

# Positive affect, well-being and the human conserved transcriptional response to adversity: a descriptive review

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## Abstract

The theoretical and philosophical foundations of human well-being are well-described in psychology research. Within the construct of well-being, psychologists distinguish eudemonic positive affect and hedonic positive affect, although they are not only nor mutually exclusive approaches. Empirical findings demonstrate a correlation between the general positive affect and favorable health outcomes. Recent discoveries also show a biological pattern, which underlines the correlation. Thanks to describing the conserved transcriptional response to adversity (CTRA) mechanism, a new direction of research is emerging, exploring a relationship between profile of gene expression in immune cells and positive affect.

**Keywords:** well-being · eudemonic positive affect · hedonic positive affect · CTRA

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## Introduction

While the injurious effects of chronic stress on the human body are well-known and described in the literature [1], the question of the impact of positive psychological processes on health still requires thorough investigation. Physiological mechanisms that underlie the correlation between positive

affect and improved health results are particularly underdescribed. In recent studies the evidence is becoming apparent that there is an explicit link between positive affect and health involving reduced psychobiological activation of immune, neuroendocrine, autonomic and inflammatory pathways [2].

Positive affect, defined as experiencing emotional states which are positive in valence, can be distinguished

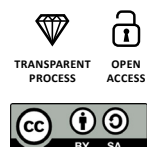
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between hedonic affect and eudaimonic affect. Hedonic positive affect describes experiencing positive feelings such as happiness, contentment, pleasure with low intensity of negative emotions and high life satisfaction. Eudaimonic positive affect describes also emotions such as vitality, curiosity and engagement that accompanies the movement towards one's potential, beyond simple self-gratification [3]. Experiencing eudaimonic/hedonic positive affect translates into the person's eudaimonic/hedonic well-being (respectively). Hedonic versus eudaimonic well-being has been found to be associated with differing inflammatory gene expression profiles in leukocytes from healthy individuals [4]. Similar in their affective and behavioral correlates, hedonia and eudaimonia are seen to have highly divergent transcriptome profiles, namely, they differ in up-regulated expression of proinflammatory genes, down-regulated expression of genes involved in antibody synthesis, and down-regulated expression of genes mediating type I IFN responses [4].

The aim of this paper is to present research that has been conducted so far in the field of positive affect and its link with psychobiological processes in human body. We provide a closer look into the literature to determine a body of existing knowledge and reveal interpretable patterns and trends in a collective field of physiology and psychology.

## Materials and methods

To find studies for inclusion in this review, we searched PubMed and Web of Science. Searches were narrowed down to human studies both in English and Polish language. The search was conducted by applying the following terms: "conserved transcriptional response to adversity," "positive affect," "eudaimonic well-being," "hedonic well-being." Also, we screened the reference lists of selected publications for additional sources.

## Results

The search retrieved 38 full text articles. After screening, 12 articles were included in the analysis.

## Discussion

### The CTRA mechanism

Conserved transcriptional response to adversity (CTRA) is a physiological pattern, arbitrated by the sympathetic nervous system "fight-or-flight" response. Within

the pattern, upregulated expression of genes involved in inflammation and downregulated expression of genes involved in Type I interferon responses, is observed [5]. When a person is exposed to prolong hostile environmental conditions (such as loss, trauma, etc.) central nervous system is affected. The "fight-or-flight" stress response is activated from the sympathetic nervous system and it is followed by releasing a neurotransmitter, which is norepinephrine. These signals result in the activation of intracellular second messenger systems which have different effect on numerous transcription control pathways. At the time, the upregulated transcription of pro-inflammatory genes and downregulated transcription of Type I interferon antiviral genes, is observed [5]. Teleological analyses proposed that the CTRA's adaptive implication is that it turns the fundamental anti-microbial stance of the immune system away from its baseline condition of counteracting viral infections (also other intracellular pathogens, which are mediated by Type I interferons and cellular immune responses) and directs the system toward a more pro-inflammatory activity that would give an optimum level of defense against bacterial infections and tissue damage related to injury wounds [6]. In ancestral times, when threat experiences were intense but temporary, activation of such a molecular defense by the sympathetic nervous system (in response to potential or perceived threat) guaranteed a mechanism for expecting changing microbial exposures and taking advantage of an impact of microbial exposure. Nowadays, when a human being is under a circumstance of more chronic low-grade threat, the CTRA pattern, by promoting chronic low-grade inflammation, seems to be conducive to the development of inflammation-related diseases (e.g. cardiovascular disease, neurodegenerative disease, neoplastic disease) [5]. In the studies presented below, when mentioning examination of the CTRA mechanism, gene expression levels were assessed in peripheral blood samples, and it is noteworthy that all analyses were conducted at the UCLA Social Genomics Core Laboratory which makes the results highly comparable and reliable (as the same protocols and methods were used to analyse all of the blood samples).

