Journal of Gynecological Oncology

Research Article
Published: 15 Feb, 2022

Neural Correlates of Pain Empathy Impairment in Chemotherapy-Treated Breast Cancer Survivors

*Wen Li, Yue Lv, Shaochun Liu, Senbang Yao, Sheng Yu, Lingxue Tang and Huaidong Cheng**

Department of Oncology, The Second Affiliated Hospital of Anhui Medical University, China

Abstract

Purpose: To investigate the potential effects of chemotherapy on pain empathy in breast cancer patients and the neural correlates in an Event-Related Potentials (ERP) study.

Methods: Twenty-two breast cancer patients were evaluated with a pain empathy task during recording of ERP before and after chemotherapy. Pictures depicting people in pain or in neutral emotions were presented to the participants, who were to determine whether the person felt pain (pain task) or to identify the affected side of the body part (laterality task).

Primary Outcome: Compared to the baseline (before chemotherapy), patients showed lower scores in empathic concern and higher scores in personal distress on the Chinese version of Interpersonal Reactivity Index (IRI-C) after chemotherapy. In both pain and laterality tasks, there was no significant differences in the response time before and after chemotherapy. However, patients showed a lower accuracy rate after than before chemotherapy. Further, the peak amplitude of N1 and P2 was significantly higher and lower, respectively, after as compared to before chemotherapy.

Results: The results suggested pain empathy impairment in chemotherapy-treated breast cancer patients. The deficits may be related to altered N1and P2 components of the ERP.

Implications for Cancer Survivors: These findings provide helpful information with substantial positive consequences for breast cancer survivorship, and add to the literature of chemotherapy-induced cognitive impairment in breast cancer.

Keywords: Breast cancer; Empathy; Chemotherapy; Event-related potentials

OPEN ACCESS

Correspondence:
Huaidong Cheng, Department of Oncology, The Second Affiliated Hospital of Anhui Medical University, Hefei, Anhui, 230601, China, E-mail: chd1975ay@126.com

Received Date: *24 Jan 2022*
Accepted Date: *07 Feb 2022*
Published Date: *15 Feb 2022*

Citation:
Li W, Lv Y, Liu S, Yao S, Yu S, Tang L, et al. Neural Correlates of Pain Empathy Impairment in Chemotherapy-Treated Breast Cancer Survivors. J Gynecol Oncol. 2022; 5(1): 1072.

Introduction

Breast cancer is one of the most common malignancies [1], and many breast cancer patients receive chemotherapy for treatment [2]. Numerous neuropsychological studies have shown cognitive impairment in breast cancer patients undergoing chemotherapy [1], a condition known as Chemotherapy-Related Cognitive Impairment (CRCI) or "chemo brain" [4]. CRCI is defined by the American Cancer Society as increasing forgetfulness, trouble with concentrating and remembering details, difficulty in multitasking, and need of longer time to complete tasks [5]. Structural and functional brain changes have been found to underlie CRCI in breast cancer patients [6,7]. In the first prospective longitudinal neuroimaging study of breast cancer patients, McDonald et al. [8] reported a reduction in gray matter density one month after chemotherapy, particularly in frontal regions [8]. Deprez et al. [9] reported decreases in gray matter volumes in the prefrontal cortex, temporal cortex, hippocampus and cerebellum, and in the fractional anisotropy, an index of white matter integrity, in the frontal, parietal and occipital tracts after chemotherapy [9,10].

Pain empathy is the ability to understand and experience the painful feelings of others, an essential component of emotional and social being [11,12]. In neuroscience research there is increasing attention to the psychological and neural processes of empathy [13,14]. The neural mechanisms of empathy can be divided into two phases. The early emotional phase is driven automatically by perceived pain, and the late, cognitive phase can be modulated more consciously with reappraisal [15]. These two aspects of empathy can be considered as affective (or pre-reflective) and cognitive (reflective) empathy [16]. Affective empathy is associated with the activation of in frontoparietal, temporal, and subcortical regions that support movement, sensation, and emotion, whereas cognitive empathy is associated with activity of the neural circuits of cognitive control and decision making, including the cingulate, prefrontal and temporal regions [17].

