training	T3 after standard 30 sessions					SWITCH TO LOWER SEVERITY
	NORMAL	MILD	MODERATE	SEVERE	EXTREMELY SEVERE	
NORMAL	80%	9%	11%	0%	0%	
MILD	50%	10%	20%	20%	0%	50%
MODERATE	41%	29%	24%	6%	0%	70%
SEVERE	25%	8%	25%	33%	8%	58%
EXTREMELY SEVERE	40%	10%	0%	40%	10%	90%

Figure 4: Tinnitus Patient Profile after NeurOptimal® Training: T0 before start of training and T3 after standard 30 sessions – Dass-21 Depression Questionnaire switched to lower severity.

The means for the Anxiety score at time T3 (3,3) and at time T0 (4,7) are statistically significantly different from one another, with significance level (alpha level) equal to 1% (p-value 0,0010). % variation for Anxiety score at time T3 vs. T0 is -29%.

The Extremely Severe went goes from 12% at time T0 to 6% at time T3, the Mild class from 21% at time T0 to 12% at time T3 and the Normal class from 45% at time T0 to 62% at time T3 (Figure 5).

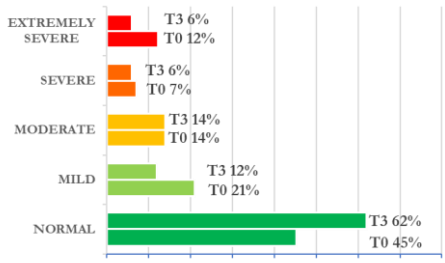

Figure 5: Tinnitus Patient Profile after NeurOptimal® Training: T0 before start of training and T3 after standard 30 sessions – DASS-21 Anxiety Questionnaire class % on a sample of 115 tinnitus patients who completed the training up to time T3.

For each DASS-21 class declared at time T0, at least 61% of the subjects, at the end of the NeurOptimal® Training, passed to one of the lower Anxiety severity class (Figure 6).

T0 before start of training	T3 after standard 30 sessions					SWITCH TO LOWER SEVERITY
	NORMAL	MILD	MODERATE	SEVERE	EXTREMELY SEVERE	
NORMAL	76%	16%	8%	0%	0%	
MILD	61%	6%	11%	17%	6%	61%
MODERATE	50%	17%	33%	0%	0%	67%
SEVERE	33%	17%	17%	17%	17%	67%
EXTREMELY SEVERE	40%	0%	20%	10%	30%	70%

Figure 6: Tinnitus Patient Profile after NeurOptimal® Training: T0 before start of training and T3 after standard 30 sessions – Dass-21 Anxiety Questionnaire switched to lower severity.

The means for the Stress score at time T3 (6.5) and at time T0 (8.3) are statistically significantly different from one another, with a significance level (alpha level) equal to 1% (p-value is = 0,0004). % variation for Anxiety score at time T3 vs. T0 is -22%.

The Extremely Severe class went from 6% at time T0 to 1% at time T3, the Severe class from 17% at time T0 to 11% at time T3 and the Normal class from 54% at time T0 to 65% at time T3 (Figure 7).

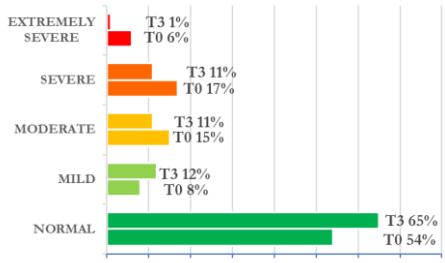

Figure 7: Tinnitus Patient Profile after NeurOptimal® Training: T0 before start of training and T3 after standard 30 sessions – DASS-21 Stress Questionnaire class % on a sample of 115 tinnitus pa-tients who completed the training up to time T3.

For each DASS-21 class declared at time T0, at least 57% of the subjects, at the end of the NeurOptimal® Training, passed to one of the less severe Stress classes (Figure 8).

