

Effect of Cognitive Behavioral Intervention on Plasma Cortisol in Patients with Breast Cancer PTSD

Yanling Zhou, Min Guo* 💿

President Office, The Fourth People's Hospital of Haikou City, Haikou, China Email: *g2002m@163.com

How to cite this paper: Zhou, Y.L. and Guo, M. (2024) Effect of Cognitive Behavioral Intervention on Plasma Cortisol in Patients with Breast Cancer PTSD. *Journal of Cancer Therapy*, **15**, 62-70. https://doi.org/10.4236/jct.2024.153007

Received: February 10, 2024 **Accepted:** March 16, 2024 **Published:** March 19, 2024

Copyright © 2024 by author(s) and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).

http://creativecommons.org/licenses/by/4.0/

cc ① Open Access

Abstract

Objective: To investigate the effect of cognitive behavioral intervention on plasma cortisol in patients with breast cancer PTSD before surgery. **Methods:** SCL-90, EPQ-N and cognitive behavior intervention were performed on 30 patients with PTSD, 30 patients without PTSD and 30 normal subjects, and their fasting blood was collected to analyze cortisol in the morning. **Results:** The scores of SCL-90 and EPQ-N in patients with breast cancer PTSD were significantly higher than those in non-PTSD patients and normal subjects (P < 0.01). After cognitive behavioral intervention, the plasma cortisol level of breast cancer PTSD patients was significantly decreased (P < 0.05). **Conclusion:** Compared with non-PTSD breast cancer patients and normal control group, breast cancer PTSD patients had more serious psychological problems, worse emotional stability and higher plasma cortisol level. Cognitive-behavioral intervention can effectively reduce plasma cortisol levels in breast cancer patients with PTSD.

Keywords

Cognitive Behavior Intervention, Breast Cancer, PTSD, Cortisol

1. Introduction

Breast cancer is a malignant tumor with the highest incidence among women in the world. In recent years, the incidence of breast cancer in China has increased gradually, becoming one of the "number one killers" threatening women's lives. The impact of breast cancer on patients includes not only physical changes, such as endocrine abnormalities (high cortisol), decreased immune function, sleep disorders, pain, fatigue, etc. [1] [2], but also psychological aspects. These include increased negative emotions (increased depression, increased anxiety, more depression, mood disorders), impaired cognitive function, sensitivity to stress perception, and increased response to cancer-related stress [3] [4]. Tumor size, body mass index, sleep habits, family and social support, emotional stability, and life meaning also have an impact on the recovery of breast cancer patients [5] [6]. The relationship between Post-Traumatic Stress Disorder (PTSD) and breast cancer is more complex, Pre-cancer stress and trauma, such as domestic violence, family members suffering from breast cancer, anxiety disorder, depression disorder and work frustration, can all become precursors of breast cancer and affect the treatment process and prognosis of patients [7] [8] [9]. However, the diagnosis and treatment of breast cancer itself can be used as a stressful event to make individuals comorbid with PTSD [10]. The psychological intervention of breast cancer patients before or after surgery mainly focuses on cognitive adjustment and behavioral relaxation, and generally takes the change of cortisol level as the evaluation index to detect the intervention effect. For example, a number of studies conducted a 10-week intervention on postoperative breast cancer survivors using cognitive-behavioral stress management method showed that individuals' relaxation ability was improved, psychological stress was reduced and plasma cortisol was significantly reduced [11] [12]. Mindfulness and stress reduction meditation is also increasingly used in the rehabilitation treatment of breast cancer patients, which can effectively improve individual quality of life, reduce stress symptoms, promote the normal function of the HPA (Hypothalamic-pituitary-adrenal) axis, and then regulate cortisol level [13] [14]. Brief supportive therapy is often used to regulate preoperative negative emotions in breast cancer patients [15]. In addition, various types of yoga training and traditional massage are also used in this field. Yoga is effective in regulating stress hormone mechanisms, while traditional massage can temporarily reduce plasma cortisol levels [15] [16] [17]. At present, there is no research on psychological intervention for breast cancer PTSD patients before surgery. Generally, PTSD caused by any event will bring significant pain and impairment of social relations, work ability or function in a certain key area to individuals. However, the negative cognitive/emotional and avoidance reactions of PTSD patients with breast cancer are closely related to the treatment effect and prognosis [9] [10]. Therefore, this study developed a cognitive-behavioral intervention program for breast cancer PTSD patients, and used plasma cortisol levels to evaluate the effect of the intervention.

