

Case report

Impact of cognitive-behavior therapy on resilience-related neurobiological factors

Impacto da terapia cognitivo-comportamental nos fatores neurobiológicos relacionados à resiliência

Carlos Eduardo Norte¹, Gabriela Guerra Leal Souza², Ana Lucia Pedrozo¹, Ana Carolina Ferraz Mendonça-de-Souza³, Ivan Figueira⁴, Eliane Volchan³, Paula Rui Ventura¹

¹ Institute of Psychology, Federal University of Rio de Janeiro (UFRJ), Rio de Janeiro, Brazil.

² Institute of Biological and Exact Sciences, Federal University of Ouro Preto (UFOP), Ouro Preto, MG, Brazil.

³ Institute of Biophysics Carlos Chagas Filho, UFRJ, Rio de Janeiro, RJ, Brazil.

⁴ Institute of Psychiatry, UFRJ, Rio de Janeiro, RJ, Brazil.

Received: 9/6/2010 – Accepted: 7/10/2010

Abstract

Resilience, as an outcome variable, has been largely neglected in the field of therapeutics. Our aim was to investigate the effects of cognitive behavioral therapy (CBT) on neurobiological markers of resilience in posttraumatic stress disorder (PTSD) patients. In this single-case experimental research, we assessed physiological (heart rate, respiratory rate, cardiac vagal tone, sympathetic balance and skin conductance) and neuroendocrine (cortisol and dehydroepiandrosterone – DHEA) variables; and psychometric self-report measures (negative affect, resilience, PTSD symptoms, depression, anxiety and social support). Physiological, neuroendocrine and psychometric responses at rest were measured before and after four months of CBT. The patient was a 45-year-old man who had suffered two armed robberies and failed to respond adequately to pharmacological treatment with paroxetine. CBT led to a reduction in heart rate, respiratory rate, sympathetic balance, skin conductance and cortisol. It also led to an increase in cardiac vagal tone and DHEA. Furthermore, CBT promoted reduction of PTSD symptoms, depression, anxiety and negative affect scores and enhancement of resilience and social support scores. CBT in this single case enhanced resilience-related factors such as DHEA, vagal tone, self-reported resilience and social support suggesting that this therapeutic strategy not only contributed to 'anti' pathology effects but to 'pro' well-being. Additionally, our results show the relevance of investigating the effects of psychological treatments in multiple neurobiological systems in the same PTSD patients to unveil the neurobiological underpinnings of resilience factors.

Norte CE, et al. / *Rev Psiq Clín.* 2011;38(1):43-45

Keywords: Post-traumatic stress disorder, cognitive behavior therapy, resilience, neuroendocrine, psychophysiology.

Resumo

A resiliência, como uma variável de desfecho, tem sido largamente negligenciada no campo terapêutico. Nosso objetivo foi investigar os efeitos da terapia cognitivo-comportamental (TCC) nos marcadores neurobiológicos de resiliência em pacientes com transtorno de estresse pós-traumático (TEPT). Nesta pesquisa experimental de caso único, foram acessadas variáveis fisiológicas (frequência cardíaca, frequência respiratória, tônus vagal cardíaco, balanço simpático e condutância da pele) e neuroendócrinas (cortisol e de-hidroepiandrosterona – DHEA) e medidas psicométricas de autorrelato (afeto negativo, resiliência, sintomas de TEPT, depressão, ansiedade e apoio social). Foram medidas as respostas fisiológicas, neuroendócrinas e psicométricas em repouso antes e após quatro meses de TCC. O paciente era um homem de 45 anos que sofreu dois assaltos com arma de fogo e não respondeu adequadamente ao tratamento farmacológico com paroxetina. A TCC levou a uma redução da frequência cardíaca, frequência respiratória, balanço simpático, condutância da pele e cortisol, bem como a um aumento no tônus vagal e DHEA. Além disso, a TCC promoveu redução na pontuação dos sintomas de TEPT, depressão, ansiedade e afeto negativo e aumento da pontuação de resiliência e apoio social. Nossos dados sugerem que a TCC aumenta os fatores relacionados à resiliência (DHEA, tônus vagal, autorrelato de resiliência e apoio social). Isso não é somente "antipatológico", mas também pode ser considerado "pró-bem-estar". Adicionalmente, nossos resultados mostram a relevância da investigação dos efeitos do tratamento psicológico em múltiplos sistemas neurobiológicos no mesmo paciente com TEPT, visando desvendar as bases neurobiológicas dos fatores de resiliência.