T0 before start of training	T3 after standard 30 sessions					SWITCH TO LOWER SEVERITY
	NORMAL	MILD	MODERATE	SEVERE	EXTREMELY SEVERE	
NORMAL	84%	11%	4%	0%	0%	
MILD	57%	14%	14%	14%	0%	57%
MODERATE	54%	8%	23%	8%	8%	62%
SEVERE	29%	14%	14%	43%	0%	57%
EXTREMELY SEVERE	40%	20%	20%	20%	0%	100%

Figure 8: Tinnitus Patient Profile after NeurOptimal® Training: T0 before start of training and T3 after standard 30 sessions – Dass-21 Stress Questionnaire switched to lower severity.

The means for the PSWQ score at time T3 (46.1) and at time T0 (49.0) remained unchanged. Variation % for PSWQ score at time T3 vs. T0 is -6%.

The High class went from 16% at time T0 to 11% at time T3 and Low class from 17% at time T0 to 25% at time T3 (Figure 9).

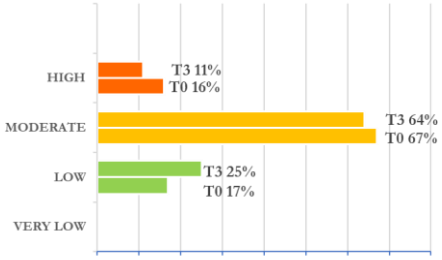

Figure 9: Tinnitus Patient Profile after NeurOptimal® Training: T0 before start of training and T3 after standard 30 sessions – PSWQ class % on sample of 115 tinnitus patients who completed the training up to time T3.

We introduced the measurement of the V/I ratio of the ABR test to evaluate whether there was centrality or cochlearity in the genesis of tinnitus (i.e. central or pe-ripheral).

The ABR test evaluates the auditory function of the brainstem in response to au-ditory stimuli. The ABR is composed of various waves, among which waves I, III and V are the most relevant and have clinical significance: they are generated respectively in the distal portion of the cochlear nerve, in the cochlear nucleus and in the inferior col-liculus.

It is generally accepted that in cases of normal wave I (in the absence of cochlear synaptopathy) elevated wave V amplitude could be related to hyperactivity responses in the central regions.

We know that in some cases tinnitus patients have altered V/I wave amplitude ra-tios (measured with the ABR test), which is a signal of compensatory hyperactivity or intrinsic central hyperactivity. We intended to verify if the efficacy of NeurOptimal® is higher in patients with tinnitus and altered V/I ratio than in patients with tinnitus and V/I ratio in normality.

Of our sample of tinnitus patients, 30% of normal hearing had an altered V/I ratio. From the first data (a small sample at the moment) it emerges that the Non-Linear Dynamic Neurofeedback NeurOptimal™ has a greater beneficial impact in subjects with normal hearing tinnitus with inversion of the V/I ratio, compared to tinnitus patients with a normal V/I ratio. This only confirms the hypothesis that the neuromodu-latory action of the Non-Linear Dynamic Neurofeedback NeurOptimal™ acts in neu-ral networks centrally rather than peripherally (Table 15).

Table 15: Average score % variation T3 vs. T0 – Normal hearing with altered ratio V/I vs. Nor-mal hearing with Normal V/I ratio.

Score	Altered V/I ratio (n=25)	Normal V/I ratio (n=56)
Thi	-43%	-24%
PSWQ	-14%	-12%
Depression	-41%	-31%
Anxiety	-31%	-28%
Stress	-36%	-15%

DISCUSSION

The study was conducted with approvation by the Ethics Committee Palermo 1 of Azienda Ospedaliera Universitaria Policlinico Paolo Giaccone of Palermo (Italy).

Subjective Tinnitus is defined as the perception of a sound in the absence of any external vibratory stimulation. Now everyone accepts the fact that this symptom de-rives mainly from activity within the CNS. Tinnitus originates from a peripheral hearing impairment but also involves the CNS. This "phantom sound" is mostly described as "ringing in the ears." P.J. Jastreboff describes it as "perception of a sound in the absence of external sound stimulation." [14,15]. Others state that tinnitus is an "unorganized acoustic perception, not actually produced by any sound source, either inside or outside our body." These descriptions of tinnitus do not appear exhaustive, at least because they do not distinguish between tinnitus and psychiatric hallucinations. The latter can also be classified as "Sound in the absence of stimulation" and, as we will see later, the distinctive character cannot be represented by the organization of the perception. A person with tinnitus can also report quite complex perceptions, including musical ones [16], and therefore well-structured ones, without being a psychiatric patient [17-19].