Many studies of pain empathy have employed human body images, such as acupunctured

hands, because they are relatively clear and easy to understand [18,19]. Images of limb pain activated sensorimotor areas, where as painful facial responses activated more strongly the midline frontal and parietal cortex as well as the amygdala [18]. Recording of Event-Related Potentials (ERP) has been used to study the neural mechanisms of brain responses during exposure to images of individuals in pain [20,21]. Previous ERP studies of pain perception have associated N1 with the early stage of sensory processing and P2 with recognition and processing of stimulus features [23]. Compared with hearing others' neutral voices, hearing others' voices of pain elicited more positive frontal-central N1 and N2 responses [24].

Emotional regulation requires process of changing one's emotions to maintain a priority emotional state [25]. Emotional regulation impairment in breast cancer patients can persist for several years after chemotherapy [26,27] and lead to elevated levels of depressive symptoms and decreased quality of life [28-30]. Emotional distress may reduce treatment adherence [31] and even increase the risk of disease progression and death [27,32]. It is thus important to understand how chemotherapy influences multiple dimensions of emotional processing, including empathy, in breast cancer patients.

On the other hand, there is little research on empathy processing in breast cancer patients. No studies to our knowledge have investigated the neural processes of pain empathy in breast cancer patients. Here, we addressed this gap in research in an electrophysiological study of 22 breast cancer patients by combining ERP and an empathy task.

Materials and Methods

Subjects and neuropsychological tests

Twenty-two female patients with breast cancer were recruited from the Second Affiliated Hospital of Anhui Medical University, Hefei, China, and were hospitalized from January to October, 2018 in the Department of Oncology. All study procedures were approved by the Research Ethics Committee of the Affiliated Second Hospital of Anhui Medical University (protocol 20131028). After receiving a detailed explanation of the study, all subjects signed informed consents in accordance with the Helsinki Declaration and the research protocol.

The participants ranged in age from 40 to 65 years (mean ± SD = 50.2 ± 6.0). All were diagnosed with stage II through IV breast cancer and treated with standard chemotherapy regimens. Patients with the following conditions were recruited: (1) To complete at least 6 cycles of chemotherapy; (2) age ≥ 18 years; (3) no impairment of vision, hearing, intelligence, or language; (4) no use of psychotropic medications; (5) no history of neurological or psychiatric illnesses; (6) no primary or secondary brain tumor or history of head injury; (7) no abuse of alcohol or use of illicit drugs; (8) Normal daily life activities, as estimated by the Karnofsky Performance Status (KPS) score ≥ 80.

All subjects participated in neuropsychological tests before and following chemotherapy. Digit Spans Tests (DST) were commonly used to quantify the capacity of verbal memory. DST consisted of forward (repeating digits in the order shown) and backward (repeating digits in reverse order as they were displayed) conditions, and probed short-term verbal memory [33]. Verbal Fluency Test (VFT) has frequently been used to evaluate the executive functions both in clinics and research [34,35]. Subjects were asked to name all of the vegetables and fruits they could as quickly as possible within 30 sec in this study.

All subjects were evaluated with Chinese version of Interpersonal Reactivity Index (IRI-C), a test widely used to assess empathy [36-38] both before and following chemotherapy.

Empathy detection paradigm

A total of 120 pictures to indicate a painful or neutral bodily state (all without showing faces) were used for the pain empathy task. The photos were divided into 30 cases, each consisting of four specific images: 1) Left body part in a pain state; 2) left body part in a neutral state; 3) right body part in a pain state; and 4) right body part in a neutral state. Images of pain depicted events that may occur in everyday life. All pictures were matched in brightness and frequency of occurrence [39] (Figure 1A).The pain empathy task was conducted in two consecutive blocks – pain and laterality task – counter-balanced in order across subjects. In the pain task block, the subject was asked to determine if the person in the picture felt pain. In the laterality task block, the subject was required to determine the laterality of the body part in the picture. Each block included 120 trials (60 pains and 60 matched neutral images). Each trial started with a fixation cross and then a blank screen for 400 ms. Next, the picture was shown for 1000 ms, followed by a blank screen that allowed the subject to respond as quickly and accurately as possible (Figure 1B). All pictures were randomly presented and the same pictures were used in both blocks. Before the experiment, participants practiced on the tasks for 20 trials with a different set of images. Participants were given a short break in between the two blocks [37].

