Chronic social stress is one of the most important factors responsible in the triggering and/or worsening of anxiety and depressive disorders in humans\textsuperscript{1-3}. In recent years, the impact of social stress on the development of psychopathologies has been thoroughly investigated in preclinical animal studies\textsuperscript{4,5}. It has been hypothesized that life stress alters the dynamic regulation of the autonomic, neuroendocrine, and immune systems\textsuperscript{6,7}.

The central nervous system (CNS) is constantly and unconsciously adapting to accommodate changes...
in the environment. Unfortunately this unconscious process hides from our perception the adaptations that are detrimental to our health and to our quality of life. Allostasis is the ability to maintain the dynamic stability of the physiological systems facing a constantly changing environment (environmental stress or allostatic load). The allostatic load\textsuperscript{8-10} is constituted by the combined environmental pressures that, when they can no longer be managed through the best physiological response, determine the allostatic state that is the comprehensive result of an altered physiological response (adaptive dysfunction) to the allostatic load. The allostatic state is unable to guarantee the good management of the physiological systems and therefore the health status and the well-being of the individual. The therapy to optimize the response to the allostatic load and the allostatic state is now available with the Neuro-Psycho-Physical-Optimization (NPPO) with a medical apparatus named the Radio Electric Asymmetric Conveyer (REAC)\textsuperscript{11,12}.

The REAC-CRM emits a radio frequency (RF) in the field of very low power microwaves. The REAC-CRM, due to the nature of its construction, can concentrate the signal emitted in the environment on specific points of the body of the patient to be treated. The interaction between the field of microwaves emitted by the instrument and the body of the patient is different to that produced by exogenous cerebral stimulation with transcranial magnetic stimulation\textsuperscript{13,14} and with vagal nerve stimulation which was recently approved by the Food and Drug Administration for treatment-resistant major depression\textsuperscript{15,16}. Indeed, REAC-CRM produces an autogenous signal which, when suitably transported and concentrated in specific points of the auricular pavilion, can produce biological responses. These biological responses have been the subject of repeated clinical observations over the years, always showing a general improvement in the physical-psychological characteristics of the subjects treated with NPPO\textsuperscript{17-21}.

In conditions of acuteness of stress, at a level of the CNS, the secretion of adrenaline and cortisol hormones stimulates memory and attention, to let the organism deal with the environmental stressors. In the case of chronic stress there is progressive damage to some structures of the nervous system and in particular there is an atrophy of the apical dendrite of the neurons of the hippocampus, of the amygdale and damages to the dendrite of the neurons of the prefrontal cortex. The most serious and frequently observed symptoms were those of the clusters for mood depression and anxiety. Anatomic pathological damage to the cerebral cortex has also been shown in mood disturbances with a reduction of the glial tissue of the prefrontal cortex\textsuperscript{22}.

The purpose of the present study was to verify whether the use of REAC-CRM was effective in reducing subjective perceptions of stress measured by a validated questionnaire, the PSM test\textsuperscript{23-25} that allows the precise classification of the subject studied in a stress well-being scale to accurately assess the effectiveness of the treatment. In particular the influence on the symptoms of anxiety and depression, according to the definition of mixed anxiety and depressive disorder given by Diagnostic and Statistical Manual of mental disorders (DSM-IV-TR)\textsuperscript{26} and correlated to stress conditions, were considered.

**Material & Methods**

*Patient selection:* Between January 1999 and December 2007, a total of 888 selected subjects, who attended at Rinaldi-Fontani Institute showing different types of stress-related symptoms (such as tension headaches, high blood pressure, migraine headaches, anxious tremors, colitis, irritable bowel syndrome, bruxism, neck and back pain, chronic pain syndrome, bronchial asthma, peptic ulcer disease, skin disorders, insomnia) gave their consent and were included in the study. No patients were taking psychotropic medication.

The subjects (randomly selected for each group) were divided into 2 groups, Group A patients were given active treatment and patients in Group B were given placebo treatment. Group A comprised 688 subjects (476 females, average age 42.3 ± 13.7 yr, and 212 males, average age 42.9 ± 15.4 yr) treated with a cycle of NPPO of “active” REAC-CRM, and Group B comprised 200 subjects (control group) (136 females, average age 42.5 ± 16 yr, and 64 males, average age 43.8 ± 16.7 yr), treated with a cycle of NPPO of “placebo” REAC-CRM.

The clinical trial reported here was registered in the Primary Register of the Australian New Zealand Clinical Trial Registry (ANZCTR) (No. ACTRN12607000429459) and reported in the International Clinical Trials Registry Platform Search Portal - WHO.

