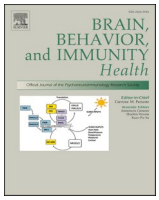
Brain, Behavior, & Immunity - Health 37 (2024) 100748

Contents lists available at ScienceDirect

Brain, Behavior, & Immunity - Health

journal homepage: www.editorialmanager.com/bbih/default.aspx



Optimism as a key factor in coping with the common cold

S. Puig-Perez [a,*], M.W. Kozusznik [b], M.M. Pulopulos [c]

[a] Sara Puig Pérez: Research Group for Psychology and Quality of Life (PsiCal), Valencian International University, Valencia, Spain
[b] Malgorzata Wanda Kozusznik: Department of Marketing, Innovation and Organization, Ghent University, Belgium
[c] Matias Miguel Pulopulos Tripiana: Department of Experimental Clinical and Health Psychology, Ghent University, Belgium

ARTICLE INFO

Keywords:
Optimism
Common cold
Jackson symptoms
Immune system

ABSTRACT

Objective: The optimism trait is considered one of the most important psychological factors in protecting and promoting health. This study aims to investigate whether trait optimism may help to cope better with the common cold by reducing the subjective perception of cold symptoms and affecting the immune response.
Methods: To do so, 212 volunteers from the Pittsburg Cold Study 3 within the Common Cold Project were exposed to Rhinovirus (RV39). On the 5 days following the inoculation, a daily symptoms scale, nasal wash, and blood samples were collected to assess Jackson Symptoms (nasal congestion, sneezing, runny nose, sore throat, cough, headache, chills, and malaise) and control the Immune System response to infection (concentrations of interleukin (IL)-1β, IL-6, IL-8, IL-10, tumour necrosis factor (TNF)-α, and interferon (IFN)-α).
Results: Results showed that approximately 30% of the inoculated participants were finally diagnosed with a common cold, showing higher Jackson Symptom severity and Immune System Response (IL-1β, IL-6, IL-8, IL-10, TNFα and IFNα). Importantly, moderation regression analyses showed that higher optimism scores were related to lower Jackson Symptom severity and TNFα response to infection in cold-diagnosed participants.
Conclusions: Our results provide important evidence for the protective role of optimism, a trait factor that promotes a better perception of wellbeing and less need for immune system resources to successfully cope with the common cold.

1. Introduction

Acute upper respiratory tract viral infections (URTIs) such as the common cold are some of the most common diseases in humans, and they are diagnosed between two to five times per year in adults (Johnston and Holgate, 2012). A total of 8 respiratory symptoms were identified by Jackson et al. (1958) as characteristic of the common cold that peak for around 2–3 days out of the 7–10 days the cold usually lasts (Eccles, 2005). Interestingly, increasing evidence shows psychological changes associated with URTIs, which are caused by the interaction of cytokines on the central nervous system (Mahoney and Ball, 2002).

Expecting good outcomes in the future may result in experiencing the situation with more positive feelings (Carver et al., 2010), which affects successful coping with environmental demands. How does optimism may affect health? First, optimism may acts on psychophysiological health by increasing health-promoting behaviours (e.g. Nabi et al., 2010; Giltay et al., 2006). In addition, it has been suggested that high optimism may interact with psychological constructs that are related to health promotion (Puig-Perez et al., 2018; Carver et al., 2010). Finally, the effect of optimism on stress perception and coping strategies in stressful situations may affect the functioning of main physiological systems promoting adaptive functioning (Puig-Perez et al., 2015, 2017; Brydon et al., 2009). Considering the suggested protective role of optimism in promoting health maintenance, it is important to explore its relevance in one of the most common physiological challenges, URTIs.

Taking into account that enduring stress situations elicit immune alterations (Miller and Cohen, 2001), the relationship between optimism and the immune system has been explored in response to stress. High optimism has been found to be related to lower interleukin-6 (Brydon et al., 2009), but a higher lymphocyte cell (Segerstrom et al., 1998; Cohen et al., 1989), T helper, and natural killer cell (NKC) (Segerstrom et al., 1998) response to acute stress. However, this relationship might depend on the persistence of the stressor. When stress exposure lasted less than one week, optimism was related to keeping high T cell concentrations in blood; whereas with longer stressors, a significant decline in helper T cell and NKC was related with high optimism (Cohen et al., 1999). In addition, the perception of control of the stressful stimuli may affect the relationship between optimism and the immune response. In

* Corresponding author. Valencian International University, Calle Pintor Sorolla, 21, 46002, Valencia, Spain.
E-mail address: sara.puig@professor.universidadviu.com (S. Puig-Perez).

https://doi.org/10.1016/j.bbih.2024.100748
Received 18 October 2023; Received in revised form 19 February 2024; Accepted 26 February 2024
Available online 8 March 2024

this regard, Sieber et al. (1992) showed that optimistic participants who perceived the situation as controllable showed higher NKC; whereas high optimism participants in perceived non-controllable situations showed lower NKC (Sieber et al., 1992). Taking previous studies together, Segerstrom (2005) proposed *the engagement hypothesis* to explain the link between optimism and the immune system observed in the literature. This hypothesis suggests that high optimists remain involved in demanding situations, and depending on the difficulty of the circumstances it would lead to higher or lower immune response. Having a cold is uncontrollable and may be considered a persistent stressor since the symptoms last 7–10 days (Cohen et al., 1999; Sieber et al., 1992). Under such a difficult circumstance, giving up or an avoidance response would be physiologically protective because it minimized the exposure to the negative effects of stress. Thus, the engagement behaviour that evokes optimism would lead to the negative relationships between optimism and the immune response to stress (Segerstrom, 2001, 2005).

In line with Lazarus and Folkman (1984), a disease makes a demand on the organism that could be perceived as stressful, which would affect immune responses. In fact, optimism may have a direct and/or stress-buffering effect on immune responses (Ah et al., 2007), moderating NKC activity, but not INF-γ, with higher NKC in highly optimistic women with breast cancer who reported being under high stress. Moreover, optimism was related to slower immune decline (Byrnes et al., 1998; Reed et al., 1999) in HIV patients. Along this line, a positive emotional style, which is positively related to the optimism trait, has been associated with reporting fewer symptoms of the common cold (Cohen et al., 2006).