ERP recording and analysis

According to the extended International 10/20 system, the electroencephalography (EEG) data were recorded *via*. 64 tin electrodes placed on the scalp using a Neuroscan recording system (NeuroScan, Sterling, VA, USA). The reference electrode was placed at the left mastoid of the subject. And the vertical and horizontal Electrooculograms (EOG) were collected using four electrodes, with vertical EOG recorded on the supraorbital and suborbital regions of the left eye and horizontal EOG on the left versus right orbital rim. All electrode impedances were maintained below 10 kΩ. EEG and EOG activities were amplified with 0.01 Hz to100 Hz band-pass filtering and continuously sampled at 1,000 Hz. De-artifact processing was performed on waveforms with amplitudes greater than ± 100 μV. In epoch of analysis we focused on the data from 200 ms before to 1,000 ms after onset of image presentation.

We performed offline processing of the data as implemented in Neuroscan editing system. Based on the averaged potential of each task condition, the time windows for peak values analysis of N1 and P2 were established. The window was 50 ms to 150 ms for N1, 150 ms to 200 ms for P2. The FZ, FCZ, CZ (2 frontal and 1 central electrodes) were selected for statistical analysis of the ERPs. Greenhouse-Geisser correction was used to correct the P values.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) (version 16.0) was employed for statistical analysis. Student's t-tests were used to analyze continuous variables such as age and years of education. Paired-sample t-tests were used to assess group differences in neurocognitive test and Chinese IRI subscale scores before and after chemotherapy. The reaction time and accuracy rate of pain and laterality tasks were submitted to repeated-measures Analyses of Variance (ANOVAs) with time point (before *vs.* after chemotherapy), task (laterality *vs.* pain task) and valence of stimulus(neutral *vs.* pain)

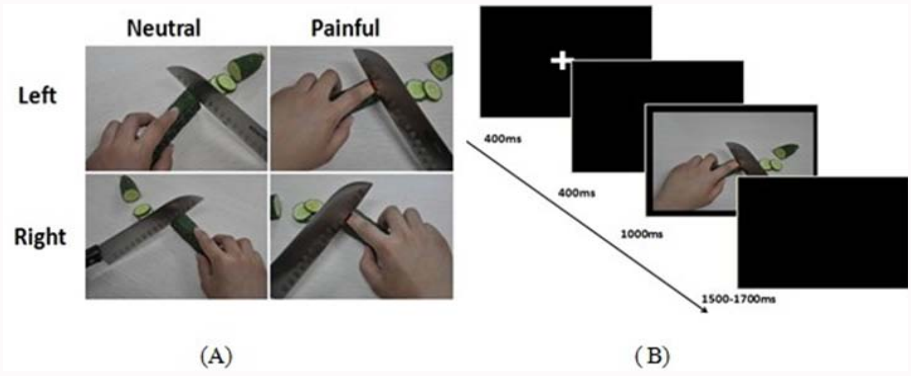

Figure 1: Empathy detection task. A) Examples of pain and neutral stimuli used in study; (B) Timing of stimulus presentation.

as within-subject factors. For the peak values of the two component ERP, ANOVAs were conducted with-subject effects of time point (before *vs.* after chemotherapy), task (laterality *vs.* pain task) and valence of stimulus (neutral *vs.* pain) as well as electrodes (FZ *vs.* FCZ *vs.* CZ). Statistical significance was defined at a level of P<0.05.

Results

Clinical characteristics and neuropsychological tests

The participants ranged from 40 to 65 years with a mean ± SD of 50.2 ± 6.0 years in age. The participants had a mean ± SD of 7.1 ± 3.0 years of education. Participants averaged 85.7 ± 6.0 in KPS (Karnofsky Performance Status) score. Participants received 8.4 ± 2.1 cycles of chemotherapy with EC4-wP4 (10), EC4-wP7 (3), EC4-wP9 (2), TEC × 7 (3), and (CTX+DOX) × 6 (4). (EC: Cyclophosphamide + epirubicin, P: Paclitaxel, W: Weekly; TEC: paclitaxel+ pirarubicin+ cyclophosphamide; CTX: Cyclophosphamide; DOX: doxorubicin).