Norte CE, et al. / *Rev Psiq Clín.* 2011;38(1):43-45

Palavras-chave: Transtorno de estresse pós-traumático, terapia cognitivo-comportamental, resiliência, neuroendócrino, psicofisiologia.

Introduction

There are many autonomic and neuroendocrine abnormalities associated with PTSD. There are still few studies about the neurobiological correlates of the treatment's response in this disorder. Effects of psychological treatment on autonomic¹ and neuroendocrine² variables have been reported in PTSD patients. These considerations underscore the need to simultaneously investigate the effects of psychological treatments on multiple neurobiological systems in PTSD using a within-patient design.

While there are abundant studies of negative psychological states, scant attention have been paid to positive psychological ones. There is, nevertheless, a growing field of research on positive

affect and well-being, the so-called positive psychology. Constructs related to positive psychology such as resilience have been largely neglected as a treatment target in the field of therapeutics, in spite of an extant literature on this subject. Resilience is a dynamic process involving an interaction between risk and protection factors, internal and external to the individual, that act to regulate the effects of an adverse life event³.

The study of psychophysiological factors is critical for the understanding of successful adaptation to stress. Studies have been suggested that higher vagal tone is associated with healthier social engagement behavior⁴. Recent results from our group, have provided evidence that cardiac recovery from an acute psychosocial stress seemed de-

Research carried out at the Integrated Laboratory of Stress Research/Institute of Psychiatry/Federal University of Rio de Janeiro, RJ, Brazil.

Correspondence to: Carlos Eduardo Norte. Laboratório Integrado de Pesquisa em Estresse – IPUB. Av. Venceslau Brás, 71, Pavilhão Prof. J. Leme Lopes, salas: 2 a 8, Urca – 22290-140 – Rio de Janeiro, RJ, Brasil. E-mail: cadulsn@gmail.com

pendent upon individual predispositions such as cardiac vagal tone and resilience⁵. Data supporting dehydroepiandrosterone hormone (DHEA), as a possible neurobiological resilience and stress protective factor include an inverse correlation between DHEA reactivity (in response to ACTH administration) and PTSD symptoms severity⁶.

There is strong evidence that changes in beliefs and behaviors is an effective psychological treatment for posttraumatic stress disorder⁷. Foa and Kozak⁸ proposed a therapeutic approach to achieve fear reduction in PTSD. This approach is based on Lang's bio-informational conceptualization of fear which posits that fear is represented in underlying memory structures serving as templates for fear behavior. Accordingly, fear reduction will be reflected in alterations in physiological activities, in reports about experience of fear, and/or in overt acts such as avoidance or escape.

The main goal of the present study is to gather evidence for the relevance of resilience-related factors both on psychometric and biological grounds as outcome measures in clinical trials. The current case-study documents the impact of CBT on autonomic and neuroendocrine variables as well as on symptoms, affective predispositions and resilience-related scales.

Case report

The patient is a 45-year-old male who has been assaulted with a gun twice in a bank where he worked as a treasurer. At the time of the first assessment in our research unit he was diagnosed using the Structured Clinical Interview for DSM-IV⁹ (SCID-I) and met criteria for current Posttraumatic stress disorder, major depressive disorder (MDD), panic disorder (PD) and obsessive compulsive disorder (OCD). During 32 months he received pharmacological treatment with paroxetine (maximum dose: 40 mg/day) showing a full remission of PD and OCD and a partial response of PTSD and MDD. Just before he started CBT treatment he still met criteria for current PTSD. His symptoms included recurrent nightmares, flashbacks, trauma-related intrusive thoughts, avoidant behaviors, emotional detachment, irritability and hypervigilance. As his PTSD symptoms presented resistance to the pharmacological treatment he was referred to an augmentation trial with cognitive behavior therapy. The study protocol and informed-consent form were approved by the Institutional Review Board of the Federal University of Rio de Janeiro (Rio de Janeiro, Brazil).

Cognitive behavioral treatment

During the entire CBT treatment the patient kept using the prescribed medication of paroxetine (40 mg/day). The psychological treatment was conducted based on the protocol developed by Foa and Rothbaum¹⁰ which included: psychoeducation; relaxation and breathing training; imaginal exposure; gradual in vivo exposure; cognitive restructuring and relapse prevention. However, we conducted sixteen sessions and introduced coaching to help with relaxation, breathing control, imaginal and graduated in vivo exposure. Forty-eight coaching sessions lasting 120 minutes each were held three times a week. Extra sessions and coaching were added since the present protocol was designed to be the "next step" strategy to patients resistant/intolerant to standard pharmacological treatment. Furthermore, the study was conducted in a tertiary PTSD outpatient clinic, in a context of frequent reexposure to traumatic events, mainly armed robbery.