2. Objects and Methods

2.1. Objects

Female breast cancer patients admitted to the Breast Surgery Department of Hainan Provincial People's Hospital from January 1, 2015 to December 31, 2015 were selected as subjects for post-traumatic stress disorder screening. 30 patients with breast cancer PTSD and 30 patients without breast cancer PTSD were selected, and 30 healthy people were selected. The groups were relatively matched in age $(43 \pm 7 \text{ years})$, occupation, education level, economic level and family status.

Inclusion criteria: Post-traumatic Stress Disorder Self-rating Scale (PTSD-SS)

for PTSD, breast cancer PTSD patients, non-breast cancer PTSD patients, and volunteers were evaluated for inclusion criteria. The post-traumatic Stress Disorder Self-Rating Scale (PTSD-SS) contains 24 items, including repeated experience, avoidance symptoms, subjective trauma evaluation, impairment of social function, and high alertness. Each item is scored with 1 to 5 points (full score is 120 points). The higher the score, the more severe the symptoms of PTSD, and 50 is the critical value. A score of \leq 50 indicates no symptoms and a score of >50 indicates PTSD.

Exclusion criteria: 1) Patients who are unable to communicate or cooperate with the study; 2) suffering from other malignant tumors; 3) Postoperative radiotherapy; 4) Cognitive impairment, hearing impairment, mental disorders; 5) lactation period; 6) Elderly patients; 7) Serious mental illness. This study was approved by the hospital Ethics Committee.

2.2. Tools

2.2.1. Symptom Checklist 90 (SCL-90) [18]

Used to assess an individual's psychological problems. A total of 90 entries were grouped into 10 factors (somatization, obsessive state, interpersonal sensitivity, depression, anxiety, hostility, terror, paranoia, psychosis, and other items). Each item is rated on a scale of 1 to 5, with the higher the score, the more serious the psychological problems.

2.2.2. Eysenck Personality Questionnaide-Neuroticism (EPQ-N) [19]

Used to assess an individual's emotional stability. It consisted of 24 items and asked subjects to answer "1 = yes" or "2 = no" based on their situation, with higher scores indicating worse emotional stability.

2.2.3. Psychological Intervention Program

Using a cognitive behavioral intervention that includes: general knowledge about breast cancer, using cognitive techniques (explaining how thoughts cause emotions; Develop new adaptive criteria and assumptions) to regulate subjects' negative cognitive/emotional and avoidance thoughts, and to use behavioral relaxation techniques (muscle relaxation training) to relieve tension and hypervigilance responses from repeated experiences. The whole process lasts 90 minutes and is completed by two researchers who have undergone unified training.

2.3. Methods

2 ml of blood samples were collected from breast cancer patients on the morning of the second day after admission and three days after the end of cognitive behavioral intervention. The normal group had blood drawn the day before the cognitive behavioral intervention began and one week after the cognitive behavioral intervention ended. The kit is provided by Guangzhou Yongnuo Biotechnology Co., Ltd.

- 1) Delayed onset and long-term persistence of mental disorders.
- 2) Fixed a form of recurrent intrudative traumatic experience recurrence.
- 3) Patients often have this "repeated experience" in a vague and extremely

painful way.

4) The patient adopts a receptive attitude towards things related to trauma.

5) Most patients develop symptoms within a few days to six months after a traumatic event, and it usually takes many years to return to normal.

An assessment test for the presence of PTSD is required after one month.

The cognitive behavioral intervention was performed 3 days after the breast cancer patients were diagnosed and admitted to hospital.

SPSS 22.0 was used for data entry and statistical analysis. The measurement data conforming to the normal distribution were described by means \pm standard deviation, the independent sample T-test was used to compare the two groups, the analysis of variance was used to compare the multiple groups, and the multiple groups with significant differences were compared after the fact. P < 0.05 was considered to be statistically significant.