As shown in Table1, participants performed similarly in Digit Span Forward (t=1.821, p=0.083) and Verbal Fluency test (t=0.388, p=0.702) before and after chemotherapy. Patients showed lower scores in Digit Span Backward test after as compared to before chemotherapy (t=2.134, p=0.045).

In the IRI-C, patients performed similarly on fantasy (t=1.593, p=0.126) and perspective taking (t=1.501, p=0.148) before and after chemotherapy. After as compared to before chemotherapy, patients scored lower on empathic concern (t=3.039, p=0.006) and higher scores in personal distress (t= -2.324, p=0.030) (Table 2).

Picture assessments and behavioral results

The behavioral data, including the Reaction Time (RT) and the Accuracy Rate (AR), are shown in Table 3 and the statistics of ANOVA are shown in Table 4. There was no significant time × stimulus (neutral *vs.* pain) × task (pain *vs.* laterality) interaction for AR (F=0.589, P=0.448). There was a significant main effect of group (BC *vs.* AC) in AR (F=9.943, P=0.005), with patients before chemotherapy showing higher scores than after chemotherapy. For the AR, both task (F=9.678, p=0.005) and stimuli (F= 10.845, p=0.003) main effects were significant, with higher AR in laterality task *vs.* pain task and lower AR for pain *vs.* neutral stimuli. For the RT, there was no statistical significance (F=0.543, p=0.469) before and after chemotherapy. There was a significant task (F=15.540, p=0.001) main effect, but not two-way or three-way interaction effects.

ERP

As shown in Figure 2, the peak amplitude of the N1 component was significantly higher after than before chemotherapy (F (1.21) =38.091, P<0.001). There was a significant time point (before *vs.* after) × stimulus (neutral *vs.* pain) × task (pain *vs.* laterality) interaction (F=5.169, P=0.035) and a significant time point (before *vs.* after) × stimulus (neutral *vs.* pain) interaction (F=11.056, P=0.004) for the N1.

The peak amplitude of the P2 component was significantly lower after than before chemotherapy (F=15.046, P=0.001). The main effect of the stimulus was significant (F=4.889, P=0.039), with the pain stimulus evoking a higher P2 peak compared to neutral stimulus.

The two components did not show other main effects and interaction effects.

Table 1: The performance of neuropsychological test before and after chemotherapy.

	N	VFT	DSF	DSB
Before	22	12.27 ± 2.69	7.91 ± 0.29	4.82 ± 1.56
After	22	12.13 ± 2.47	7.64 ± 0.58	4.18 ± 1.22*

Note: VFT: Verbal Fluency Test; DSF: Digit Span Forward; DSB: Digit Span Backward; *P<0.05. All values are mean ± SD

Table 2: Chinese version of Interpersonal Reactivity Index before and after chemotherapy.

	PT	FS	EC	PD
Before	9.68 ± 3.80	10.14 ± 3.75	11.68 ± 3.64	9.05 ± 4.21
After	9.05 ± 3.46	9.64 ± 2.80	10.27 ± 2.66*	10.14 ± 4.10*

Note: PT: Perspective Taking; FS: Fantasy; EC: Empathic Concern; PD: Personal Distress; *P<0.05. All values are mean ± SD

Table 3: Accuracy Rate (AR) and Reaction Time (RT) in the empathy task before and after chemotherapy.