In sum, optimism may affect the perception of a demanding or stressful situation (Puig-Perez et al., 2015; Endrighi et al., 2011; Carver et al., 2010), which in turn interacts with the physiological response to cope with it (Puig-Perez et al., 2015; Brydon et al., 2009). Therefore, the aim of this study is to explore the relationship between optimism, the psychological perception of common cold symptoms, and the immune response to URTIs caused by RV. Considering that a common cold lasts more than one week, it could be considered a prolonged stressor (Cohen et al., 1999), and it is uncontrollable because the disease process cannot be avoided (Sieber et al., 1992). In line with *the engagement hypothesis* (Segerstrom, 2005), it would be expected that high optimism is related to lower perception of the severity of common cold symptoms. Moreover, given the persistent and uncontrollable nature of the stressor, we expect a that high optimism would be related to lower immune response.

2. Material and methods

Data were obtained from the Pittsburg Cold Study 3. The data were collected by the Laboratory for the Study of Stress, Immunity and Disease at Carnegie Mellon University under the directorship of Sheldon Cohen, PhD; and they were accessed via the website (www.commoncoldproject.com; grant number NCCIH AT006694). The Pittsburg Cold Study 3 was a viral challenge study conducted between 2007 and 2011. This study received approval from the Carnegie Mellon University and University of Pittsburg Internal Review Boards, and all volunteers gave their informed consent by telephone during screening and in writing before the study procedures began.

2.1. Participants

A total of 212 volunteers (122 men and 90 women) were recruited from Pittsburgh, the metropolitan area of Pennsylvania. They were enrolled after responding to newspaper advertisements or invited to participate after a medical examination. Prior to participation, volunteers completed a telephone interview and gave their verbal consent before the initial screenings, and they passed an in-person physical evaluation to check that they had good health status. All the volunteers met the inclusion criteria (see www.commoncoldproject.com).

2.2. Procedure

A detailed description of the protocol for the whole study can be found on the website of the Common Cold Project (www.commoncoldproject.com). Two days before the inoculation, an assay of serum Rhinovirus (RV39) neutralizing antibody titer was performed. After the assay and checking the inclusion criteria, admitted volunteers were confined to an isolated floor of a hotel for 6 consecutive days, with Day 0 being the 24-h pre-exposure period and Days 1–5 being sequential 24-h post-exposure periods. At the end of Day 0, each subject was inoculated with RV39 by direct instillation of course drops to the nasal mucosa at an estimated dose of approximately 100 Tissue Culture Infective Dose-50% (Doyle et al., 1992). On each day of cloister, all subjects had a general physical and an Ear, Nose, and Throat examination. In order to assess subjective cold symptoms, the Daily Symptoms Scale was administered on quarantine day 0 and at the end of each subsequent post-challenge quarantine day. Additionally, daily nasal wash was performed, with samples aliquoted and frozen at −70 °C for later assay of local cytokines (IL-1β, IL-6, IL-8, IL-10) during the 5-day quarantine, and a blood sample was collected approximately 4 weeks (±28 days) after exposure to the virus. Throughout, subjects were not allowed to take prescription or over-the-counter medications, with the exception of acetaminophen, dispensed by study personnel, and birth control. At the end of Day 5, volunteers were interviewed by a doctor, provided with specific guidelines for follow-up, and discharged from quarantine.

2.3. Assessment and measures

2.3.1. Infection & clinical illness

Infection was determined through isolation of the challenge virus in nasal secretion following Gwaltney et al. (1989) criteria. The participant was considered to have developed a clinical cold based on Cohen et al. (1997) criteria and showed one of the following conditions following Doyle et al. (1988) criteria: (1) Secretion production: 10 g or more total baseline-adjusted mucus weight, or (2) Nasal congestion: time of 7 min or longer to average baseline-adjusted nasal mucociliary clearance.

2.3.2. Nasal cytokine assay and cellular immunity

Nasal wash fluid was assayed at the ENT Research Laboratory of the Children's Hospital of Pittsburgh. It was analysed in duplicate for interleukin (IL)-1β, IL-6, IL-8, IL-10, tumour necrosis factor (TNF)-α, and interferon (IFN)-α, using commercially available enzyme-linked immunosorbent assays (ELISAs; Endogen). See the Common Cold Project website (www.commoncoldproject.com) for specific details.

2.3.3. Daily symptoms scale

A self-report questionnaire was developed by the Common Cold Project to assess several symptoms of upper respiratory illness during the preceding 24 h. The questionnaire was composed of 18 5-point Likert items (0 = none to 4 = very severe) based on modified Jackson Criteria (Gwaltney et al., 1980). The questionnaire takes into account individuals' subjective ratings of 8 respiratory symptoms identified by Jackson et al. (1958) as characteristic of the common cold: nasal congestion, sneezing, runny nose, sore throat, cough, headache, chills, and malaise. Symptom severity ratings were summed within each day to create a daily Jackson Symptom Score (possible range, 0 to 32).

2.3.4. Dispositional optimism

The revised version of the Life Orientation Test (Scheier et al., 1994) was used to assess dispositional optimism through a total of 10 statements (6 scale items and 4 filler items) about which the participant had to rate his/her agreement on a 5-point Likert scale (0 = strongly disagree to 4 = strongly agree). The dispositional optimism is composed by two subscales: Optimism and Pessimism. Cronbach's alpha in this sample was 0.684 for Optimism subscale, 0.851 for Pessimism subscale, and 0.725 for the global scale of Dispositional Optimism.

2.4. Statistical analysis

Concentrations of IL-1β, IL-6, IL-8, IL-10, and IFNα and TNFα were log-10 transformed before analysis because of a skewed distribution. Subjective perception of 8 cold symptoms (nasal congestion, runny nose, sneezing, sore throat, cough, headache, chills, and malaise), the total Jackson Symptom Score, and immune responses (IL-1β, IL-6, IL-8, IL-10, IFNα and TNFα) were assessed in 6 trials (pre-challenge Day 0 and post-challenge Days 1–5). The nasal cytokine area under the curve (AUCi) was calculated from baseline-adjusted values and computed using the trapezoid formula. The delta for the Jackson Symptom Score was computed, adjusting the maximum post-challenge score to baseline values.

Repeated-measures ANOVA was used to test the progression of the 8 cold symptoms, total Jackson Symptom Score, and immune response. Main effects were followed up with post hoc tests using Bonferroni correction. The Greenhouse-Geisser procedure was used when the assumption of sphericity in the repeated-measures ANOVA was violated. Exploratory correlational analyses were used to investigate the relationship between optimism, subjective cold symptomatology, and immune response in the whole sample and in those with a cold diagnosis. Moderation models were performed using hierarchical regression analysis, and 95% confidence intervals for the interaction effect were computed using the PROCESS macro in SPSS (Model 1) with 5000 bootstrapped samples. Optimism was included as an independent variable, the Delta for the Jackson Symptom Score and the AUCi of TNFα were included as dependent variables, and Clinical Condition (Healthy vs. Cold) was included as moderator. Preliminary analysis revealed group differences (Healthy vs. Cold) in age, household income, body mass index, and trial session, and so these variables were included as covariates in the analyses. Considering theoretical formulations (Diener et al., 1999; Ryff and Singer, 1998) that supported the independence of positive and negative mental states and that it has been recommended studying the optimism and pessimism subscales separately in order to provide greater knowledge about their functions (Carver et al., 2010; Rasmussen et al., 2009), we explored optimism and pessimism subscales relationships with subjective cold symptomatology and immune response.

