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Galvanic Skin Response—Extinction Biofeedback Training for Psychogenic Abdominal Pain: A Validation Protocol

Maddalena Castelletti¹, Enrico Berné¹, Erasmo Dionigio Carlo Castagnoli², Alberto Montagna³, Giorgio Tonon³

¹Magenta Medical Center, Milan, Italy
²Castagnoli Medical Center, Garlasco, Italy
³GEA Soluzioni, Turin, Italy
Email: info@magentamedicalcenter.com

Abstract

Abdominal and pelvic pain of psychogenic origin is a widespread, disabling, difficult to identify, and often inadequately treated medical condition. This condition is often associated with poor quality of life due to high pain interference with daily activities. Cognitive behavioral psychological therapy and neuromodulation with biofeedback are validated therapies for the treatment of this condition. Aim of the present research work is the validation of a therapeutic protocol that involves the use of both techniques in combination. 20 patients diagnosed with psychogenic abdominal pain, of both sexes, aged between 18 and 60 years who had not benefited from pharmacological therapies were enrolled. 10 patients were randomly assigned to the control group (psychological treatment only), another 10 patients were assigned to the study group (neuromodulation with biofeedback-Galvanic skin response-extinction in combination with psychological therapy). For both groups, the pain score, interference of pain with daily living activities, pain relief, and the share of anxiety associated with the pain condition were evaluated (pre- and post-treatment). The patients who underwent the combined treatment achieved statistically significant better scores than patients in the control group, respectively -4.9 ± 0.9 vs -1.0 ± 0.4 for Pain; -5.1 ± 1.1 vs -0.9 ± 0.3 for Interference with life; -7.2 ± 3.7 vs -2.2 ± 2.1 for HAMA; 4.6 ± 1.2 vs 1.1 ± 0.6 for Relief.

Keywords

Chronic Abdominal and Pelvic Psychogenic Pain (PAP), Biofeedback Training, Pain Management, Galvanic Skin Response (GSR)

1. Introduction

Pain is clinically defined as an unpleasant sensory and emotional experience associated with actual or hypothetical tissue damage [1]. Abdominal pain, even in its pelvic extension, is a critical topic for emergency medicine and specialist clinics. Abdominal pain can be categorized as: intra-abdominal pain, abdominal wall pain and referred pain and can involve the entire abdomen, epigastrium, right and left subcostal areas, right and left hips, periumbilical area, and pelvic area [2].

The etiology of abdominal pain is varied, in fact pain can originate from intra-abdominal organs (parenchymal organs, gastro-intestinal tract, urogenital organs, and vascular system), it can originate from structures of the abdominal wall (skin, subcutaneous tissues and musculoskeletal system), it can finally originate from intrathoracic organs, metabolic or endocrine disorders and psychic disorders [3]. Abdominal pain of psychogenic origin (PAP) is inextricably linked to the origin of the pain and is described as severe, persistent, and experienced consistently for a period of at least 6 months without evidence of organic alterations on clinical or laboratory evaluation and diagnostic imaging [2] [4].

Psychogenic pain falls under the definition of somatic symptom disorder (SSD) introduced in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) [5] in 2013; main characteristics of this disorder is the manifestation of pain symptoms for which no biological causes are found. Failure to recognize this condition can lead doctors or surgeons to perform unnecessary diagnostic or therapeutic procedures with a high risk of iatrogenic complications. It should also be considered that recent neuroimaging studies have shown neurophysiological and neuropsychological alterations in patients with PAP [6] [7]. Such abnormalities would result in a pathogenetic neural mechanism related to central and peripheral sensitization process [8]; in particular, images obtained by functional Magnetic Resonance Imaging (fMRI) of subjects with PAP displayed increased levels of combined glutamine-glutamate (Glx) within the anterior insula and greater anterior insula connectivity to the medial prefrontal cortex (mPFC). Increased connectivity between these regions was positively correlated with anterior insula Glx concentrations and with psychopathological outcomes [4]. This evidence supports a multifactorial clinical approach for the treatment of PAP and any other form of SSD. The validated treatments for SSD are: psychological therapy of cognitive behavioral approach, biofeedback and pharmacological treatments with selective serotonin reuptake inhibitors (SSRIs)/tricyclic antidepressants [9] [10].

The evaluation and correct diagnosis of abdominal pain of psychogenic origin (PAP) can be complex for clinicians even when there are no positive organic findings. An appropriate diagnosis is the only way to an effective treatment by improving the quality of life of patients, avoiding unnecessary medical treatments and hospitalizations, while also reducing costs for the health system [11].