### CTRA and psychological dimensions

Fredrickson et. al [4] focused on the biological implications (changes in the CTRA gene expression) of hedonic and eudaimonic well-being in a group of 80 healthy Americans (35 to 64 years of age) and revealed a correlation between eudaimonia and decreased expression of the CTRA mechanism, the correlation between hedonic well-being and significant up-regulation of the CTRA mechanism as well as that CTRA transcriptome profile was not different as a function of overall well-being (hedonic plus eudaimonic). In this

research CTRA gene expression was significantly down-regulated in a group of individuals showing a relative dominance of eudaimonia vs. hedonia, therefore gene regulatory architecture of the response of individuals' immune system may be more sensitive to the eudaimonic well-being vs. hedonic well-being as a source of human happiness than are conscious experiences.

In order to verify whether the findings described above extended to non-Western cultures, Lee et. al [7] examined a group of 152 healthy Korean adults. Their outcomes were consistent with those published by Fredrickson et. al [4] and showed significant correlation between eudaimonic well-being and CTRA in the Korean cohort. Furthermore, they indicated that the correlation between eudaimonia and CTRA is evident to become higher with age.

A relationship between dispositional optimism (defined as one's personality trait which inclined them towards positive expectations) and CTRA gene expression has been examined [8]. In a sample of 114 male Japanese workers, it was found that individual differences in optimism were inversely associated with CTRA expression. The results are consistent with the outcomes published by Kitayama et al. [9], where general eudaimonic well-being was associated with lower CTRA gene expression while general hedonic well-being was associated with higher CTRA gene expression in a group of 106 male workers of a Japanese IT company.

These results, which describe the link between general eudaimonia with CTRA, are consistent with one of studies conducted among highly involved videogame players (those who present significantly strong engagement with virtual world) [10]. The researchers have shown that higher level of a gamer's eudaimonic well-being is linked to lesser genomic dysregulation in CTRA mechanism and that the eudaimonia-CTRA correlation is strongest among the most highly involved players. The authors also performed more detailed follow-up analyses and investigated the social and psychological aspects of eudaimonia and their influence on CTRA mechanism. Consistent with the authors' hypothesis, their results showed a stronger association between social well-being with lessened expression of CTRA than with psychological well-being and the hedonia did not show statistical significance with the CTRA. The sample consisted of 56 avid online videogame players, which is a limitation, nevertheless it suggests that committed social activity may help reduce CTRA expression.

A study based on a similar notion, namely that prosocial behavior is linked to lifespan [11-12] and that might be mediated by the pathway which implicates changes in gene expression, which consequently may affect disease development (or resistance), examined changes in CTRA in 159 adults. They were randomly divided into 4 groups

and for 4 weeks, they engaged in either prosocial behavior directed towards specific people, or prosocial behavior directed towards the world in general or self-focused kindness or a neutral control task [13]. As expected in a randomized study, kindness-to-world, kindness-to-other, kindness-to-self and the control groups showed no difference in average sex, race/ethnicity, age, current illness symptoms, nor the initial level of CTRA gene expression. The analyses showed significant decrease in CTRA gene expression in the kindness-to-other group over time. The decrease was not observed in any other group. This study adds to the body of research that points out the importance of the social well-being dimension of eudaimonia in the CTRA gene expression.

Slightly different outcomes were observed in a study of 18 volunteers (aged 50+), placed in a third-grade kindergarten classroom, where their task was to work with students on academic skill development (e.g. reading proficiency and math) for 9 months [14]. Analyses, which were conducted at the baseline and the 9-month follow-up, revealed the correlation between measure of individual decrease in CTRA mechanisms with the measure of individual increase in eudaimonia over time. It is necessary to point out that the social component of eudaimonia increased significantly from base level to the 9-month follow-up, while the psychological component demonstrated no significant change over time, and neither of the components correlated significantly with change over time in CTRA mechanism. Only total of social and psychological components of eudaimonia was prognostic for CTRA gene expression changes.