Due to missing data in AUCi, 5 participants were removed from the analysis for IL-1 β and IL-8, 4 for IL-10 and IFNα, 3 for IL-6, and 1 for TNFα. Participants more than ±3SD were identified as outliers and removed from the analysis: 5 for AUCi of TNFα, 3 for AUCi of IL-1 β, 4 for AUCi of IL-6, IL-8 and AUCi of IFNα, and 6 for AUCi of IL-10. Two participants were removed from the analyses of the Delta for the Jackson Symptom Score, given that they were ±3SD.

All p values reported are two-tailed, and the level of significance was set at $p < 0.05$. We used SPSS 24.0 to perform the statistical analyses.

3. Results

3.1. Preliminary results

The enrolled volunteers were between 18 and 55 years old; 59.9% were employed, and 40.1% were unemployed (see Table 1 for further details). Following Cohen et al. (1997) criteria, 63 (29.7%) volunteers clinically displayed a common cold, whereas 149 (70.3%) did not. The Cold group was older, and their household income and body mass index (BMI) were higher, compared to the Healthy group (all $p < 0.029$). Additionally, there were differences between groups in trial infection, with a higher prevalence of volunteers with doctor-diagnosed colds who performed the trial in the summer, compared to other seasons ($\chi^2 = 9.367$, $p = 0.009$). In contrast, there were no differences in sex, race/-ethnicity, educational level, or smoking status between the Healthy and Cold groups (all $p > 0.075$).

Table 1
General sample characteristics.

Table 1	Total Sample ($N = 212$)	Healthy Group ($N = 149$)	Cold Group ($N = 63$)
Sex	*N* (%)	*N* (%)	*N* (%)
Men	122 (57.5)	91 (61.1)	31 (49.2)
Women	90 (42.5)	58 (38.9)	32 (50.8)
Season Trial	*N* (%)	*N* (%)	*N* (%)
Winter	57 (26.9)	37 (24.8)	20 (31.7)
Spring	69 (32.5)	58 (38.9)	11 (17.5)
Summer	86 (40.6)	54 (36.2)	32 (50.8)
Race/ethnicity	*N* (%)	*N* (%)	*N* (%)
White, Caucasian	142 (67)	103 (69.1)	39 (61.9)
Black, African-American	57 (26.9)	38 (25.5)	19 (30.2)
Other	13 (6.1)	8 (5.3)	5 (8.0)
Educational Level	*N* (%)	*N* (%)	*N* (%)
Didn't finish High School	5 (2.4)	4 (2.7)	1 (1.6)
Didn't finish High School but completed a Tech Program	2 (0.9)	1 (0.7)	1 (1.6)
High School grad	44 (20.8)	28 (18.8)	16 (25.4)
High School grad and Tech Program	15 (7.1)	9 (6.0)	6 (9.5)
Less than 2 years College	42 (19.8)	33 (22.1)	9 (14.3)
More than 2 years College and associates degree	50 (23.6)	37 (24.8)	13 (20.6)
Bachelor's degree	44 (20.8)	30 (20.1)	14 (22.2)
Master's degree	8 (3.8)	7 (4.7)	1 (1.6)
Doctoral degree	2 (0.9)	0 (0.0)	2 (3.2)
Smoking Status	*N* (%)	*N* (%)	*N* (%)
No	140 (66)	104 (69.8)	36 (57.1)
Yes	34 (34)	45 (30.2)	27 (42.9)

3.2. Cold symptomatology and immune response

ANOVA for repeated measures showed significant main effects of Time (all $p < 0.001$) and Clinical Condition (all $p < 0.028$) on sneezing, runny nose, nasal congestion, cough, sore throat, headache, and malaise. The time effect was significant for the Chills symptom ($F_{3.790,795.806} = 4.416$, $p = 0.002$, $\eta^2 = 0.021$), but the Clinical Condition was not ($F_{1,210} = 0.740$, $p = 0.391$, $\eta^2 = 0.004$). As Fig. 1 shows, all the symptoms vary across the days, regardless of the condition. However, in general,

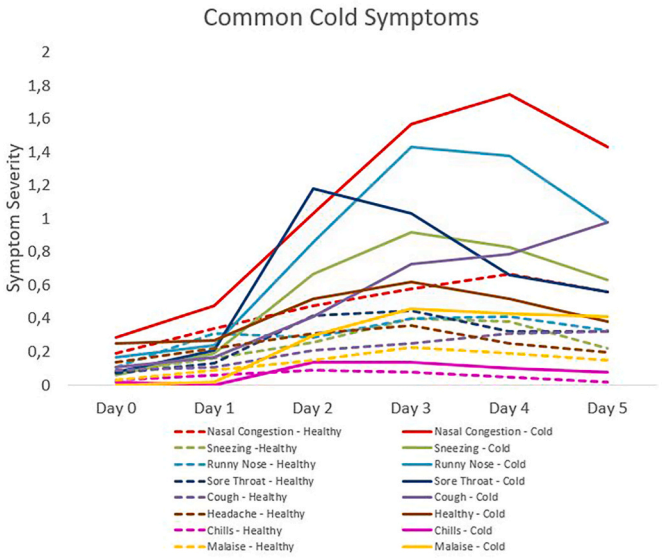


Fig. 1. Common Cold Symptom progression from pre-challenge day to 5th postchallenge RV39 inoculation.

volunteers with a cold referred to greater severity of sneezing, runny nose, nasal congestion, cough, headache, and malaise (all $p < 0.006$), but not chills ($p = 0.391$), than healthy volunteers.