Outcome	Time point	Laterality Task		Pain Task	
		Neutral	Pain	Neutral	Pain
AR (%)	Before	96 ± 5	0.92 ± 0.05	0.90 ± 0.09	0.81 ± 0.14
	After	0.93 ± 0.11	0.88 ± 0.12	0.91 ± 0.08	0.78 ± 0.17
RT (ms)	Before	644 ± 47	643 ± 45	650 ± 79	664 ± 35
	After	627 ± 43	629 ± 46	670 ± 45	654 ± 68

Note: All values are mean ± SD

Discussion

Empathy, the ability to understand other people's emotions, is achieved by observing and sharing experiences. The present study examined changes in pain empathy in breast cancer patients before and after chemotherapy by using the Chinese version of Interpersonal Reactivity Index and an empathy detection task with concurrent

Table 4: ANOVAs of Accuracy Rate (AR) and Reaction Time (RT).

Time	Task	Stimuli	Time × Task	Time × Stimuli	Task × Stimuli	Time × Task × Stimuli
F=9.943	F=9.678	F=10.845	F=1.221	F=2.729	F=3.822	F=0.598
P=0.005*	P=0.005*	P=0.003*	P=0.282	P=0.113	P=0.064	P=0.448
F=0.543	F=15.540	F=0.056	F=1.603	F=1.549	F=.000	F=1.292
P=0.469	P=0.001*	P=0.815	P=0.219	P=0.227	P=0.991	P=0.269

Note: *P<0.05. Within-subject effects (DF=1, 21)

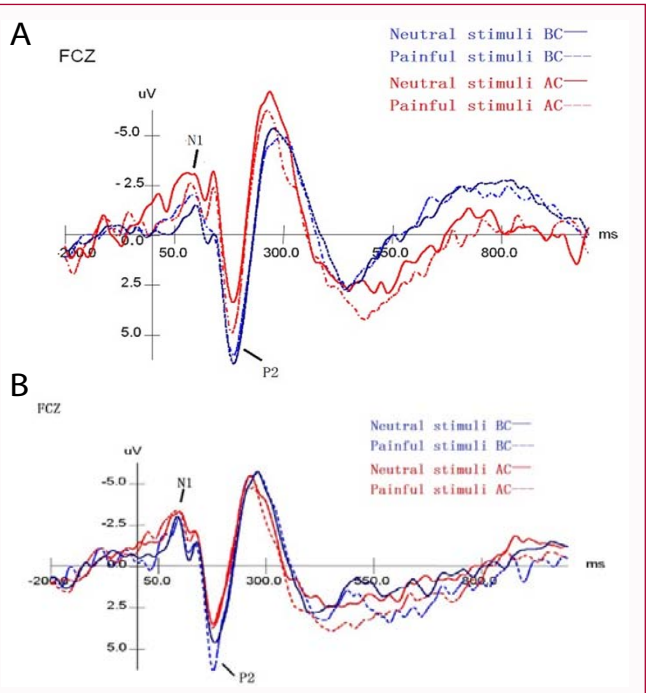

Figure 2: Event-related potentials. The mean ERP amplitude of (A) the laterality and (B) pain task before (BC) and after (AC) chemotherapy. Blue/red lines represent the findings before/after chemotherapy. The solid/dotted lines represent the results of neutral/pain blocks.

recording of ERP. Patients after chemotherapy showed significantly lower scores in Digit Span Backward test, lower empathic concern and higher personal distress as compared to the baseline. During pain and laterality judgments in the empathy task, patients showed lower accuracy rate for pain as compared to neutral images and lower accuracy rate for both pain and neutral blocks after chemotherapy treatment. The ERP study indicated that the peak amplitude of the N1 was significantly higher while the peak value of the P2 was significantly lower after chemotherapy as compared to before chemotherapy.

These findings support impairment of cognitive function and pain empathy among breast cancer patients following chemotherapy. Previous studies have demonstrated that Chemotherapy-Related Cognitive Impairment (CRCI) is associated with dysfunction of the prefrontal cortex and temporal cortex, including the hippocampus [8-10]. Imaging studies suggest that pain empathy is related to the activation of the frontoparietal, temporal, and subcortical regions [16,17,40-42]. It is possible that pain empathy impairment may be related to chemotherapy-elicited functional alterations of these cortical and subcortical structures in breast cancer patients.

The ERP results revealed significant changes in N1 and P2 components after chemotherapy. The N1 component is related to the early stage of emotional perception [37] and visual selective attention [43]. The elevation of N1 peak after chemotherapy may be related to the need of the patients to invest more cognitive resources in emotion, attention and visual perception.