We need a more exhaustive definition of tinnitus for correctly identifying the clinical picture, to avoid the confusion that is also reflected in both epidemiological and therapeutic statistical studies and finally to indicate new therapeutic paths.

A. Messina [20,21] et Al. give the following definition of tinnitus: "It is a sound not justified by any internal or external vibration, which is perceived for at least 5 minutes more than once a week. Tinnitus is an auditory dysperception that can be classified in the field of positive auditory hallucinosis which, as such, recognizes a pathogenesis in the phenomena of dysneuro-plasticity resulting 'almost always' from an organic cochlear peripheral lesion. Being a form of hallucinosis, tinnitus can take on a coherent structure but does not determine delusional attitudes and behaviors. Tinni-tus is clinically evident only if there is an altered evaluation of its signal by the fron-to-limbus striatal system."

During a NeurOptimal® Session, the trainer applies sensors to the ears and crani-al case to analyze the electrical activity of the patient's brain, over a whole frequency range from 0 to 64 Hz. Receptor sensors are connected to an amplifier which trans-forms the signal so that it is readable by the computer. The training lasts about 33 minutes, during which the patient listens to music with headphones. The patient is re-laxed, and no mental effort or intense concentration is required. The software receives the EEG in real time and searches for signals of shift, change or inconsistency in the brain in terms of duration, intensity, frequency, or a shift in the electrical signal. which usually corresponds to a marked and sudden variation in amplitude. As these changes or inconsistencies are registered, the music stops for a fraction of a second and this is the feedback. The interruption of the music disregards the coherence expectations of the brain regarding the music it is listening to at the exact moment in which the brain behaves inconsistently with respect to the way it was behaving a moment before. It is a mirroring effect that allows the brain to mirror itself and become aware of the changes taking place at that moment.

The interrupted brain activity goes in search of the cause of this interruption. The activity is then suspended, and the brain can appropriate the feedback by immediately self-regulating so as to stabilize itself again in its comfort zone. Session after session, these hundreds and then thousands of micro-reorganizations promote better functioning of the patient's nervous system. Each session is unique and unrepeatable, be-cause the system adapts to each brain and its particular state at that moment.

After NeurOptimal® Training 54% of sample declares a nil or mild tinnitus hand-icap (it was 37% before); 74% declares a normal or mild level of depression (it was 55% before), 77% declares a normal or mild level of anxiety (it was 58% before) and the subjects who declare a normal or mild level of stress is 78% (it was 51% before).

On a small number of patients, we measured level of THI, PSWQ and DASS-21, 6 months, 12 months and 24 months after time T3 (end of 30 sessions).

These follow-ups highlight the long-lasting efficacy of NeurOptimal® Training on tinnitus-related symptoms Table 16.

Table 16: Tinnitus Patient Profile (scores) at follow-up times (6 months, 12 months and 24 months after T3) – variation % vs. T0.

Score	T3 n=115	6 months after T3 n=6	12 months after T3 n=10	24 months after T3 n=14
Thi	-22%	-21%	-19%	-18%
PSWQ	-6%	-6%	-5%	-5%
Depression	-29%	-28%	-25%	-24%
Anxiety	-29%	-27%	-25%	-25%
Stress	-22%	-22%	-19%	-18%

CONCLUSION

NeurOptimal® Training improves both perception of handicap and levels of depression, anxiety and stress.

NeurOptimal® Training, like any other valid treatment for tinnitus, does not eliminate tinnitus, but it has the ability to reduce the perception and attention to it, aspects that represent the crux of the treatment of this disorder. In some cases, at the end of the treatment, perception is reduced to such an extent that the problem almost disappears in the subject, together with an improvement in the psychophysical state.

The results highlighted so far are promising and seem to confirm the peculiar characteristic of this technique, namely that it is based on the key principles of brain activity: self-regulation, neuroplasticity and learning. According to these preliminary results, the result of this pilot study, NeurOptimal® represents a valid aid for tinnitus patients.

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