Moreover, ANOVA showed a significant Time × Clinical Condition interaction for sneezing, runny nose, nasal congestion, cough, sore throat, and malaise (all $p < 0.001$), but not for headache ($F_{4.535,952.273} = 1.154$, $p = 0.330$, $\eta^2 = 0.005$) or chills ($F_{3.790,795.806} = 1.613$, $p = 0.172$, $\eta^2 = 0.008$). There were no significant differences between the Healthy and Cold groups on pre-challenge Day 0, and in sneezing, runny nose, nasal congestion, cough, and sore throat symptomatology on post-challenge Day 1 (all $p > 0.133$). The symptomatology severity becomes higher for sneezing, runny nose, nasal congestion, cough, and sore throat in the Cold group compared to the Healthy group from post-challenge Day 2 to Day 5 (all $p < 0.025$). Regarding the malaise symptom, there were no differences between the Cold and Healthy groups from pre-challenge Day 0 to post-challenge Day 2 (all $p > 0.095$), but the Cold group reported greater malaise symptom severity compared to the Healthy group from post-challenge Day 3 to Day 5 (all $p < 0.038$).

Considering all the cold symptoms using modified Jackson Criteria (Gwaltney et al., 1980), the ANOVA for repeated measures (see Fig. 2) showed significant main effects of Time ($F_{3.528,740.956} = 99.123$, $p < 0.001$, $\eta^2 = 0.321$) and Condition ($F_{1,210} = 67.934$, $p < 0.001$, $\eta^2 = 0.244$). The Cold group showed a higher Jackson Symptom Score than the Healthy group. In spite of the condition, the Jackson Symptom Score increased significantly from pre-challenge Day 0, peaking at post-challenge Day 3 (all $p < 0.001$). After that, the Jackson Symptom Score decreased significantly until post-challenge Day 5, without recovering baseline status (all $p < 0.015$). The analyses also revealed a significant Time × Condition interaction ($F_{3.528,740.956} = 30.228$, $p < 0.001$, $\eta^2 = 0.126$). Post hoc analyses showed that there were no significant differences between the Cold and Healthy groups on the Jackson Symptom Score on pre-challenge Day 0 and post-challenge Day 1 (both $p > 0.204$). However, the Cold group reported a significantly higher Jackson Symptom Score than the Healthy group from post-challenge Day 3 to Day 5 (all $p < 0.001$).

Regarding the Immune Response to RV39, ANOVA for repeated measures showed significant main effects of Time (all $p < 0.001$) and Clinical Condition (all $p < 0.007$) for IL-1β, IL-6, IL-8 and TNFα. The time effect was significant for IL-10 ($F_{4.334,\ 333.323} = 31.489$, $p < 0.001$, $\eta^2 = 0.131$), but Clinical Condition was not ($F_{1,208} = 1.018$, $p = 0.314$, $\eta^2 = 0.005$). In contrast, the time effect was not significant for IFNα ($F_{3.857,802.304} = 1.966$, $p = 0.100$, $\eta^2 = 0.009$), but the Clinical Condition effect was ($F_{1,208} = 0.267$, $p = 0.606$, $\eta^2 = 0.001$). As Fig. 3 shows, IL-1β, IL-6, IL-8, IL-10, and TNFα concentration vary across the days, in spite of the condition. In addition, in general, the Cold group showed a higher concentration of IL-1β, IL-6, IL-8, and TNFα (all $p < 0.006$) than the Healthy group, but the two groups did not differ on IL-10 and IFNα concentrations (both $p = 0.314$).

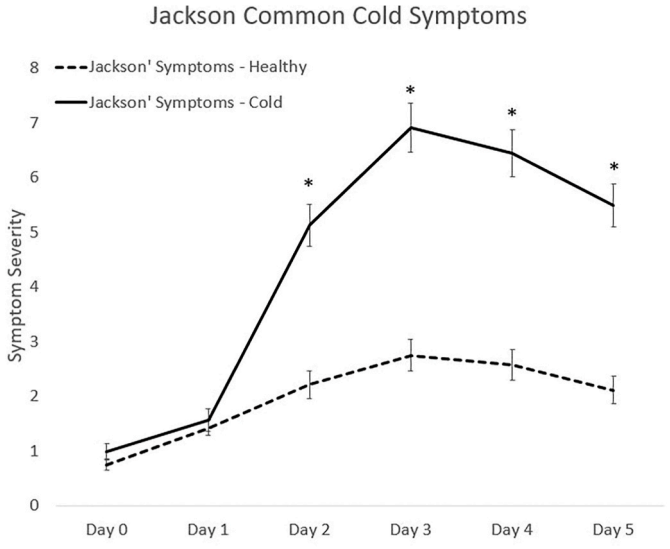


Fig. 2. ANOVA for repeated measures with cold and healthy volunteers, considering all cold symptoms using modified Jackson criteria.

The analyses showed significant Time × Clinical Condition interactions for IL-1β, IL-6, IL-8, IL-10, and TNFα (all $p < 0.001$), but not for IFNα ($F_{3.857,802.304} = 1.453$, $p = 0.217$, $\eta^2 = 0.007$). There were no significant differences between the Healthy and Cold groups on pre-challenge Day 0 and post-challenge Day 1 for IL-1β (Day 0, $p = 0.520$; Day 1, $p = 0.585$), IL-6 (Day 0, $p = 0.802$; Day 1, $p = 0.866$), IL-8 (Day 0, $p = 0.543$; Day 1, $p = 0.691$), IL-10 (Day 0, $p = 0.090$; Day 1, $p = 0.064$), and TNFα (Day 0, $p = 0.304$; Day 1, $p = 0.425$). The concentration becomes higher in the Cold group compared to the Healthy group from post-challenge Day 2 to Day 5 for IL-1β, IL-6, and IL-8 (all $p < 0.025$). Regarding IL-10 in the Cold group, there was a higher concentration on post-challenge Days 2 and 3 (all $p < 0.020$), but not Days 4 and 5, compared to the Healthy group (all $p > 0.120$). With regard to TNFα, the cold volunteers reported higher concentrations on post-challenge Days 2, 3, and 4 (all $p < 0.002$), but not on Day 5, compared to the healthy group ($p > 0.281$).

3.3. Optimism and the common cold

Correlation analyses were performed to explore the relationship between the optimism trait, the average subjective perception of cold symptoms during the post-challenge period (Jackson Symptom Score), and the immune response to infection (AUCi of IL-1β, IL-6, IL-8, IL-10, IFNα or TNFα).