3. Results

3.1. Analysis of Personality and Mental Health Status of Breast Cancer Patients

Variance analysis was performed on the factors and total scores of SCL-90, EPQ-N scores and plasma cortisol levels before cognitive behavioral intervention in breast cancer PTSD group, breast cancer non-PTSD group and normal group. According to the existence of inter-group differences and the homogeneity of variance in each group, LSD method was used to make post-hoc comparison between groups. The results showed as follows: There were significant differences in interpersonal relationship, depression and anxiety among the three groups (P < 0.001), and the PTSD group was higher than the non-PTSD group than the normal group. The scores of somatization, compulsion, hostility, terror, paranoia, psychosis, other, SCL-90 score and EPQ-N score in breast cancer PTSD group were significantly higher than those in breast cancer non-PTSD group and normal group (P < 0.01). Before cognitive behavior intervention, plasma cortisol levels of breast cancer PTSD group and breast cancer non-PTSD group had no significant difference, but were significantly higher than normal group (P < 0.05). See Table 1.

3.2. Analysis of the Influence of Cognitive Behavioral Intervention on Serum Glucocorticoid in Patients with Breast Cancer PTSD

A paired t-test was performed on plasma cortisol levels in all groups (breast cancer PTSD group, breast cancer non-PTSD group, and normal group) before and after the cognitive behavioral intervention. The results showed that compared with before cognitive behavioral intervention, plasma cortisol level in breast cancer PTSD group was significantly decreased after cognitive behavioral intervention (P < 0.05). There were no significant differences in plasma cortisol levels between breast cancer non-PTSD and normal groups before and after the cognitive-behavioral intervention (see Table 2).

| | Breast cancer PTSD group a | Breast cancer non-PTSD group b | Normal group c | F | Р | Post inspectior |
|----------------------------|----------------------------|-----------------------------------|--------------------|----------|-------|-----------------|
| Somatization | 21.80 ± 4.84 | 18.67 ± 1.63 | 17.10 ± 4.38 | 11.39*** | 0.000 | a > b, c |
| Force | 16.73 ± 4.00 | 14.27 ± 1.11 | 12.70 ± 3.27 | 13.31*** | 0.000 | a > b, c |
| Interpersonal relationship | 14.57 ± 3.47 | 11.50 ± 0.82 | 9.97 ± 2.75 | 24.36*** | 0.000 | a > b > c |
| Depressed | 22.17 ± 4.57 | 19.40 ± 1.65 | 17.34 ± 4.31 | 12.53*** | 0.000 | a > b > c |
| Anxiety | 19.93 ± 3.42 | 17.80 ± 1.30 | 16.17 ± 3.87 | 11.28*** | 0.000 | a > b > c |
| Antagonize | 10.33 ± 2.23 | 8.83 ± 0.91 | 8.27 ± 2.08 | 10.07*** | 0.000 | a > b, c |
| Horror | 10.93 ± 2.63 | 9.53 ± 0.97 | 8.70 ± 2.41 | 8.37*** | 0.000 | a > b, c |
| Bigoted | 8.27 ± 2.79 | 6.70 ± 0.95 | 6.27 ± 1.84 | 8.26** | 0.001 | a > b, c |
| Psychosis | 14.93 ± 4.84 | 11.60 ± 1.28 | 10.04 ± 2.71 | 17.36*** | 0.000 | a > b, c |
| Other | 15.10 ± 3.03 | 13.50 ± 1.33 | 12.53 ± 3.37 | 6.77** | 0.002 | a > b, c |
| SCL-90 | 154.77 ± 34.13 | 131.80 ± 5.35 | 121.97 ± 21.74 | 15.31*** | 0.000 | a > b, c |
| EPQ-N | 43.80 ± 9.47 | 37.97 ± 2.31 | 34.53 ± 7.26 | 2.66** | 0.008 | a > b, c |
| Cortisol (ng/ml) | 23.06 ± 14.08 | 23.28 ± 10.45 | 14.39 ± 14.07 | 4.58* | 0.013 | a > c, b > c |

Table 1. Comparison of SCL-90 and EPQ-N scores among all groups ($\overline{x} \pm s$).

Note: * means P < 0.05, ** means P < 0.01, *** means P < 0.001.

| | Breast cancer PTSD group a | Breast cancer non-PTSD group b | Normal group c |
|-------------------|----------------------------|--------------------------------|-------------------|
| Pre-intervention | 23.06 ± 14.08 | 23.28 ± 10.45 | 14.39 ± 14.07 |
| Post-intervention | 17.76 ± 12.12 | 20.37 ± 18.36 | 13.18 ± 9.23 |
| Pair t | 2.08 | 0.94 | 0.54 |
| Р | 0.038* | 0.357 | 0.594 |

Note: *means P < 0.05, ** means P < 0.01, *** means P < 0.001.

