



Lymphocyte subsets are influenced by positivity levels in healthy subjects before and after mild acute stress



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ABSTRACT

In the current study, the possible association of positivity (POS), recently defined as general disposition to view life under positive outlook, with immune markers and post-stress modifications, was analyzed.

Circulating lymphocyte subsets and serum cytokine levels were evaluated before and after a standard mild acute stress test, in 41 healthy students, previously selected by a questionnaire for their level of POS (high [POS-H] and low [POS-L]).

The CD3⁺ and CD4⁺ cell frequency was higher in the POS-H students before and after acute stress. CD4⁺ subpopulation analysis revealed baseline higher terminally differentiated frequency in the POS-H, whereas higher effector memory frequency was present in the POS-L students. Moreover, the frequency of post-stress B cells was higher in the POS-H students.

The mild-stress test was associated to an increase of the IL-10 mean values, while mean values of the other cytokines tested did not change significantly.

It is tempting to speculate that IL-10 may work as biomarker of response to acute mild stress and that POS-H may be associated to a better capacity of the immune system to contrast the disturbing effects of mild acute stress. Yet further studies on lymphocyte subset absolute number and function of larger and different populations are needed to definitively prove these preliminary observations.

1. Introduction

A growing body of research is focusing on the role that individual differences in personality may play in promoting health and in moderating vulnerability to adversities and illness. Whereas personality can be viewed as the self-regulating system accounting for the manifold ways people manage themselves and interact with the outside world, individual differences in traits, self-beliefs, attitudes and habits are in various degree associated to biological variations affecting health and well-being.

Several authors have pointed to a number of self-referent constructs like self-esteem [1], life satisfaction [2,3], and optimism [4,5] as

psychological assets that are crucial to manage the changes that occur in people's physical and psychological functioning during the course of their lives.

Likely people who are convinced of their own worth are satisfied with their lives, and expect that their future will be full of rewarding experiences, are better equipped to cope with adversities and to benefit of rewarding experiences than those who, on the contrary, are self-doubting, unsatisfied with their lives and worried about the future.

Indeed, self-esteem, optimism and life satisfaction not only are all associated to a variety of positive outcomes and highly correlated to each other, but rest upon a common basis. Earlier findings from cross-cultural and twin studies have shown that standard measures of self-

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esteem, optimism and life satisfaction can be traced to a common latent factor [6–8], which was first named “positive orientation” and then “positivity” (POS). Heritability accounted for about 70% of variance of this latent factor whereas unshared environment accounted for the remaining 30%.

Subsequent findings have documented the close association of POS with a large variety of positive outcomes including social adjustment, psychological well-being and health [9–11]. The development of the POS scale [12], namely a direct measure of POS, has been followed by several studies that have corroborated its pervasive impact over well adjustment and well-being and further supported the view of POS as a basic disposition that it is needed to grow and to manage human existence despite adversities, failures and loss [7,13].

Longitudinal findings have corroborated a concept that posits POS stays at the basis of “positive affect” (PA) over the course of development. This is particularly worth of note since PA has been associated with many positive healthy outcomes through its apparent effects on social relationship [14], cognition [15], coping [16], and resiliency [17], as well as because of its associations with various physiological functions (e.g., cardiovascular, endocrine, and immune systems [18,19]).

POS resulted uniquely and pervasively associated to brain structures’ activation in the posterior cingulate, that are essential for integrating self referential thought and biographic memories and for assigning a positive valence to one’s experience [20].

POS proved to moderate the impact of cancer severity on the quality of life of patients [21] and the negative impact of aging on health problems as reported by old people [22].

In all above studies self esteem, life satisfaction and optimism showed limited or no impact once POS was taken under control.

The current study has been conceived to investigate the relationship of POS with immune system before and after mild/acute stress. Freier et al. [23] showed that acute psychological stress alerts the adaptive immune response by inducing a reduction of peripheral CD4 and CD8 naïve (N) and CD8 central memory (CM) T cell subsets, while CD4 effector memory (EM) and CD8 terminally differentiated (TD) T cells remained stable or increased. Interestingly, peripheral T regulatory cells (Tregs) decreased. Moreover, transiently reduced natural killer (NK) cell cytotoxicity has been found associated with moderate life stress [24]. Edwards et al. [25] observed increased antibody response to the T-dependent influenza and to the T-independent meningococcal polysaccharide vaccine antigens [26] after acute mental stress in healthy people.