Another study which analyzed the link between eudaimonic well-being and CTRA, though from a different perspective, examined the strength of CTRA in relation to loneliness [15]. In this study loneliness, defined as social isolation, was a risk factor, while eudaimonic well-being was a resilience factor. Data was collected from 108 community-dwelling older adults (mean age 73), and contain blood samples and an assessment of loneliness and eudaimonic well-being via psychological scales. In separate analysis, the results showed up-regulation of CTRA gene expression in association with loneliness and down-regulation in association with eudaimonia. In joint analyses, loneliness' effect was fully abrogated while eudaimonia continued to be associated with CTRA down-regulation. The results were independent of behavioral and demographic health-related risk factors. Reviewing outcomes and conclusions of the studies, a question about the direction of the association appears. Nevertheless, a person with lower CTRA might be psychosomatically healthy in ways that enhance their social relations, hence also their eudaimonic well-being.

## CTRA, affect and health implications

The CTRA pattern also has been found to be associated with adverse hematopoietic stem-cell transplantation (HCT) clinical outcomes. A group of 78 HCT recipients who differed with socioeconomic status (SES) were compared in terms of pretransplant leukocyte CTRA gene expression. Data compiled from peripheral blood mononuclear cells collected pre-HCT from low SES patients showed significant CTRA upregulation compared with paired HCT individuals of high SES [16]. According to the literature, individuals with low SES have higher likelihood of being depressed [17] and it is necessary to consider that in depression the positive affect is significantly reduced [18].

Chronic adversity and distress triggers cancer initiation, progression and cancer metastasis, also plays an unfavorable role for anti-tumor immune function and therapy response [19]. Due to that, relationships between cognitive behavioral stress management (CBSM), disease-free survival (DFS), and CTRA have been investigated among breast cancer patients. CBSM is an empirically-validated group-based psychosocial intervention which assures greater DFS vs. a control condition. It builds an individual's emotional skills (e.g. positive coping skills, a high sense of coping self-efficacy), which works in favor of positive affect. The research revealed that patients (n = 28) randomized to the CBSM group (10-weeks program) showed lesser change in CTRA gene expression, while patients randomized to the control group (n = 23) showed increased CTRA expression in 6-12-month period. What is more, greater 6-12 month CTRA increases were associated with shorter DFS over 8-15 years of follow-up [20].

Another study of breast cancer survivors confirms that eudaimonic positive affect may be a significant mechanism in interventions intended to enhance health in vulnerable groups. A group of 22 women completed self-report surveys and provided blood samples before and after a 6-week mindfulness meditation practice [21]. This study demonstrated that increases in eudaimonic positive affect were correlated with a rise in the inversely weighted CTRA subcomponent connected to antiviral response. Interestingly, changes in eudaimonic positive affect were not significantly associated with changes in the pro-inflammatory CTRA subcomponent. Also, the study indicated no significant association between hedonic positive affect, nor depressive syndromes with overall CTRA gene expression. Nevertheless, there are findings of Antoni et al. [22] which suggest that negative affect is related to the pro-inflammatory, but not the antiviral component of the CTRA among breast cancer survivors.

It is necessary to bear in mind that hedonia and eudaimonia are not reciprocally exclusive approaches to happiness. Both, eudaimonic well-being and hedonic well-being,

have common origins (e.g. recognized social connections) [23] and can have an effect on each other [23], i.e., positive affect inclines people to find positive meaning [24-25] and finding positive meaning causes a growth of positive affect [26].

## Conclusions

CTRA is a significant framework for an understanding of psychoneuroimmunology relationships. It links a micro-level biology of illness and health with a macro-level of psychosocial processes. A possible neuroimmunological mechanism involved in the interactions of immune function and social behavior is a dopamine signaling, as it plays an important role in behavioral and brain development [27].

There is a growing body of literature examining the link between well-being and CTRA gene expression. However, it is necessary to acknowledge limitations of the presented studies, which include small sample size, lack of control group in some studies, short duration of the studies and lack of extended follow-ups. It is necessary to conduct further research of the CTRA components and its psychological correlates in order to accurately understand the pathway between positive affect/well-being and the CTRA mechanism. The understanding of the association could be especially beneficial for clinical groups including patients with inflammation related diseases, as CTRA gene expression is indicative of greater expression of proinflammatory genes and hence greater inflammation process. Further research conducted in that field could be a promising support in the treatment process. At present, it is necessary to be careful in interpreting the link between CTRA expression and clinical health outcomes, as the majority of studies contain no measures of clinical health outcomes at all. Questions about other potential variables mediated in the process still need to be investigated, as for the time being, drawing more general conclusion is limited. Heretofore, we can conclude that there is no biological toxicity in experiencing overall well-being, and the various routes of experiencing positive affect/well-being have distinct biological correlates.

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## Conflicts of interests

None.

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