Analysis with the total sample revealed that higher optimism was related to a lower Delta for the Jackson Symptom Score ($r = -0.166$, $p = 0.016$) and AUCi of TNFα ($r = -0.176$, $p = 0.012$) in the total sample. Correlation analysis performed only with the Cold group showed that participants with a higher optimism score reported a lower Delta for the Jackson Symptom Score ($r = -0.303$, $p = 0.016$) as well as a lower AUCi of TNFα ($r = -0.343$, $p = 0.006$). However, no significant relationships were found between optimism and AUCi of IL-1β, IL-6, IL-8, IL-10, or IFNα in the total sample or the Cold group sample (all $p > 0.060$). Moderation regression analyses were performed including Optimism as predictor variable, the Delta for the Jackson Symptom Score and the AUCi of TNFα as predictor variables, Clinical Condition (Cold vs. Healthy) as moderator variable, and Age, BMI, income, and trial season as covariates.[1] Results showed (see Table 2) that clinical condition significantly moderates the relationship between Optimism, the Delta for the Jackson Symptom Score ($p = 0.044$), and the AUCi of TNFα ($p < 0.001$). Optimism was not related to changes in the Jackson Symptom Score or to changes in the TNFα concentration in healthy volunteers (both $p > 0.556$). However, those participants with a cold diagnosis and higher optimism reported less increase in cold symptoms and TNFα concentration during the post-challenge period (both $p < 0.007$).

3.4. Optimism, pessimism and the common cold

Correlation analysis were performed to explore whether the optimism and pessimism subscales were related to both the average subjective perception of cold symptoms during the post-challenge period (Jackson Symptom Score), and the immune response to infection (AUCi of IL-1β, IL-6, IL-8, IL-10, IFNα or TNFα). The analyses revealed a marginally significant negative relationship between optimism subscale and the Delta for the Jackson Symptom Score in the total sample ($r = -0.134$, $p = 0.053$). The Delta for the Jackson Symptom Score was not

[1] The statistical conclusions of the study remain the same if the analyses are performed without covariates.

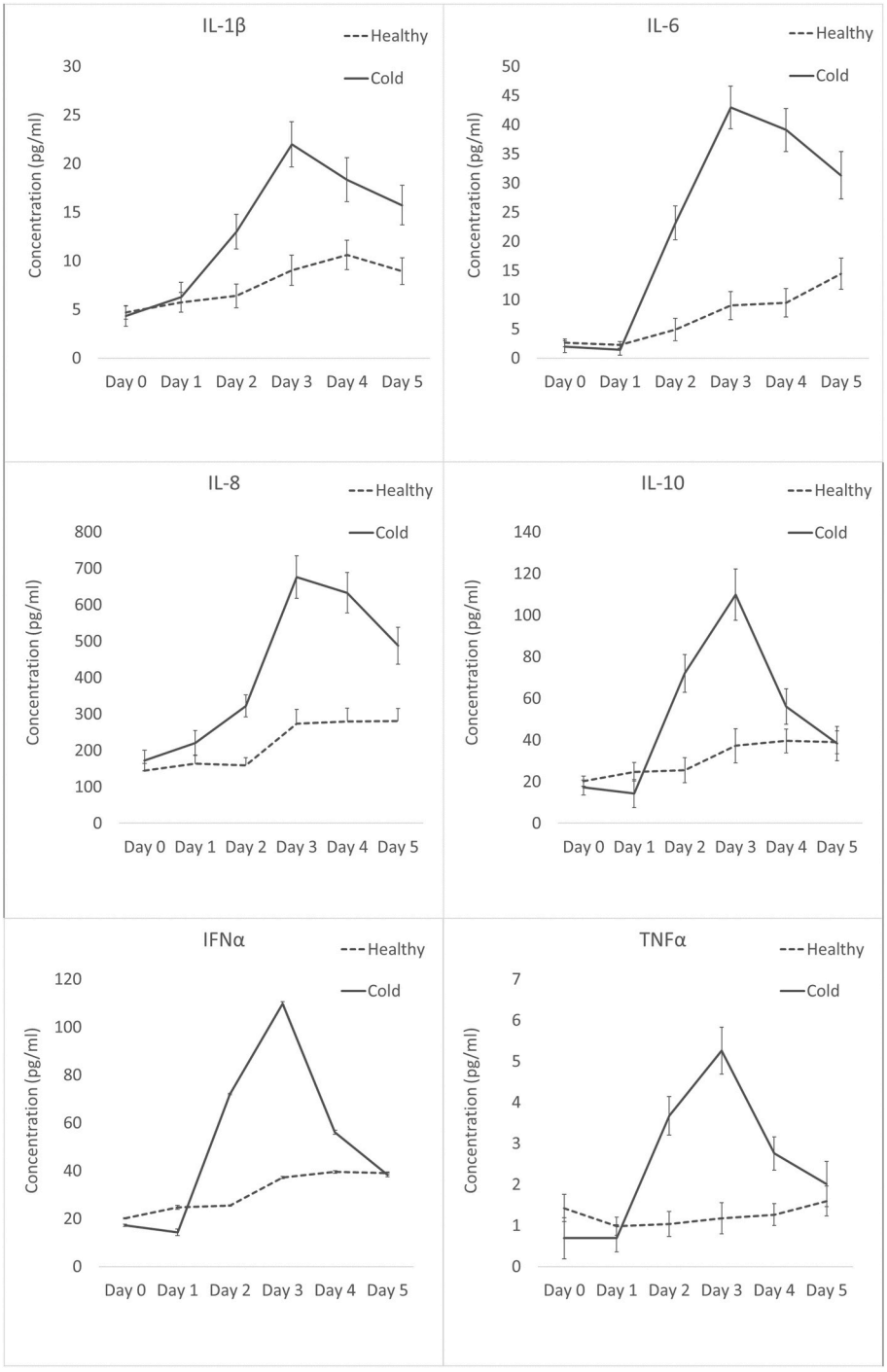


Fig. 3. ANOVA for repeated measures with cold and healthy volunteers, considering immune response to RV39.

significantly associated with the pessimism subscale in the total sample ($r = 0.210$, $p = 0.069$). Moreover, the Delta for the Jackson Symptom Score was not significantly associated with the optimism and pessimism subscales for the Healthy Group and the Cold Group separately (all p's $>$ 0.076). Regarding the immune response, the correlation analysis showed a significant positive relationship between higher pessimism and the AUCi of TNFα in the total sample ($r = 0.190$, $p = 0.006$), and in the Cold Group ($r = 0.286$, $p = 0.024$), but not in Healthy Group ($r = 0.314$, $p = 0.144$). Moreover, the optimism subscale was not related with AUCi of TNFα in the total sample or the Healthy Group and the Cold Group separately (all $p > 0.201$). The optimism and pessimism subscales were not related to AUCi of IL-1β, IL-6, IL-8, IL-10 or IFNα in the total sample or the Healthy Group and the Cold Group separately (all $p >$ 0.075).