*Psychological test and psychiatric assessment:* The Psychological Stress Measure (PSM)\textsuperscript{23-25} was specifically developed to detect the stress levels in non-clinical population. The PSM is usually a 49-item self-
The REAC-CRM is an instrument (2.4 or 5.8 or 10.5 GHz, measurable electromagnetic field of the human body (~30-300 MHz) and that produced by the instrument (2.4 or 5.8 or 10.5 GHz, measurable from the emitter about 0.1 mW/m2) which lasts approximately a few milliseconds. This emission is dispersed into the environment and it is then received by a probe (conveyor) placed on the body of the patient. During the receiving process this probe (conveyor) allows an interaction between the emitted electromagnetic field and that of the treated patient. The target of the process is to allow the CNS to self-perceive the dysfunctional adjustments occurred, without the conditioning of the dysfunctional cognitive filters that maintain the neuro-psycho physical-pathological alterations (dysfunctional adjustments). This allows optimization of the allostatic responses, progressively reducing the various dysfunctions.

The instrument that we used is registered under the trademark of CRM (ASMED, Florence, Italy). The result is an activation of the central nervous system that can optimize neuropsycomotorial function and reduce the adaptive dysfunctional modification of the nervous system induced by stress. The NPPO auricular therapy protocol was used to manage and optimize these modifications. The REAC-CRM probe was applied to seven specific points of the auricular pavilion, the same points that are also used in auricular therapy to treat neurovegetative symptoms and diseases (Syenmen, kidney, stomach, heart, occiput, ipotalamus, prefrontal cortex). Only 18 sessions of NPPO with the REAC-CRM active (group A) and inactive (group B) were administered to each patient on alternate days, during a 4 wk therapy cycle after the first PSM test. The aim of REAC-CRM therapy was to optimize the responses of the CNS and of the whole organism against unknown alterations due to stress from continuous interaction with the environment.

Each therapeutic session lasted for approximately three seconds. The protocol was painful, non invasive, did not require the collaboration of the patient and was completely without side effects.

After 18 sessions of NPPO with the active REAC-CRM (group A) and the inactive REAC-CRM (group B), the PSM test was repeated (t1).

Statistical analysis: Statistical analysis of Total points and Point T scored at t0 and t1 was performed using the Wilcoxon Signed Ranks test and P<0.05 was considered significant. The number of patients showing anxiety/depression before and after therapy in both groups was
compared using the McNemar test of Symmetry for statistical significance. The mean percentage change of Total points and T points before and after therapy between Groups A and B was calculated and compared by the Wilcoxon-Mann Whitney Rank Sum Test.

**Results**

The mean of Total Points and T Points obtained by the PSM test before and after “active” and “placebo” REAC-CRM therapy in both groups of patients are shown in the Table.

In Group A, before the treatment 312 patients (45%) reported stress related symptoms of anxiety/depression, whereas only 84 (12%) reported the persistence of these clinical targets after a cycle of “active” REAC-CRM therapy. In particular, the mean of Total Points and T Points decreased from 107.9 to 87.3 and from 57.1 to 48.2, respectively and was statistically significant (Wilcoxon Signed Rank Test $P<0.001$ for Total Points).

In Group B, before the treatment 76 patients (38%) reported stress related symptoms of anxiety/depression, and after the cycle of “placebo” REAC-CRM therapy 72 patients (36%) reported the presence of these clinical targets. The difference was not significant.

In Group A, the PSM scores (Total Points and T Points) after the cycle of REAC-CRM treatment were lower and less variable (Fig. 1). In contrast, the distribution of scores for the “placebo” group (Group B) was similar in both the first and second tests (Fig. 2).

The McNemar test was used to analyze the difference in number of patients showing anxiety/depression before and after therapy. Only 8 patients of Group B, who reported stress related symptoms of anxiety/depression before the cycle of “placebo” REAC-CRM therapy, did not show the same symptoms after the cycle of placebo. On the contrary, 240 patients belonging to Group A found relief from anxiety/depression as they did not report these symptoms after the cycle of REAC-CRM therapy ($P<0.001$).

The mean percentage change of Total Points and Points T between Group A and B was also analysed. The difference between the two groups was significant ($P<0.001$) for both Total points and Point T, confirming the positive effect of the REAC-CRM therapy on anxiety/depression.