4. Discussion

This study showed that patients with breast cancer PTSD had significantly worse psychological problems and emotional stability than patients with breast cancer non-PTSD and normal control group, and patients with breast cancer non-PTSD had more serious problems in interpersonal relationships, depression and anxiety than normal control group. First of all, the diagnosis of breast cancer brings serious physical and psychological pressure and accompanied by psychological problems to patients, which is consistent with the conclusions of previous studies [2] [3], because patients not only have to face the pain of disease development and treatment, but also worry about the prognosis. For most patients, they face financial burdens due to medical expenses, interrupted career development, unbalanced social relationships, and impaired family functioning. Secondly, this study distinguished whether the breast cancer patients had PTSD or not. When the breast cancer patients had no comorbidities of PTSD, they only had more serious problems in interpersonal relationship, depression and anxiety than the normal control group. But when breast cancer comorbidities PTSD, patients have more and more severe psychological problems and poorer emotional stability than the other two groups. Previous studies have shown that cancer individuals with more severe PTSD have less social support, more pre-cancer trauma history, shorter survival time after treatment, and a higher incidence of serious diseases [20]. PTSD is associated with major depression in cancer individuals [7]. This is similar to the conclusion of this study. However, further research is needed on the interaction mechanism between breast cancer and PTSD. Thirdly, in terms of interpersonal sensitivity, depression and anxiety, breast cancer PTSD patients were significantly higher than breast cancer non-PTSD patients than the normal control group, which is similar to the conclusions of previous studies. A diagnosis of cancer can lead to feelings of inferiority and despair, depression, fear, anger, depression, and anxiety, which can also affect their interpersonal relationships. However, the existence of PTSD will aggravate these three aspects of patients' problems. Kangas found in the exploration of factors affecting the occurrence of PTSD in cancer patients that poor social function and interpersonal relationship and avoidant coping style are typical predictors of PTSD symptoms in cancer patients [21]. Golden-Kreutz et al. showed through longitudinal studies that severe invasive and avoidance symptoms in cancer PTSD patients predicted the development of depressive symptoms [22]. In addition, numerous studies have shown that PTSD patients have a very high probability of comorbidity anxiety disorder and depression disorder. Therefore, in addition to the psychological problems of general cancer patients, breast cancer PTSD patients will be more obvious in the problems associated with PTSD symptoms, such as the avoidance of breast cancer problems will easily lead to the aggravation of depression, the self-blame caused by negative cognition or blame others will worsen their interpersonal relationships, and the overvigilance of cancer-related things will easily develop into obvious anxiety disorders. These findings suggest that screening for PTSD in breast cancer patients is necessary for more targeted psychosomatic treatment.

This study showed that the plasma cortisol level of breast cancer patients was higher than that of the normal group, which was consistent with the conclusions of previous studies [1] [2] [3] [4]. For non-cancer individuals or healthy individuals, the daily cortisol curve is often abnormal under long-term stress, and the diagnosis of breast cancer, as a major stressor, will increase the activation of the HPA axis of patients, thus keeping the body's cortisol at a high level and generating tension, anxiety or anxiety.

5. Conclusion

This study developed a cognitive-behavioral intervention program for breast cancer PTSD patients, including a general discussion of breast cancer knowledge and more targeted cognitive-behavioral regulation of PTSD symptoms in breast cancer patients. The study showed that after cognitive behavioral intervention, the changes in plasma cortisol in the breast cancer PTSD group were statistically significant, indicating that our cognitive behavioral intervention for PTSD symptoms in breast cancer patients is effective and can significantly improve plasma cortisol levels. This cognitive behavioral intervention mainly used two cognitive techniques: first, to explain how thoughts cause emotions; first, to explain the relationship between negative cognition and negative emotions and behaviors to patients with PTSD in breast cancer; Secondly, the negative cognition and avoidance thoughts related to breast cancer were identified through the self-monitoring of patients, and the unreasonable ideas were directly questioned. Finally, the patient was asked to self-state rational ideas to replace the previous irrational ideas. The development of new adaptive standards and hypotheses and the diagnosis of breast cancer will inevitably lead to an increase in patients' negative cognition and emotions. However, as a consequence of traumatic events, individuals can also experience good aspects, such as resetting of life prospects and rebuilding of relationships with others [23], that is, post-traumatic growth. New adaptive standards and hypotheses can bring positive psychological changes. And then promote endocrine function. In addition, in view of the tension and hypervigilance caused by repeated experiences of PTSD patients with breast cancer, this study mainly taught muscle relaxation training in behavioral therapy to patients to help them reduce the excitability of sympathetic nerve activity and physiological alertness level, so as to relieve tension and anxiety.