Previous studies have shown that the P2 component is associated with recognition and processing of stimulus features [44,45]. Breast cancer patients showed a significant decrease in P2 amplitude, suggesting that the recognition and processing of stimulus pictures are hindered, after chemotherapy. The main effect of the stimulus on P2 was significant, which indicated that pain as compared to neutral stimuli evoked greater P2 amplitude, consistent with previous studies [46]. As a special physiological experience, pain is of critical significance to human survival. When facing neutral and painful stimuli, individuals tend to be more sensitive to painful stimuli and exhibit higher emotional arousal at the sight of pain in others [47].

Together, the current results suggested that pain empathy was impaired in breast cancer patients following chemotherapy. The study thus provided direct evidence that empathy impairment was part of CRCI in breast cancer. As CRCI could persist for months to years after chemotherapy and negatively impact cognitive aging and quality of life [30,48], more studies are warranted to examine other dimensions of emotional deficits in cancer survivors. In particular, deficits in emotion regulation may affect psychological health, and exacerbate depression and anxiety [49] and interpersonal functioning [50]. Deficits in pain empathy may influence emotion regulation and social interaction in breast cancer survivors.

It should be noted that the present study comprised just a small sample of subjects. Thus, the findings should be considered as preliminary. Future research with a larger sample size and a longitudinal design and perhaps in combination with brain imaging would help replicating the findings and evaluate the neural bases as well as the clinical impact of pain empathy impairment.

In summary, the present study demonstrated empathy impairment in breast cancer patients after chemotherapy. The findings extend the list of chemotherapy-induced cognitive and affective dysfunction in breast cancer.

Funding

This research was supported by the National Natural Science Foundation of China (Grant No. 81872504).

References

1. DeSantis CE, Ma J, Sauer AG, Newman LA, Jemal A. Breast cancer statistics, 2017, racial disparity in mortality by state. CA Cancer J Clin. 2017;67(6):439-48.

2. Goto W, Shinichiro K, Koji T, Yuka A, Tak K, Fujita H, et al. Significance of intrinsic breast cancer subtypes on the long-term prognosis after neoadjuvant chemotherapy. J Transl Med. 2018;16(1):307.

3. Wefel JS, Janette V, Tim A, Sanne BS. International cognition and cancer task force recommendations to harmonise studies of cognitive function in patients with cancer. Lancet Oncol. 2011;12(7):703-8.

4. Kovalchuk A, Yaroslav I, Rocio RJ, Svitlana S, Stepan M, Igor P, et al. Chemo brain or tumor brain - that is the question: the presence of extracranial tumors profoundly affects molecular processes in the prefrontal cortex of tumor graft mice. Aging (Albany NY). 2017;9(7):1660-76.

5. Christine DC, Bradley JM, John HF, Dana MC. Cognitive impairment in gynecologic cancers: A systematic review of current approaches to diagnosis and treatment. Support Care Cancer. 2014;22(1):279-87.

6. Andryszak P, Monika W, Paweł I, Bogdan Ż. A systemic literature review of neuroimaging studies in women with breast cancer treated with adjuvant chemotherapy. Contemp Oncol (Pozn). 2017;21(1):6-15.

7. Biegler KA, Chaoul MA, Cohen L. Cancer, cognitive impairment, and meditation. Acta Oncol. 2009;48(1):18-26.

8. McDonald BC, Susan KC, Dori JS, John DW, Andrew JS. Frontal gray matter reduction after breast cancer chemotherapy and association with executive symptoms: A replication and extension study. Brain Behav Immun. 2013;30(Suppl):S117-25.

9. Sabine D, Frederic A, Ann S, Ronald P, Alexander L, Wim VH, et al. Longitudinal assessment of chemotherapy-induced structural changes in cerebral white matter and its correlation with impaired cognitive functioning. J Clin Oncol. 2012;30(3):274-81.

10. Li X, Haijun C, Yue L, Herta HC, Liang G, Chiang-Shan RL, et al. Diminished gray matter density mediates chemotherapy dosage-related cognitive impairment in breast cancer patients. Sci Rep. 2018;8(1):13801.