Considering the results observed for the AUCi of TNFα, we investigated whether the clinical condition (Cold vs. Healthy) moderated the relationship between the pessimism subscale and the AUCi of TNFα. Moderated regression analyses were performed including Pessimism subscale as a predictor variable, the AUCi of TNFα as the dependent variable, Clinical Condition (Cold vs. Healthy) as the moderator, and Age, BMI, income, and trial season as covariates.[1] Results showed that clinical condition does not moderate the relationship between Pessimism and the AUCi of TNFα ($R^2 = 0.005$, $F_{1,202} = 1.152$, $p = 0.284$), and that Pessimism was not related to AUCi of TNFα in the total sample

Table 2
Moderation analyses where optimism scores predict the Delta for the Jackson Symptoms Score and the AUCi of TNFα; $p < 0.05$, are marked in bold.

	Delta Jackson Symptoms Score				AUCi of TNFα			
Model	R^2	ΔR^2	$F_{7, 201}$	*p*	R^2	ΔR^2	$F_{7, 197}$	*p*
	0.584	0.341	11.417	**<0.001**	0.540	0.291	11.570	**<0.001**
Variable	β	S.E.	t	*p*	β	S.E.	t	*p*
Constant	0.399	1.609	0.248	0.804	5.260	3.519	1.495	0.137
Age	−0.032	0.024	−1.363	0.175	−0.035	0.052	−0.681	0.497
BMI	0.113	0.039	2.880	**0.004**	−0.115	0.086	−1.342	0.181
Income	<0.001	<0.001	−1.851	0.066	<0.001	<0.001	1.358	0.176
Season	0.839	0.293	2.866	**0.005**	0.824	0.635	1.299	0.196
Condition	8.011	1.882	4.257	**<0.001**	21.717	4.083	5.319	**<0.001**
Optimism	−0.039	0.066	−0.590	0.556	−0.047	0.145	−0.321	0.749
Optimism × Condition	−0.253	0.125	−2.023	**0.044**	−0.953	0.272	−3.496	**<0.001**
Healthy	−0.039	0.066	−0.590	0.556	−0.047	0.145	−0.321	0.749
Cold	−0.292	0.107	−2.734	**0.007**	−0.999	0.231	−4.324	**<0.001**

(Model: $R^2 = 0.278$, $F_{3,202} = 5.628$, $p = 0.001$; Pessimism × AUCi of TNα: $t = 0.131$, $p = 0.896$, $CI = -0.808$ to 0.923).

4. Discussion

The aim of this study was to investigate the role of trait optimism in the subjective perception of the severity of common cold symptoms, as well as its influence on the physiological response to common cold infection. Results showed that, after RV39 exposure, volunteers who met objective criteria of infection and clinical illness showed significantly higher severity of cold symptoms, separately and integrated in a total score defined by the Jackson Criteria (Gwaltney et al., 1980), than their healthy counterparts. Additionally, volunteers diagnosed with a common cold showed significantly higher concentrations of IL-1β, IL-6, IL-8, IL-10, IFNα or TNFα during the quarantine days than healthy volunteers. Correlational analyses showed that a higher dispositional optimism score was related to a lower subjective perception of the severity of common cold symptoms, as well as a lower TNFα response, regardless of clinical condition, and only in the cold-volunteer subsample. Moderation analyses confirmed that higher dispositional optimism was related to a lower subjective perception of the severity of common cold symptoms and lower TNFα response to RV39 exposure in ill volunteers, but not in their healthy counterparts, even after controlling for several covariates. Finally, although the exploratory correlation analysis showed that the pessimism subscale was positively related to TNFα response, this relationship was not supported in the moderated regression analyses.

In line with previous literature (Tyrrell et al., 1993), approximately 30% of volunteers exposed to RV39 developed a clinical cold with the usual progression of symptoms, that is, a significant increase from inoculation, peaking between 2nd-4th days later. Specifically, participants infected and diagnosed with a cold reported more symptoms severity of cold symptoms and an increase in immune system activity.

Regarding the dispositional optimism trait, our results showed that high dispositional optimism were related to lower cold symptom severity only in cold-diagnosed participants. It is possible that a lower perception of the severity of cold symptoms may be related to better management of the disease process and reduced disruption in daily responsibilities. A large body of evidence shows that trait optimism (Carver and Scheier, 2014) is related to better overcome a disease process, and this study provides important evidence to understand how this trait helps the organism to cope with demanding situations. Assuming that optimism trait is related to a reduction in the perceived severity of the symptomatology, it could be related to an increase of the perception of wellbeing and better cope of the common cold, thus confirming the protective role of optimism. This is the first study that confirmed a direct relationship between optimism and subjective perception of common cold severity, and our results support previous studies (Cohen et al., 2006) showing that a positive emotional style is associated with reporting fewer symptoms of the common cold.

Furthermore, our results showed that higher dispositional optimism in cold-diagnosed participants were related to lower TNFα concentrations. According to *the engagement hypothesis*, a lower immune response should be expected in highly optimistic people under uncontrollable and persistent stressors (Segerstrom, 2005). Assuming that illness can be considered a persistent stressor (Ah et al., 2007; Cohen et al., 1999), including the common cold (with symptoms lasting 7–10 days), our results go in line with the engagement hypothesis by showing that optimism would be related to lower immune response. Our results help to consolidate previous results observed in people with sustained and uncontrollable stress conditions, showing a lower immune response in high optimists (Segerstrom, 2001, 2005; Cohen et al., 1999). It is important to note that previous studies showing that high optimism is related to a higher immune response studied this relationship under acute stress situations (Brydon et al., 2009; Segerstrom et al., 1998; Cohen et al., 1989), where a rapid and high immune response may be adaptive. Assuming that the length of the stressor is crucial in the relationship between optimism and the immune response (Segerstrom, 2001, 2005; Cohen et al., 1999), the contrasting results observed could be explained by the fact that this study investigated a prolonged stressor, in contrast to previous studies (Brydon et al., 2009; Segerstrom et al., 1998; Cohen et al., 1989). Importantly, although the common cold can be considered a persistent stressor (symptoms last 7–10 days), in this study, the psychological and immune response was assessed during the first 5 days after the inoculation due to methodological reasons (i.e., a peak in symptoms is expected during these days). Thus, it is also possible that the expectation of experiencing a cold for a long period, not only the persistence of the stressor, influences the immune response associated with optimism. This idea aligns with the protective role of positive expectancies during stress anticipation (De Raedt and Hooley, 2016; Pulopulos et al., 2020, Pulopulos et al., 2021; Pulopulos et al., 2023). Future research should investigate whether it is the actual duration of the stressor or the expectation of being exposed to a persistent stressor that explains most of the variability.