Psychometric assessment

The following clinician-rated and self-report measures of personal traits were used: the PTSD Checklist-Civilian¹¹ (PCL-C), Beck Depression Inventory¹² (BDI), Beck Anxiety Inventory¹³ (BAI), Positive and Negative Affect Schedule – Trait Version¹⁴ (PANAS-T), Ego-Resiliency Scale¹⁵ and Medical Outcomes Study's Social Support Scale¹⁶.

Physiological recordings

The experiment was performed during the afternoon. The patient was asked to abstain from food and drink (except for water) for 1 hour before the physiological assessment. The patient was comfortably seated and asked to fill out some questionnaires. A respiratory belt transducer and electrocardiogram and skin conductance electrodes were attached. After a 5 min period of adaptation a stimulated saliva sample was collected using a Salivette[®] device. This was followed by 5 min of physiological recordings. Both physiological and psychometric assessments were conducted before and after CBT treatment. As this is a single case report, no statistical analyses were performed.

Respiratory effort, electrocardiographic and electrodermic recordings were collected simultaneously employing the MP100 system (BIOPAC Systems Inc). We performed spectral analyses on electrocardiographic recordings to extract the amplitudes of the high (HF) and the low (LF) frequency power and analyze vagal tone (HF) and sympathetic balance (LF/HF). Electrodermic signals were expressed as the mean amplitude of skin conductance responses. Saliva samples were analyzed using Enzyme Immunoassay (EIA) to measure the concentration of the hormones cortisol and dehydroepiandrosterone (DHEA).

Results

The patient reported improvement in cognitions and behaviors related to PTSD symptoms. The CBT's effects were mediated by changes in maladaptive cognitions, as predicted by cognitive models of PTSD. Vulnerable cognitions like "I am always in serious risk, something bad could happen to me at any time", "I always suspect people" and "The world is dangerous" changed for adaptive and realistic cognitions in accordance with the present situations, which correlates with reduced anxiety. There was also a reduction in avoidance behaviors and, nowadays, the patient is able to take public transportation, and he goes to places he used to avoid, like malls, supermarket, relatives' houses, banks, with low if any anxiety. Nowadays, he speaks easily about the trauma. More importantly, he had an improvement in his interpersonal relationships becoming more tolerant toward people.

Scores in psychometric "negative" signs were lower post treatment. This includes negative affect (reduction of 40%) and symptoms of PTSD (reduction of 19,6%), depression (reduction of 15,8%) and anxiety (reduction of 28,6%). On the other hand, changes in scores of "positive" signs such as social support (enhancement of 33,3%) and resilience (enhancement of 23,1%) were driven in the opposite direction, which is of being higher following treatment.

Physiological indexes of autonomic activation showed lower levels after CBT treatment: heart rate (reduction of 3,2%), sympathetic balance (reduction of 39,4%), respiratory rate (reduction of 5,7%) and skin conductance responses (reduction of 19,6%). Cardiac vagal tone, an autonomic index related to physical and mental healthier states, was higher after the CBT treatment with an enhancement of 40,6%. Salivary cortisol was slightly lower after CBT treatment, reduction of 5,4%, while DHEA was much higher after the psychotherapy with an enhancement of 118,2%.

Discussion

The present study applied Cognitive Behavioral Therapy to a patient with PTSD resistant to pharmacological treatment. Cognitive and behavioral aspects as well as psychometric and physiological recordings were evaluated before and after treatment with CBT. CBT promoted reduction in unfavorable psychometric parameters such as PTSD, depression and anxiety symptoms as well as negative affect scores. There was a concomitant reduction in physiological basal levels of heart rate, respiratory rate, skin conductance and salivary cortisol. Importantly, the therapy increased the following resilience-related factors: the scores on social support and resilience questionnaires, and the basal levels of cardiac vagal tone and dehydroepiandrosterone.

Considering that the treatment with CBT began after 32 months of pharmacological treatment with paroxetine, without the expected results, the effects showed in the present study strongly suggest that the patient's improvement was caused by CBT.

These results highlight the importance of this therapy not only in helping the patient to relieve the negative aspects of the disorder, but also in building positive features like resilience, social support and a healthier physiology. As pointed out by Fredrickson and Levenson¹⁷ building positive resources may accelerate internal homeostatic process, restore equilibrium both in terms of physiological activation and psychological openness to a wide range of action possibilities. The enhancement of positive resources may also help counteract negative symptoms and buffer against their future recurrence.