2. Materials and Methods

For the present study, 20 patients of both sexes aged 18 - 60 years were enrolled who turned to Magenta Medical Center and Castagnoli Medical Center because of chronic abdominal pain that lasted for more than 6 months with partial benefit from pharmacological therapies prescribed by physicians of the territorial primary care services.

After the compilation of the informed consent and the collection of the anamnestic interview, a first level clinical examination with Carnett test [12] was performed by physicians and surgeons, followed by laboratory diagnostic investigations (biochemical, hematological) and, where necessary, by diagnostic imaging (abdominal and pelvic ultrasound) [13].

Once the diagnosis of PAP was made, all patients underwent pre-treatment clinical assessments (T0) *i.e.* psychometric assessment for anxiety disorder through Hamilton anxiety rating scale (HAMA) [14], multidimensional assessment of pain with Brief Pain Inventory short version (BPI) [15], monitoring of baseline values of galvanic skin response extinction capacity (GSR-extinction)

Galvanic skin response (GSR) reflects the electrical properties of the patient skin, which is mainly associated to the activity of eccrine sweat glands and is usually derived by the conductance value using strap electrodes composed of conductive carbon rubber placed on index and middle finger of left (or right) hand [16].

A low current is applied between these two electrodes and an electric circuit can measure the resistance of the skin by Ohm's Law ($R = V/I$ where V is a tension, I is a low current and R is the skin resistance). The inverse of resistance is the conductance measured in μS (microSiemens), which is the parameter mainly used for clinical and research applications. The variation of skin conductance is a result of the amount of Na^+ and Cl^- ions on the area where electrodes are placed.

The conductance of the skin increases when the intensity of the patient's emotional arousal increases, which happens when an alert situation triggered by the Autonomic Nervous System (ANS) increases the body and mind activity [16].

GSR parameter can be decomposed in two kinds of components: Tonic and Phasic [16], the first one is a signal with very slow and gradual changes, also known as skin conductance level (SCL), the Tonic component is useful to understand the baseline emotion level of each patient and his stress level, it increases when patient is under stress and decreases during relax. Arousal level variations are slow and Tonic component can be assessable after a variable time, from tens of seconds to few minutes.

The Phasic component is a faster response with fast fluctuations, more suitable for the emotional state of the patient after stimulus, also known as skin conductance response (SCR). It can be triggered by external or internal stimuli, the ER-SCR is a response based on images, sound, videos or other external provocative stimulus, NS-SCR is a response based on emotions, thoughts, memories and other internal positive or negative feels.

Participants were randomly assigned to two homogeneous groups conditions called respectively *control group*: 10 subjects (4 females and 6 males); *study group*: 10 subjects (5 females and 5 males). The study was double-blind: different clinicians performed the treatments and pre-post assessments.

The *control group* underwent clinical treatment with psychological sessions with a cognitive behavioral approach once a week for 10 weeks; the *study group* performed clinical treatment with psychological sessions with a cognitive behavioral approach once a week for 10 weeks and at the same time ten sessions of GSR-extinction biofeedback training once a week for 10 weeks were performed.

At the end of treatment (T1) patients were re-evaluated with HAMA, BPI and GSR-extinction capacity.

2.1. Hamilton Anxiety Rating Scale (HAMA)

Evaluation of clinical anxiety referred to a population of adults and adolescents. A correlation between SSD and anxiety disorders is known in the literature [17] [9]. The scale is made up of 14 points, each of which is defined by a series of symptoms, measures of both psychological anxiety (mental agitation and psychological stress) and somatic anxiety (physical disorders related to anxiety). The score is obtained by evaluating the sum of the items. Each item is scored on a scale from 0 (not present) to 4 (severe). Score >17 is considered to be of clinical relevance [14].

2.2. Brief Pain Inventory (PBI)

Multidimensional pain scales allow for a better structured assessment of pain that is not limited to measuring pain intensity and localization but also assesses the impact of pain on quality of life, psychological well-being and social activities; the BPI is a questionnaire that measures pain severity and interference with the patient's daily living activities. The localization of pain, drugs intake and pain relief are also evaluated. This test can be self-reported or investigated with a structured interview. The PBI short form is validated for clinical trials in the Italian population [15].

2.3. Cognitive Behavioral Therapy (CBT)

The efficacy of psychosocial interventions in the treatment of chronic pain of both organic and psychogenic origin is known in the literature [18]. It is crucial to consider that psychological distress is one of the main mediators between chronic pain and disability. Psychological treatment is an important part of multidisciplinary care and a potential alternative to medication depending on the severity and nature of pain [19] [20] [21] [22]. With regard to chronic pain, the Italian Consensus Conference of Pain in Rehabilitation assigns primary recommendation of CBT psychological intervention compared to all other approaches, especially recommended in combination with neuromodulation treatments for pain management [18].