It is important to highlight that the increase in TNFα, along with IL-1β, IL-2, and IL-6, is responsible for what is known as "sickness behaviour" (Capuron and Miller, 2004). In fact, these cytokines have been related to URTI's, mediating mood changes in this kind of infection. Based on the above, the relationship between high dispositional optimism and reduced TNFα concentrations in cold-diagnosed participants contributes to understanding why our results showed a negative relationship between optimism and subjective perceptions of cold symptom severity: higher optimism may be related to lower TNFα concentration, which has been related to reduced sickness behaviour, helping to generate a healthier perception in situations of infection.

Apart from the novel results, some limitations warrant discussion.

The present study was performed in a well-controlled situation; therefore, the extrapolation of the results to non-controlled conditions should be done with caution. Further research in more ecological environments is clearly needed to replicate the results of this study. Moreover, although the proportion of people who developed a common cold after infection was expected (Tyrrell et al., 1993), the group with common cold disease is significantly smaller than the group of healthy participants.

In conclusion, our observations provide relevant evidence supporting the role of optimism as a protective factor that helps to more successfully cope with disease conditions.

Funding

The data were collected by the Laboratory for the Study of Stress, Immunity, and Disease at Carnegie Mellon University under the directorship of Sheldon Cohen, PhD; and they were accessed via the Common Cold Project website (www.commoncoldproject.com). The Common Cold Project was supported by the National Center for Complementary and Integrative Health (grant number NCCIH AT006694). Primary funding for the Pittsburg Cold Study 3 study was supported by the National Institute of Allergy and Infectious Diseases (grant number NIAID R01 AI066367). Clinical and regulatory assistance for the Pittsburg Cold Study 3 was supported by the National Institutes of Health grant awarded to the University of Pittsburg (grant number NIH UL1 RR024153 and UL1 TR0005). Supplementary funding for cytokine analyses was received by the Pennsylvania Department of Health through a Commonwealth Enhancement Grant (grant number 08-01-2).

CRediT authorship contribution statement

S. Puig-Perez: Conceptualization, Formal analysis, Methodology, Writing – original draft, Writing – review & editing. **M.W. Kozusznik:** Writing – original draft, Writing – review & editing. **M.M. Pulopulos:** Supervision, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors report no conflicts of interest. Authors has full control of all primary data and agree to allow the journal to review their data if requested. Moreover, there were no potential conflicts of interest with the organization that sponsored the research.

Data availability

All data is public and available

Acknowledgements

The authors wish to thank Cindy de Poy for the revision of the English text. The authors have no competing interests to report.

References

Ah, D.V., Kang, D.H., Carpenter, J.S., 2007. Stress, optimism, and social support: impact on immune responses in breast cancer. Res. Nurs. Health 30 (1), 72–83. https://doi.org/10.1002/nur.20164.

Brydon, L., Walker, C., Wawrzyniak, A.J., Chart, H., Steptoe, A., 2009. Dispositional optimism and stress-induced changes in immunity and negative mood. Brain Behav. Immun. 23 (6), 810–816. https://doi.org/10.1016/j.bbi.2009.02.018.

Byrnes, D.M., Antoni, M.H., Goodkin, K., Efantis-Potter, J., Asthana, D., Simon, T., et al., 1998. Stressful events, pessimism, natural killer cell cytotoxicity, and cytotoxic/suppressor T cells in HIV+ black women at risk for cervical cancer. Psychosom. Med. 60 (6), 714–722. https://doi.org/10.1097/00006842-199811000-00009.

Capuron, L., Miller, A.H., 2004. Cytokines and psychopathology: lessons from interferon-α. Biol. Psychiatr. 56 (11), 819–824. https://doi.org/10.1016/j.biopsych.2004.02.009.

Carver, C.S., Scheier, M.F., 2014. Dispositional optimism. Trends Cognit. Sci. 18 (6), 293–299. https://doi.org/10.1016/j.tics.2014.02.003.

Carver, C.S., Scheier, M.F., Segerstrom, S.C., 2010. Clinical psychology review optimism. Clin. Psychol. Rev. 30, 879–889. https://doi.org/10.1016/j.cpr.2010.01.006.

Cohen, F., Kearney, K.A., Kemeny, M.E., Zegans, L.S., 1989. Acute stress, chronic stress, and immunity, and the role of optimism as a moderator, 255-255 Psychosom. Med. 51 (No. 2), 351 West Camden St, Baltimore, Md 21201-2436: Williams & Wilkins.

Cohen, F., Kearney, K.A., Zegans, L.S., Kemeny, M.E., Neuhaus, J.M., Stites, D.P., 1999. Differential immune system changes with acute and persistent stress for optimists vs pessimists. Brain Behav. Immun. 13 (2), 155–174. https://doi.org/10.1006/brbi.1998.0531.

Cohen, S., Alper, C.M., Doyle, W.J., Treanor, J.J., Turner, R.B., 2006. Positive emotional style predicts resistance to illness after experimental exposure to rhinovirus or influenza A virus. Psychosom. Med. 68 (6), 809–815. https://doi.org/10.1097/01.psy.0000245867.92364.3c.

Cohen, S., Doyle, W.J., Skoner, D.P., Rabin, B.S., Gwaltney Jr., J.M., 1997. Social ties and susceptibility to the common cold. J. Am. Med. Assoc. 277, 1940–1944. https://doi.org/10.1001/jama.1997.03540480040036.

De Raedt, R., Hooley, J.M., 2016. The role of expectancy and proactive control in stress regulation: a neurocognitive framework for regulation expectation. Clin. Psychol. Rev. 45, 45–55. https://doi.org/10.1016/j.cpr.2016.03.005.

Diener, E., Suh, E.M., Lucas, R.E., Smith, H.L., 1999. Subjective well-being: three decades of progress. Psychol. Bull. 125 (2), 276. https://doi.org/10.1037/0033-2909.125.2.276.

Doyle, W.J., McBride, T.P., Skoner, D.P., Maddern, B.R., Gwaltney, J.J., Uhrin, M., 1988. A double-blind, placebo-controlled clinical trial of the effect of chlorpheniramine on the response of the nasal airway, middle ear and eustachian tube to provocative rhinovirus challenge. Pediatr. Infect. Dis. J. 7 (3), 229–238. https://doi.org/10.1097/00006454-198803000-00033.

Doyle, W.J., Skoner, D.P., Fireman, P., Seroky, J.T., Green, I., Ruben, F., et al., 1992. Rhinovirus 39 infection in allergic and nonallergic subjects. J. Allergy Clin. Immunol. 89 (5), 968–978. https://doi.org/10.1016/0091-6749(92)90219-R.