The role of resilience-related factors in psychotherapy is an uncharted field of study. Establishing that CBT improves resilience may reinforce this choice of treatment for those who have suffered traumatic life events. This case report illustrates that resilience should be considered as another important outcome domain of assessment in clinical trials. Therapeutic efficacy in clinical trials commonly focus on a single outcome domain, prioritizing the reduction of psychopathological symptoms and neglecting the assessment of important domains such as quality of life and resilience. The assessment of multiple outcome domains should be mandatory considering that it captures the complexity and richness of the suffering associated with PTSD extending the evaluation beyond the signs and symptoms dimension.

The main strength of the present case report is the simultaneous assessment of psychometric, psychophysiological parameters and behaviors related to distress and well-being in the context of a psychotherapeutic intervention. As far as we know, this is the first study to use this all-encompassing approach.

An obvious limitation of the current investigation derives from being a single-case study. Large scale randomized controlled trials are necessary to corroborate the promising findings of this investigation.

Acknowledgments

The authors wish to thank Jose Magalhães de Oliveira for valuable technical support and Dr. Sonia Gleiser for project managing. And also thanks Carla Marques Portela, Dr. William Berger and Tania Fagundes Macedo for the clinical assistance in this case.

This research was supported by Fundação Carlos Chagas Filho de Amparo à Pesquisa do Estado do Rio de Janeiro (Faperj) and Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq).

References

1. Lindauer RTL, van Meijel EPM, Jalink M, Olf M, Carlier IVE, Gersons BPR. Heart rate responsivity to script-driven imagery in posttraumatic stress disorder: specificity of response and effects of psychotherapy. *Psy Medicine*. 2006;68:33-40.
2. Olf M, de Vries GJ, Guzelcan Y, Assies J, Gersons BPR. Changes in cortisol and DHEA plasma levels after psychotherapy for PTSD. *Psychoneuroendocrinology*. 2007;32:619-26.
3. Rutter M. Resilience concepts and findings: implications for family therapy. *J Family Therapy*. 1999;21:119-44.
4. Porges SW. The polyvagal perspective. *Biol Psychol*. 2007;74:116-43.
5. Souza GG, Mendonca-de-Souza AC, Barros EM, Coutinho EF, Oliveira L, Mendlowicz MV, et al. Resilience and vagal tone predict cardiac recovery from acute social stress. *Stress*. 2007;10:368-74.
6. Rasmusson AM, Vasek J, Lipschitz DS, Vojvodan D, Mustone ME, Shi QH, et al. An increased capacity for adrenal DHEA release is associated with decreased avoidance and negative mood symptoms in women with PTSD. *Neuropsychopharmacology*. 2004;29:1546-57.
7. Passarela CM, Mendes DD, Mari JJ. A systematic review to study the efficacy of cognitive behavioral therapy for sexually abused children and adolescents with posttraumatic stress disorder. *Rev Psiq Clín*. 2010;37(2):60-5.
8. Foa EB, Kozak MJ. Emotional processing of fear: exposure to corrective information. *Psychol Bull*. 1986;99:20-35.
9. Del-Ben CM, Vilela JAA, Crippa JAS, Hallak JEC, Labate CM, Zuardi AW. Reliability of the structured clinical interview for DSM-IV – Clinical version translated into Portuguese. *Rev Bras Psiquiatr*. 2001;23:156-9.
10. Foa E, Rothbaum B. Treating de trauma of rape – Cognitive behavioral therapy for PTSD. New York: The Guilford Press; 1998.
11. Weathers FW, Litz BT, Herman D, Huska JA, Keane TM. The PTSD Checklist (PCL): reliability, validity, and diagnostic utility. Paper present at the Annual Meeting of International Society for Traumatic Stress Studies, San Antonio, TX, October; 1993.
12. Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh G. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961;4:53-63.
13. Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. *J Consult Clin Psychol*. 1988;56:893-7.
14. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect – The panas scales. *J Pers Soc Psychol*. 1988;54:1063-70.
15. Block J, Kremen AM. IQ and ego-resiliency: conceptual and empirical connections and separateness. *J Pers Soc Psychol*. 1996;70:349-61.
16. Griep RH, et al. Construct validity of the Medical Outcomes Study's social support scale adapted to Portuguese in the Pró-Saúde Study. *Cad Saúde Pública*. 2005;21(3):703-14.
17. Fredrickson BL, Levenson RW. Positive emotions speed recovery from the cardiovascular sequelae of negative emotions. *Cogand Emotion*. 1998;12:191-220.