2.4. GSR-Extinction Biofeedback Training

The training procedure is performed using two displays, one monitor dedicated to the patient and another one to the clinical operator.

The patient display shows video/audio stimulation effect and the signal trace of the patient's GSR value. This scenario is able to make the patient aware of his emotional response and manage his/her stress state, limiting the increasing of GSR signal.

The clinical display shows to the operator the GSR signal and its trend, expressed as a percentage, with a specific mark during stimulus event [16]. The software associated with the medical device performs a real-time measurement of the self-regulation capacity of the GSR signal—both absolute values and percentage values—that allow the pre- and post-treatment results to be mathematically compared.

Patient is comfortably seated on a chair inclined to help relaxation of the abdomen and legs, the monitor is placed on a small table in front of the eyes reducing any kind of eyes movement.

A complete patient procedure is structured by 10 sessions once a week and each session takes 18 minutes. The single session is composed by 4 stages, the first 2 minutes are dedicated to an initial background stage in which the device acquires the baseline value of GSR, the second stage shown neutral images and sound to the patient in order to facilitate the spontaneous relaxation with breathing exercise, muscles relaxation and trying to avoid thinking about the pain, the third and fourth stage are specific training to teach the patient how to manage his emotional state during activation of acoustic stimuli (thunder, shattered glass, cars in sudden braking), a red band appears 5 seconds before the delivering stimulus, it helps the patient to make him aware about being in close proximity of a stressor event and manage to reduce the alert state.

During each training stage, the threshold, calculated during baseline, determines the quality of sound and video element. If the GSR value goes over the threshold, a noise is added to the sound and the brightness of the images is reduced.

3. Results

The violin plots presented in Figure 1 show the comparison between pre- and post-treatment scores for both groups. The considered scores are hereby explained in detail:

1) BPI Interference with Life score: This score is obtained by computing the average of the scores provided for each of the last 7 items of the BPI questionnaire, which specifically focus on the interference the pain has on the daily activities of the patient, on a scale 0 - 10.

2) BPI Pain score: This score is obtained by computing the average of the 4 scores regarding the intensity of the pain felt, specifically the mean intensity, the pain felt at the moment of the questionnaire, the maximum and minimum intensities in the 24 hours prior to the questionnaire, on a scale 0 - 10.

3) BPI Relief from Pain score: This score specifies the level of relief obtained from the medication therapy, on a scale 0 - 10.
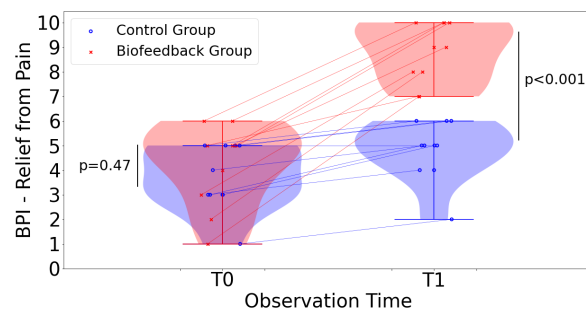
4) HAMA score: This score, as explained in section 2.2, is a measure for psychometric assessment for anxiety disorder, on a scale 0 - 56.
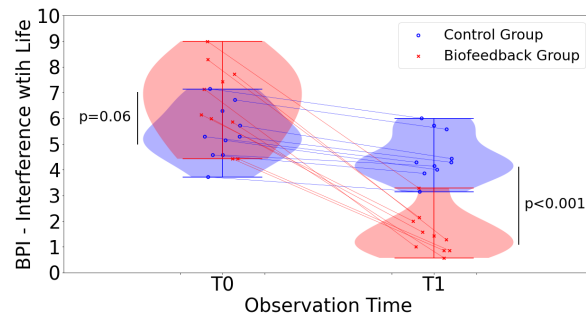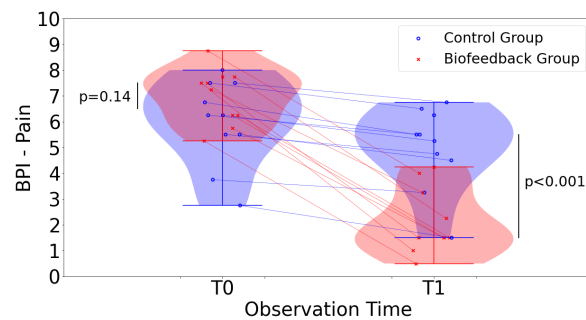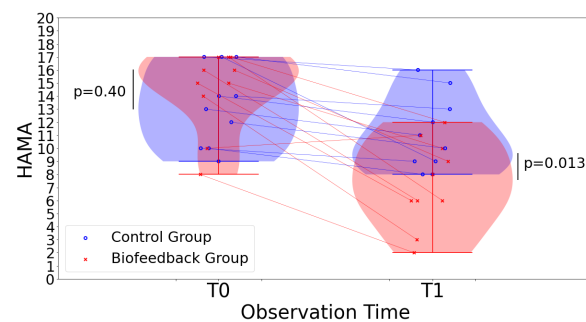