Eccles, R., 2005. Understanding the symptoms of the common cold and influenza. The Lancet infectious diseases 5 (11), 718–725.

Endrighi, R., Hamer, M., Steptoe, A., 2011. Associations of trait optimism with diurnal neuroendocrine activity, cortisol responses to mental stress, and subjective stress measures in healthy men and women. Psychosom. Med. 73 (8), 672–678. https://doi.org/10.1097/PSY.0b013e31822f9cd7.

Giltay, E.J., Kamphuis, M.H., Kalmijn, S., Zitman, F.G., Kromhout, D., 2006. Dispositional optimism and the risk of cardiovascular death: the Zutphen Elderly Study. Arch. Intern. Med. 166 (4), 431–436. https://doi.org/10.1001/.431.

Gwaltney Jr., J.M., Colonno, R.J., Hamparian, V.V., Turner, R.B., 1989. Rhinovirus. In: Schmidt, N.J., Emmons, R.W. (Eds.), Diagnostic Procedures for Viral, Rickettsial, and Chlamydial Infections, 6th Ed. American Public Health Association, Washington, D. C., pp. 579–614

Gwaltney Jr., J.M., Moskalski, P.B., Hendley, J.O., 1980. Interruption of experimental rhinovirus transmission. JID (J. Infect. Dis.) 142, 811–815.

Jackson, G.G., Dowling, H.F., Spiesman, I.G., Boand, A.V., 1958. Transmission of the common cold to volunteers under controlled conditions. I. The common cold as a clinical entity. Arch. Intern. Med. 101, 267–278.

Johnston, S., Holgate, S., 2012. Epidemiology of viral respiratory infections. In: Myint, S., Taylor-Robinson, D. (Eds.), Viral and Other Infections of the Human Respiratory Tract. Springer Science & Business Media.

Lazarus, R.S., Folkman, S., 1984. Stress, Appraisal, and Coping. Springer, New York.

Mahoney, T., Ball, P., 2002. Common respiratory tract infections as psychological entities: a review of the mood and performance effects of being ill. Aust. Psychol. 37 (2), 86–94. https://doi.org/10.1080/00050060210001706726.

Miller, Gregory, Cohen, S., 2001. Psych Interventions and Immune Sys. Health Psychology, pp. 47–83.

Nabi, H., Koskenvuo, M., Singh-Manoux, A., Korkeila, J., Suominen, S., Korkeila, K., et al., 2010. Low pessimism protects against stroke: the health and social support (hessup) prospective cohort study. Stroke 41 (1), 187–190. https://doi.org/10.1161/STROKEAHA.109.565440.

Puig-Perez, S., Hackett, R.A., Salvador, A., Steptoe, A., 2017. Optimism moderates psychophysiological responses to stress in older people with Type 2 diabetes. Psychophysiology 54 (4), 536–543. https://doi.org/10.1111/psyp.12806.

Puig-Perez, S., Pulopulos, M.M., Hidalgo, V., Salvador, A., 2018. Being an optimist or a pessimist and its relationship with morning cortisol release and past life review in healthy older people. Psychol. Health 33 (6), 783–799. https://doi.org/10.1080/08870446.2017.1408807.

Puig-Perez, S., Villada, C., Pulopulos, M.M., Almela, M., Hidalgo, V., Salvador, A., 2015. Optimism and pessimism are related to different components of the stress response in healthy older people. Int. J. Psychophysiol. 98 (2), 213–221. https://doi.org/10.1016/j.ijpsycho.2015.09.002.

Pulopulos, M.M., Baeken, C., De Raedt, R., 2020. Cortisol response to stress: the role of expectancy and anticipatory stress regulation. Horm. Behav. 117, 104587 https://doi.org/10.1016/j.yhbeh.2019.104587.

Pulopulos, M.M., Boccagno, C., De Raedt, R., Hooley, J.M., 2021. Attenuated beta-adrenergic response to stress and increased anticipation and perception of social threat in women high on perceived criticism. Psychoneuroendocrinology 133, 105421. https://doi.org/10.1016/j.psyneuen.2021.105421.

Pulopulos, M.M., Hoorelbeke, K., Vandenbroucke, S., Van Durme, K., Hooley, J.M., De Raedt, R., 2023. The interplay between self-esteem, expectancy, cognitive control, rumination, and the experience of stress: a network analysis. Curr. Psychol. 42 (18), 15403–15411. https://doi.org/10.1007/s12144-022-02840-6.

Rasmussen, H.N., Scheier, M.F., Greenhouse, J.B., 2009. Optimism and physical health: a meta-analytic review. Ann. Behav. Med. 37 (3), 239–256. https://doi.org/10.1007/s12160-009-9111-x.

Reed, G.M., Kemeny, M.E., Taylor, S.E., Visscher, B.R., 1999. Negative HIV-specific expectancies and AIDS-related bereavement as predictors of symptom onset in asymptomatic HIV-positive gay men. Health Psychology 18 (4), 354.

Ryff, C.D., Singer, B., 1998. The contours of positive human health. Psychol. Inq. 9 (1), 1–28. https://doi.org/10.1207/s15327965pli0901_1.

Scheier, M.F., Carver, C.S., Bridges, M.W., 1994. Distinguishing optimism from neuroticism (and trait anxiety, self-mastery, and self-esteem): a reevaluation of the Life Orientation Test. J. Pers. Soc. Psychol. 67 (6), 1063.

Segerstrom, S.C., 2001. Optimism, goal conflict, and stressor-related immune change. J. Behav. Med. 24 (5), 441–467. https://doi.org/10.1023/A:1012271410485.

Segerstrom, S.C., 2005. Optimism and immunity: do positive thoughts always lead to positive effects? Brain Behav. Immun. 19 (3), 195–200. https://doi.org/10.1016/j.bbi.2004.08.003.

Segerstrom, S.C., Taylor, S.E., Kemeny, M.E., Fahey, J.L., 1998. Optimism is associated with mood, coping, and immune change in response to stress. J. Pers. Soc. Psychol. 74 (6), 1646–1655. https://doi.org/10.1037/0022-3514.74.6.1646.

Sieber, W.J., Rodin, J., Larson, L., Ortega, S., Cummings, N., Levy, S., et al., 1992. Modulation of human natural killer cell activity by exposure to uncontrollable stress. Brain Behav. Immun. 6 (2), 141–156. https://doi.org/10.1016/0889-1591(92)90014-F.

Tyrrell, D.A.J., Cohen, S., Schlarb, J.E., 1993. Symptoms and signs in common colds. Epidemiol. Infect. 111, 143–156.