Fund Project

2022 Hainan Provincial Key Research and Development Program, project number: ZDYF2022SHFZ110.

Conflicts of Interest

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

References

- Schmidt, M.E., Semik, J., Habermann, N., *et al.* (2016) Cancer-Related Fatigue Shows a Stable Association with Diurnal Cortisol Dysregulation in Breast Cancer Patients. *Brain Behavior and Immunity*, **52**, 98-105. <u>https://doi.org/10.1016/j.bbi.2015.10.005</u>
- [2] Tell, D., Mathews, H.L. and Janusek, L.W. (2014) Day-to-Day Dynamics of Associations between Sleep, Napping, Fatigue, and the Cortisol Diurnal Rhythm in Women Diagnosed as Having Breast Cancer. *Psychosomatic Medicine*, **76**, 519-528. https://doi.org/10.1097/PSY.000000000000097
- [3] Ho, R.T., Fong, T.C., Chan, C.K., *et al.* (2013) The Associations between Diurnal Cortisol Patterns, Self-Perceived Social Support, and Sleep Behavior in Chinese Breast Cancer Patients. *Psychoneuroendocrinology*, **38**, 2337-2342. <u>https://doi.org/10.1016/j.psyneuen.2013.05.004</u>
- [4] Hsiao, F.H., Chang, K.J., Kuo, W.H., et al. (2013) A Longitudinal Study of Cortisol Responses, Sleep Problems, and Psychological Well-Being as the Predictors of Changes in Depressive Symptoms among Breast Cancer Survivors. *Psychoneuroendocrinology*,