11. Bernhardt BC, Singer T. The neural basis of empathy. Annu Rev Neurosci. 2012;35:1-23.

12. Coll MP, Essi V, Markus R, Giorgia S, Claus L, Caroline C, et al. Are we really measuring empathy? Proposal for a new measurement framework. Neurosci Biobehav Rev. 2017;83:132-9.

13. Caruana F, Jezzini A, Beatrice SF, Giacomo R, Vittorio G. Emotional and social behaviors elicited by electrical stimulation of the insula in the macaque monkey. Curr Biol. 2011;21(3):195-9.

14. Rogers-Carter MM, Juan AV, Katherine BG, Anne FP, Morgan TM, Maureen R, et al. Insular cortex mediates approach and avoidance responses to social affective stimuli. Nat Neurosci. 2018;21(3):404-14.

15. Christov-Moore L, Elizabeth AS, Gino C, Grigaityte K, Iacoboni M, Ferrari PF. Empathy: Gender effects in brain and behavior. Neurosci Biobehav Rev. 2014;46(Pt 4):604-27.

16. Singer T. The neuronal basis and ontogeny of empathy and mind reading: Review of literature and implications for future research. Neurosci Biobehav Rev. 2006;30(6):855-63.

17. Zaki J, Ochsner KN. The neuroscience of empathy: Progress, pitfalls and promise. Nat Neurosci. 2012.15(5):675-80.

18. Vachon-Presseau E, Roy M, Martel MO, Albouy G, Chen J, Budell L, et al. Neural processing of sensory and emotional-communicative information associated with the perception of vicarious pain. Neuroimage. 2012;63(1):54-62.

19. Timmers I, Anna LP, Molly DF, Corey AK, Lauren CH, Maya JH, et al. Is empathy for pain unique in its neural correlates? A meta-analysis of neuroimaging studies of empathy. Front Behav Neurosci. 2018;12:289.

20. Luo P, Pang Y, Li B, Jie J, Zhuang M, Yang S, et al. Competitive intensity modulates the pain empathy response: An event-related potentials study. Front Psychol. 2018;9:1854.

21. Coll MP. Meta-analysis of ERP investigations of pain empathy underlines methodological issues in ERP research. Soc Cogn Affect Neurosci. 2018;13(10):1003-17.

22. Levy J, Goldstein A, Maayan P, Ruth F. Maturation of pain empathy from child to adult shifts from single to multiple neural rhythms to support interoceptive representations. Sci Rep. 2018;8(1):1810.

23. Fan Y, Han S. Temporal dynamic of neural mechanisms involved in empathy for pain: An event-related brain potential study. Neuropsychologia. 2008;46(1):160-73.

24. Liu Y, Meng J, Yao M, Qian Y, Bi F, Weiwei P. Hearing other's pain is associated with sensitivity to physical pain: An ERP study. Biol Psychol. 2019;145:150-8.

25. Thompson RA. Emotion regulation: A theme in search of definition. Monogr Soc Res Child Dev. 1994;59:25-52.

26. Maher EJ, Fenlon D. The psychosocial issues of survivorship in breast cancer. Adv Breast Cancer. 2010;7(2):17-22.

27. Conley CC, Bishop BT, Andersen BL. Emotions and emotion regulation in breast cancer survivorship. Health-care (Basel). 2016;4(3):56.

28. Peh CX, Kua EH, Mahendran R. Hope, emotion regulation, and psychosocial well-being in patients newly diagnosed with cancer. Support Care Cancer. 2016;24(5):1955-62.

29. Lu Q, Tsai W, Chu Q, Jing X. Is expressive suppression harmful for Chinese American breast cancer survivors? J Psychosom Res. 2018;109:51-6.

30. Tang L, Fritzsche K, Leonhart R, Ying P, Jinjiang L, Lili S, et al. Emotional distress and dysfunctional illness perception are associated with low mental and physical quality of life in Chinese breast cancer patients. Health Qual Life Outcomes. 2017;15(1):231.