**Table.** Total points and T points obtained in group A and in group B by the PSM test before (t0) and after (t1) therapy/placebo

<table>
<thead>
<tr>
<th>Patients</th>
<th>Total points PSM test</th>
<th>T points PSM test</th>
<th>Anxiety/depression No. of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>107.9 ± 23.13</td>
<td>57.06 ± 9.70</td>
<td>312 (45)</td>
</tr>
<tr>
<td>(n=688)</td>
<td>(t0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group A</td>
<td>87.3 ± 16.21</td>
<td>48.25 ± 6.90</td>
<td>84* (12)</td>
</tr>
<tr>
<td>(t1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group B</td>
<td>107.86 ± 25.80</td>
<td>57.05 ± 10.62</td>
<td>76 (38)</td>
</tr>
<tr>
<td>(n=200)</td>
<td>(t0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group B</td>
<td>106.32 ± 25.88</td>
<td>56.09 ± 11.02</td>
<td>72 (36)</td>
</tr>
<tr>
<td>(t1)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Values are mean ± SD
* $P<0.05$ compare to before therapy

![Fig. 1. Distribution of the PSM scores in treated patients (Group A, n°688). Scores obtained in the first test were significantly different ($P<0.05$) to those of the second test performed after the therapy. The scores after therapy were lower.](image1)

![Fig. 2. Distribution of the PSM scores in untreated patients (Group B, n°200). The distribution of scores was similar in both the first and second tests.](image2)
Discussion

The use of electricity and magnetic fields in biomedical studies, and particularly in the treatment of disturbances of the nervous system, is not a new idea. The weak environmental emission of a radiofrequency field and its dispersion due to the interaction with the body was able to induce weak currents in the human body that activated the nervous system. Preliminary studies have suggested a reduction in general stress levels and especially in correlated stress disorders when REAC-CRM therapy is applied.

This study was aimed at assessing the significant possible improvement of stress conditions in examined patients treated with REAC-CRM therapy, in particular on behavioural anxiety/depression. After a cycle of REAC-CRM therapy, a significant reduction in the scores measuring subjective perceptions of stress in the studied patients was observed. In particular, a significant reduction of symptoms was reported by the group showing signs of behavioural anxiety-depression. On the other hand, in the untreated control group, no significant difference was found. Also, the cluster measuring behavioural anxiety/depression remained unchanged.

Growing literature indicates that the symptoms of stress-related anxiety and depression are the results of allostatic processes on specific cerebral areas and our data also showed that REAC-CRM was an effective instrument to optimize the responses of the CNS. Recently Collodel et al. suggested that NPPO therapy with REAC-CRM treatment may realize a general improvement in spermatogenetic condition, as demonstrated with sophisticated tools such as TEM and FISH, in males with idiopathic infertility.

The results of this study showed that NPPO therapy with REAC-CRM could reduce subjective perceptions of stress measured with the PSM psychometric test and in particular the symptoms of stress-related anxiety and depression. Hendriks et al. reported that cognitive behavioural therapy is efficacious for the treatment of late-life anxiety disorders.

This new therapy has the advantage of being painless, non-invasive and totally free of side-effects. Moreover, REAC-CRM therapy is not pharmacological and can represent an efficient support in many medical fields, as it does not interfere with the simultaneous use of other therapeutic approaches. This research highlights the efficacy of NPPO with REAC-CRM therapy on anxious-depressive scale only in non-psychiatric subjects; these conditions represent the most comprehensive mental suffering in the general population.

The main limitation of this research was that the efficacy of NPPO with REAC-CRM therapy was demonstrated on subjects who although identified as psychometric anxious-depressive, did not need any clinical intervention. In current psychiatric terminology, the observed affective phenomenology is classified as “below threshold” (presence of certain symptoms of anxiety or depression, which are however insufficient to set up a “primary diagnostic entity”) or “sub-clinical” (complete clinical picture, but without serious symptoms). Moreover, the patients who have responded positively to REAC-CRM therapy, showed clearly stress-related symptoms and therefore “reactive” psychic symptoms. They did not show any “endogenetic” features such as “melancholic” forms of depression, for which, the best choice in terms of speed of response and global therapeutic efficacy was a psychopharmacological treatment.

Further studies are needed to verify the stability over time when using more than one cycle, although it could be very difficult to obtain and maintain a selected group, especially after therapy.

In conclusion, our results showed that REAC-CRM therapy will help to speed up the physiological capability of recovery of the person, optimising the adaptive response to environmental stressors and contributing to the elimination of dysfunctional adaptive responses.

Acknowledgment

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