38, 356-366. https://doi.org/10.1016/j.psyneuen.2012.06.010

- [5] Hsiao, F.H., Kuo, W.H., Jow, G.M., et al. (2015) Habitual Sleep-Wake Behaviors and Lifestyle as Predictors of Diurnal Cortisol Patterns in Young Breast Cancer Survivors: A Longitudinal Study. Psychoneuroendocrinology, 53, 60-68. https://doi.org/10.1016/j.psyneuen.2014.12.014
- [6] Hsiao, F.H., Jow, G.M., Kuo, W.H., et al. (2014) The Partner's Insecure Attachment, Depression and Psychological Well-Being as Predictors of Diurnal Cortisol Patterns for Breast Cancer Survivors and Their Spouses. Stress, 17, 169-175. https://doi.org/10.3109/10253890.2014.880833
- [7] Luecken, L.J., Dausch, B., Gulla, V., et al. (2004) Alterations in Morning Cortisol Associated with PTSD in Women with Breast Cancer. Journal of Psychosomatic Research, 56, 13-15. <u>https://doi.org/10.1016/S0022-3999(03)00561-0</u>
- [8] Dettenborn, L., James, G.D., Berge-Landry, H., et al. (2005) Heightened Cortisol Responses to Daily Stress in Working Women at Familial Risk for Breast Cancer. Biological Psychology, 69, 167-179. <u>https://doi.org/10.1016/j.biopsycho.2004.07.004</u>
- [9] Shelby, R.A., Golden-Kreutz, D.M. and Andersen, B.L. (2008) PTSD Diagnoses, Subsyndromal Symptoms, and Comorbidities Contribute to Impairments for Breast Cancer Survivors. *Journal of Traumatic Stress*, 21, 165-172. https://doi.org/10.1002/jts.20316
- [10] Arnaboldi, P., Lucchiari, C., Santoro, L., *et al.* (2014) PTSD Symptoms as a Consequence of Breast Cancer Diagnosis: Clinical Implications. *SpringerPlus*, **3**, Article No. 392. <u>https://doi.org/10.1186/2193-1801-3-392</u>
- [11] Cruess, D.G., Antoni, M.H., McGregor, B.A., *et al.* (2000) Cognitive-Behavioral Stress Management Reduces Serum Cortisol by Enhancing Benefit Finding among Women Being Treated for Early Stage Breast Cancer. *Psychosomatic Medicine*, **62**, 304-308. <u>https://doi.org/10.1097/00006842-200005000-00002</u>
- [12] Phillips, K.M., Antoni, M.H., Lechner, S.C., *et al.* (2008) Stress Management Intervention Reduces Serum Cortisol and Increases Relaxation during Treatment for Nonmetastatic Breast Cancer. *Psychosomatic Medicine*, **70**, 1044-1049. <u>https://doi.org/10.1097/PSY.0b013e318186fb27</u>
- [13] Carlson, L.E., Speca, M., Patel, K.D., *et al.* (2004) Mindfulness-Based Stress Reduction in Relation to Quality of Life, Mood, Symptoms of Stress and Levels of Cortisol, Dehydroepiandrosterone Sulfate (DHEAS) and Melatonin in Breast and Prostate Cancer Outpatients. *Psychoneuroendocrinology*, **29**, 448-474. https://doi.org/10.1016/S0306-4530(03)00054-4
- [14] Matousek, R.H., Pruessner, J.C. and Dobkin, P.L. (2011) Changes in the Cortisol Awakening Response (CAR) Following Participation in Mindfulness-Based Stress Reduction in Women Who Completed Treatment for Breast Cancer. *Complementary Therapies in Clinical Practice*, **17**, 65-70. <u>https://doi.org/10.1016/j.ctcp.2010.10.005</u>
- [15] Vadiraja, H.S., Raghavendra, R.M., Nagarathna, R., *et al.* (2009) Effects of a Yoga Program on Cortisol Rhythm and Mood States in Early Breast Cancer Patients Undergoing Adjuvant Radiotherapy: A Randomized Controlled Trial. *Integrative Cancer Therapies*, 8, 37-46. <u>https://doi.org/10.1177/1534735409331456</u>
- [16] Banasik, J., Williams, H., Haberman, M., et al. (2011) Effect of Iyengar Yoga Practice on Fatigue and Diurnal Salivary Cortisol Concentration in Breast Cancer Survivors. Journal of the American Academy of Nurse Practitioners, 23, 135-142. https://doi.org/10.1111/j.1745-7599.2010.00573.x
- [17] Listing, M., Krohn, M., Liezmann, C., et al. (2010) The Efficacy of Classical Massage

on Stress Perception and Cortisol Following Primary Treatment of Breast Cancer. *Archives of Women's Mental Health*, **13**, 165-173. https://doi.org/10.1007/s00737-009-0143-9

- [18] Chen, C.H. (1993) Symptom Self-Rating Scale. *Chinese Journal of Mental Health*, 31-36. (In Chinese)
- [19] Gong, Y.X. (1993) Revision of Eysenck Personality Traits Questionnaire Manual. Hunan Medical College Press, Changsha, 31.
- [20] Andrykowski, M.A. and Cordova, M.J. (1998) Factors Associated with PTSD Symptoms Following Treatment for Breast Cancer: Test of the Andersen Model. *Journal of Traumatic Stress*, 11, 189-203. <u>https://doi.org/10.1023/A:1024490718043</u>
- [21] Kangas, M., Henry, J.L. and Bryant, R.A. (2005) Predictors of Posttraumatic Stress Disorder Following Cancer. *Health Psychology*, 24, 579-585. https://doi.org/10.1037/0278-6133.24.6.579
- [22] Golden-Kreutz, D. and Andersen, B.L. (2004) Depressive Symptoms after Breast Cancer Surgery: Relationships with Stress. *Psycho-Oncology*, 13, 211-220. <u>https://doi.org/10.1002/pon.736</u>
- [23] Diaz, M., Aldridge-Gerry, A. and Spiegel, D. (2014) Posttraumatic Growth and Diurnal Cortisol Slope among Women with Metastatic Breast Cancer. *Psychoneuroendocrinology*, 44, 83-87. <u>https://doi.org/10.1016/j.psyneuen.2014.03.001</u>