31. Greer JA, William FP, Elyse RP, Thomas JL, Jennifer ST. Behavioral and psychological predictors of chemotherapy adherence in patients with advanced non-small cell lung cancer. J Psychosom Res. 2008;65(6):549-52.

32. Satin JR, Linden W, Phillips MJ. Depression as a predictor of disease progression and mortality in cancer patients: A meta-analysis. Cancer. 2009;112(22):5349-61.

33. Baddeley A. Working memory and language: an overview. J Commun Disord. 2003;36(3):189-208.

34. Steiner VAG, Leticia LM, Sonia MDB, Ricardo N. Phonemic verbal fluency and age: A preliminary study. Dement Neuropsychol. 2008;2(4):328-32.

35. Andryszak P, Monika W, Bogdan Ż, Paweł I. Verbal fluency in breast cancer patients treated with chemotherapy. Breast Cancer. 2017;24(3):376-83.

36. Zhang F, Yi D, Kai W. Reliability and validity of the Chinese version of the interpersonal reactivity index-C. Chinese J Clin Psychol. 2010;8:155-7.

37. Yang J, Hu X, Li X, Zhang L, Dong Y, Li X, et al. Decreased empathy response to other people's pain in bipolar disorder: Evidence from an event-related potential study. Sci Rep. 2017;7:39903.

38. Massey SH, Daniel S, Eva CA, Julie EP, Derin JC, Lei W, et al. Cortical thickness of neural substrates supporting cognitive empathy in individuals with schizophrenia. Schizophr Res. 2017;179:119-24.

39. Gu X, Xun L, Kevin GG, Thomas PN, Patrick RH, Jin F. Functional dissociation of the front insular and anterior cingulate cortices in empathy for pain. J Neurosci. 2010;30(10):3739-44.

40. Kral TRA, Solis E, Mumford JA, Schuyler BS, Flook L, Rifken K, et al. Neural correlates of empathic accuracy in adolescence. Soc Cogn Affect Neurosci. 2017;12(11):1701-10.

41. Rutgen M, Seidel EM, Silani G, Riečanský I, Hummer A, Windischberger C, et al. Placebo analgesia and its opioidergic regulation suggest that empathy for pain is grounded in self pain. Proc Natl Acad Sci U S A. 2015;112(41):E5638-46.

42. Lamm C, Decety J, Singer T. Meta-analytic evidence for common and distinct neural networks associated with directly experienced pain and empathy for pain. Neuroimage. 2011;54(3):2492-502.

43. Yuan J, He Y, Lei Y, Yang J, Li H. Event-related potential correlates of the extraverts' sensitivity to valence changes in positive stimuli. Neuroreport.

2009;20(12):1071-6.

44. Schulz C, Kaufmann JM, Kurt A, Schweinberger SR. Faces forming traces: Neurophysiological correlates of learning naturally distinctive and caricatured faces. Neuroimage. 2012;63(1):491-500.

45. Kaufmann JM, Schulz C, Schweinberger SR. High and low performers differ in the use of shape information for face recognition. Neuropsychologia. 2013;51(7):1310-9.

46. Ikezawa S, Corbera S, Wexler BE. Emotion self-regulation and empathy depend upon longer stimulus exposure. Soc Cogn Affect Neurosci. 2014;9(10):1561-8.

47. Mazza M, Pino MC, Mariano M, Daniela T, Michele F, De Berardis D, et al. Affective and cognitive empathy in adolescents with autism spectrum disorder. Front Hum Neurosci. 2014;8:791.

48. Vega JN, Dumas J, Newhouse PA. Cognitive effects of chemotherapy and cancer-related treatments in older adults. Am J Geriatr Psychiatry. 2017;25(12):1415-26.

49. Mennin DS, Holaway RM, Fresco DM, Moore MT, Heimberg RG. Delineating components of emotion and its dysregulation in anxiety and mood psychopathology. Behav Ther. 2007;38:284-302.

50. Webb TL, Miles E, Sheeran P. Dealing with feeling: A meta-analysis of the effectiveness of strategies derived from the process model of emotion regulation. Psychol Bull. 2012;138(4):775-808.