Figure 1. Violin plots showing the distribution of the scores of both groups. Interference with Life score (a), Pain score (b), Relief from Pain score (c) and HAMA score (d).

3.1. Scores Comparison between Pre- and Post-Treatment

Violin plots are used to observe the distribution of numeric data, and are especially useful to make a comparison of distributions between multiple groups. The peaks, valleys, and tails of each group's density curve can be compared to see where groups are similar or different. The violin plots were chosen as the best way to represent the data due to their ability to highlight the distribution of the two populations both pre- and post-treatment. By comparing the distributions of each group at T0, for each of the scores considered, the Biofeedback group shows an overall worse situation compared to the Control group, due to the higher scores of Pain, Interference with Life and HAMA. For each score, a paired t-test between the two distributions at T0 was therefore performed, in order to assess if an initial statistically relevant difference was present, which could affect the final results. However, the differences between each pair of distributions were not statistically relevant, thus implying that the two distributions come from the same population.

On the other hand, for each considered score at T1, the results show a statistically significant improvement for the patients who underwent a Biofeedback treatment, who recorded lower values of Pain, Interference with Life and HAMA, while increasing the Relief from Pain score, thus implying that the Biofeedback treatment improves the overall situation of the patient more than the standard treatment used for the Control group.

In Table 1, these results are summed up, showing for each score the difference between the pre- and post-treatment on average for each group of patients.

3.2. GSR Variation

Since the Biofeedback training was based on the Galvanic Skin Response, great attention was given to the analysis of this parameter.

Figure 2 shows the patient specific GSR, expressed as the percentage variation with respect to the baseline, pre- and post-Biofeedback treatment. For each subject, the minimum and maximum variations during the training phase were extracted.

The GSR of the control group was acquired at T0 but, due to a 60% dropout rate, the data could not be retrieved at T1 and a post-treatment comparison between the two groups was therefore not applicable. The number of subjects and the high dropout of the control group could constitute an attrition bias. It would be desirable to conduct future studies with larger groups also to monitor the pre-post-treatment GSR values in the control group.

The results show that the Biofeedback treatment produced a clear decrease both in minimum and maximum variations for each patient, thus implying that the entire group learned to regulate the GSR.

The numerical results are presented in Table A1 and Table A2 in the Appendix.

Table 1. Comparison between pre- and post-treatment for both groups.

Time	Group	Scores (Mean ± SD)			
		Pain*	Interference*	Relief*	HAMA**
ΔT (T1 - T0)	Biofeedback	**−4.9 ± 0.9**	**−5.1 ± 1.1**	**4.6 ± 1.2**	**−7.2 ± 3.7**
	Control	−1.0 ± 0.4	−0.9 ± 0.3	1.1 ± 0.6	−2.2 ± 2.1

*The paired t-test provided a p value $p < 0.001$; **The paired t-test provided a p value $p = 0.002$.
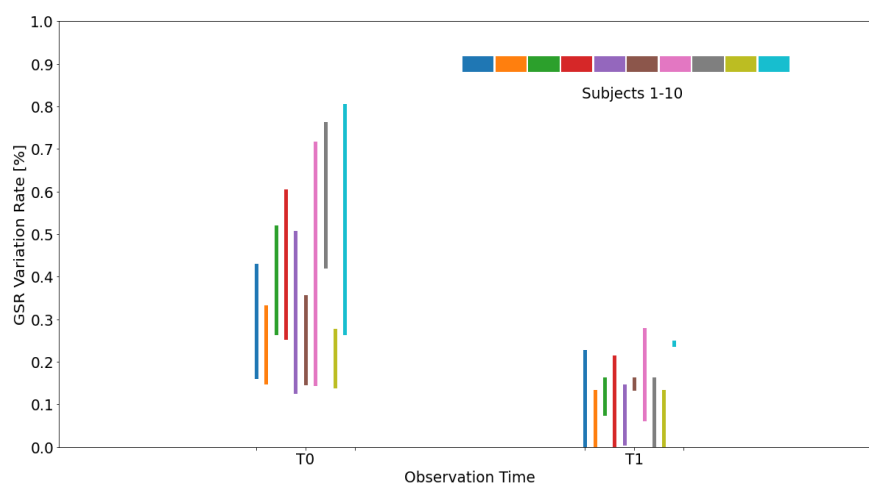

Figure 2. Variation Rate of the Galvanic Skin Response specific for each subject of the Biofeedback group. Each bar spans from the minimum to the maximum GSR variation recorded during the first (T0) and last (T1) training sessions.