Likely, individual differences in personality can moderate the immune response to stress. Previous studies have pointed to an association of PA with secretory IgA specific response [27]. Moreover, an association of optimism with cell-mediated immunity has also been observed, within-person changes in optimism being able to predict changes in cell-mediated immunity, as explored through delayed-type hypersensitivity skin tests [28]. Patients with temporo-mandibular disorders high in optimism showed smaller increase in stress-induced IL6 levels and normal subjects ranking high in optimism displayed enhanced antibody response to the polysaccharide typhoid vaccine after exposure to acute psychological stress [29–31]. However, despite several studies underline the positive effect of optimism on immunity, other studies document instead a negative effect, especially in presence of difficult (e.g., complex, persistent, and uncontrollable) stressors [32]. No study, to our knowledge, has examined POS so far. Yet we believe that most individual differences in POS, as a basic vital disposition, may help to clarify the associations between personality and immune system and how they may affect each other under various situations. On this assumption, the present study examined the frequencies of peripheral blood NK, B and T lymphocyte subsets and of serum Th1/Th2 cytokine levels in 41 healthy subjects scoring high (POS-H) or low (POS-L) in POS before and after an acute mild stress procedure.

2. Materials and methods

2.1. Participants

Forty-one students (51.2% females) took part in this study. Participants were selected on a sample of 300 students of the Medical School at Sapienza University of Rome because of their POS level (M Age = 21.49 years, SD = 1.24) scored as previously described [12]. Ten students were smokers (6 in POS-H subgroups and 4 in POS-L subgroups), 11 students practiced physical activity (8 in POS-H subgroups and 3 in POS-L subgroups), the average body mass index (BMI) was 22.2 (22.1 in POS-H subgroups and 22.5 in POS-L subgroups).

The Ethics Committee of the S. Andrea University Hospital approved the study (approval number 353/12).

Participants received all measures by mail and returned them after completion. Youths’ consents, as well as approval from University councils, were obtained. Experimenters informed participants that their responses would be confidential and offered clarification regarding the variables measured. Participants were asked to complete the scales independently of others. The POS scale was used to select participants enrolled in the study. Participants rated (1 = strongly disagree, to 5 = strongly agree) their responses on items of the P-Scale [12]. Inclusion criteria were POS mean level > 75th percentile or POS mean level < 25th percentile. Subjects meeting the inclusion criteria were contacted by phone and invited to participate in the study, for which they received a small payment. Ultimately 12 POS-H and 8 POS-L females, and 11 POS-H and 10 POS-L males accepted to participate to the subsequent session of the study.

2.2. Procedure

The Trier Social Stress Test (TSST) is designed to exploit the vulnerability of the stress response to socially evaluative situations [33]. The TSST is one of the most prominent and well-validated stress induction measures used in immunological research. The period of induced stress lasted approximately 15 min, and was divided into 5-min components. Before the test start, the participant was fitted with a butterfly needle for collecting blood. Stress induction started with the participant being taken into a room, where a panel of three judges was waiting. The first 5-min component was the anticipatory stress phase, during which the judges asked the participant to prepare a 5-min presentation. In most studies this presentation was framed as part of a job interview. In addition the judges had been trained to maintain neutral expressions throughout the test. The participants were allowed to use paper and pen to organize their presentation, but this paper was then unexpectedly taken away from them when it was time to begin the presentation. During the 5-min presentation component, the judges observed the participant without comment. If the participant did not use the entire 5 min, they asked him or her to continue. This went on until the entire 5 min had been used. The presentation was immediately followed by the mental arithmetic component, during which the participant was asked to count backwards from 1022 in steps of 13. If a mistake was made, then they had to start again from the beginning. This component lasted for 5 min and was followed by a recovery period. Immediately after the test there was a debriefing, in which the participant was told that the purpose of the test was to create stress, and that the results were in no way a reflection on his or her personal abilities. The blood was collected 20 min after the end of the stress procedure.

2.3. Lymphocyte subpopulations (Immunofluorescence and analysis)

Peripheral blood mononuclear cells (PBMCs) were isolated from heparinized whole blood by density gradient centrifugation using Ficoll-hypaque (Bio-Lynx, Brockville, Canada) and washed three times

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