4. Discussion

One of the first concerns during this study was the assessment of the initial clinical condition at T0 and the repartition of the patients in the two groups. Although the differences on average between the two groups were not sufficient to be statistically significant, the paired t-test between the two distributions of Interference with Life score at T0 (left graph of Figure 1(a)) resulted in a p-value of 0.06, very close to a value that would imply a statistically relevant difference. The fact that the Biofeedback group shows on average higher scores compared to the control group could be arguably explained by the fact that patients with an overall worse clinical situation are incentivized to try novel approaches which could result in a higher benefit at the end of the treatment.

The main limitation of the study lies in the high dropout rate of the control group which was not available for the acquisition of the GSR data at T1, thus limiting the possible comparison about the GSR to the pre- and post-treatment only for the Biofeedback group. For future studies it would be interesting to collect these data to evaluate if the GSR at T0 and T1 for the control group do not show any relevant differences, as expected. This behavior would confirm that the reduction of GSR variations would be related to the Biofeedback training. Another

critical issue is that the age range of participants (18 - 60 years) is very board, potentially introducing confounding variables that aren't accounted for in the analysis.

Nevertheless, the collected data provide interesting insights which confirm that the treatment reduces the GSR variation when the patients undergo a Biofeedback treatment.

The data relating to the HAMA scores for the clinical evaluation of anxiety should also be considered: both the patients in the control group and those in the study group had obtained scores < 17, *i.e.* not indicative of anxiety disorder. However, the treated patients reduced their anxiety levels compared to the scores measured pre-treatment.

5. Conclusions

The statistical significance of the above data suggests a better efficacy of the combined GSR biofeedback protocol and psychological therapy compared to psychological treatment alone. This is in line with the multifactorial clinical etiology of PAP and with the associated peripheral and central neurophysiological alterations [6] [7] [8] that predispose patients to process neutral stimuli as painful stimuli (intestinal peristalsis, physiological bladder distention, slight contractions of the abdominal and pelvic muscles). The conductance of the skin increases when the intensity of the patient's emotional arousal increases, which happens when an alert situation triggered by the Autonomic Nervous System (ANS) increases the body and mind activity [16]. The organic and psychological nature of this pathology requires a combined therapy that allows on the one hand a solid cognitive restructuring, and on the other hand allows reducing the hyperactivation of the sympathetic nervous system at the peripheral level. It is therefore essential to guide the patient in self-monitoring and self-regulating of the psychophysiological state both through a cognitive behavioral psychological approach [18] and through biofeedback training (e.g. GSR-extinction) which facilitates spontaneous relaxation, muscle relaxation and teaches how to regulate one's emotional state.

Through the combined clinical treatment, the patient learns how to avoid focusing on pain and, subsequently, is able to distinguish actually painful stimuli from stimuli of a non-painful nature, reducing his state of alertness.

Acknowledgements

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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Appendix

Table A1. Comparison between pre- and post-treatment of GSR maximum variation.

Time	Max GSR (%)									
	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10
T0	0.43	0.33	0.52	0.60	0.50	0.35	0.71	0.76	0.27	0.80
T1	0.22	0.13	0.16	0.21	0.14	0.16	0.28	0.16	0.13	0.25
ΔT	**−0.20**	**−0.20**	**−0.36**	**−0.39**	**−0.36**	**−0.19**	**−0.44**	**−0.60**	**−0.14**	**−0.55**

Table A2. Comparison between pre- and post-treatment of GSR minimum variation.

Time	Min GSR (%)									
	S1	S2	S3	S4	S5	S6	S7	S8	S9	S10
T0	0.17	0.15	0.27	0.26	0.13	0.15	0.15	0.43	0.14	0.27
T1	0.01	0.00	0.08	0.01	0.01	0.14	0.07	0.00	0.00	0.24
ΔT	**−0.16**	**−0.15**	**−0.19**	**−0.25**	**−0.12**	**−0.01**	**−0.08**	**−0.42**	**−0.14**	**−0.03**