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Individual Differences in Self-Regulatory Failure and Menstrual Dysfunction Predict Upper Respiratory Infection Symptoms and Antibody Response to Flu Immunization

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Abstract

Prior research indicates that cognitive priming manipulations that activate personal goals acutely increase or decrease natural killer cell cytotoxicity depending on whether individuals see themselves as making or failing to make progress toward their goals. Those findings in a laboratory setting revealed a psychobiological pathway whereby experiences of failure can influence health, but did not assess the impact of chronic perceived success/failure in goal pursuit on actual health outcomes. Three new studies investigated whether individual differences in perceived failure to attain personal goals influenced the self-reported symptoms of upper respiratory infections (URIs) as well as antibody response to flu immunization. Based on pilot data in young women, it also was hypothesized that the occurrence of menstrual dysfunction might interact with goal pursuit failure to more specifically predict cold and flu symptoms and optimal responses to vaccination. Perceived failure to attain goals did predict the reporting of URI symptoms as well as antibody levels post-immunization, both alone and in combination with menstrual dysfunction.

Keywords

self-regulation; self-discrepancy; influenza; upper respiratory infection; menstrual dysfunction; antibody

1. Introduction

A growing body of research has shown that psychological factors can have a significant influence on vulnerability to infectious disease (Cohen and Herbert, 1996; Cohen and Williamson, 1991; Segerstrom and Miller, 2004). Upper respiratory infections (URIs) such as influenza and the common cold are familiar occurrences among healthy adults, and have been widely used as outcome measures to investigate psychological processes in illness (Bonneau, Padgett, and Sheridan, 2007). For example, one personality variable, positive emotional style, was reliably associated with a decreased vulnerability to colds and flu (Cohen et al., 2003).

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Another variable that differs markedly across individuals, dispositional optimism, has been associated with positive health outcomes, but also with an inhibition of immune responses when a person's optimistic outlook is challenged by failure (Segerstrom, 2006). The occurrence of emotional distress and arousal may mediate some of the associations observed between personality variables and health outcomes (Segerstrom and Smith, 2006).

This paper presents three studies testing the hypothesis that individual differences in self-regulation, specifically in *perceived success versus failure in personal goal pursuit*, can affect the occurrences of colds and flu and the underlying immunobiology. The research was based on prior studies showing that cognitive priming manipulations activating personal goals can differentially alter the lytic activity of natural killer (NK) cells depending on whether individuals see themselves as making or failing to make progress toward their goals (Strauman, Lemieux, and Coe, 1993; Strauman et al., 2004). The impact of chronic success/failure in goal pursuit was evaluated in undergraduate women, both because women vary more in self-discrepancy than men (Moretti and Wiebe, 1999) and because our pilot research indicated that self-discrepancy was correlated with reports of menstrual dysfunction and distress, which is known to be associated with the incidence and severity of several infectious diseases.

1.1 Self-regulation, goal pursuit, and affect

Self-regulation is defined here as the process of evaluating and modifying one's behavior and attributes with respect to attainment or nonattainment of goals (Carver and Scheier, 1990). As such, self-regulation provides a proximal locus for the influence of situational and individual difference variables on physiology (Strauman, 2002). A perceived discrepancy between an individual's behavior and personal goals has predictable affective consequences (Carver, Lawrence, and Scheier, 1996; Higgins et al., 1986). Negative emotions occur when efforts at attaining personal goals are perceived as unsuccessful. If self-regulation is chronically unsuccessful, the result will be sustained negative affect, decreasing the likelihood of goal attainment and increasing the likelihood of continued distress.

Regulatory focus theory (RFT; Higgins, 1997) distinguishes between two types of goals or desired outcomes, each of which is associated with different positive and negative emotional states. *Promotion goals* involve aspirations and accomplishments, and reflect a self-regulatory orientation for attaining positive outcomes by "making good things happen". When a person believes they are failing to attain a promotion goal, dejected emotions such as sadness, disappointment, and dissatisfaction result. *Prevention goals* involve safety, obligation, and responsibility, and reflect a self-regulatory orientation toward "keeping bad things from happening" as a means to achieve positive outcomes. When a person believes they are failing to attain a prevention goal, agitated emotions such as anxiety and worry result. Chronic promotion and prevention goal failure are associated with dysphoric and anxious emotions, as well as with clinical mood and anxiety disorders, respectively (Strauman, 1992).

The experience of failing to make progress toward a personal goal is a ubiquitous feature of everyday life. When people see themselves as failing to attain an important goal, they experience momentary negative affect, which then motivates them to increase efforts, change strategies, or pursue a different goal (Carver and Scheier, 1990). The continuous emotional feedback from ongoing self-regulation is adaptive as long as the individual is able to respond effectively to reduce the discrepancy. However, if failure is more prolonged or intense, it leads to enduring negative affect, which can have consequences for health. For example, susceptibility to colds and flu has been shown to vary as a function of everyday experiences of frustration and disappointment (Cohen, Doyle, and Stoner, 1999). Similarly, students' views about their academic performance can influence the occurrence of URIs (Kiecolt-Glaser and Glaser, 1992).

1.2 Immune reactivity following goal pursuit success/failure priming

Given that many stressful events involve a perceived failure to attain goals, self-regulatory processes could account for some of the demonstrated influence of negative affect on immune responses. Moreover, the impact of perceived self-discrepancy on immunity should reflect the motivational significance of the mismatch between goals and behavior. These hypotheses were tested in anxious, dysphoric, and non-distressed undergraduates (Strauman et al., 1993), who were exposed to their own promotion (“ideal”) and prevention (“ought”) goals and, in a separate control session, to the goals of another participant. The anxious and dysphoric participants were primed with goals they believed they were failing to attain, whereas the nondistressed subjects were primed with goals they believed they were attaining. Goal failure priming resulted in decreased cytolytic activity in both distressed groups and increased cortisol in the anxious participants. In contrast, the priming of goal success in the non-distressed students led to higher NK activity relative to the yoked control condition.

Strauman et al. (2004) extended these findings by exposing undergraduate women who reported low versus high levels of perceived goal pursuit failure to goal success/failure priming in a repeated-measures design. Goal priming conditions were associated with significant alterations in NK lysis. Participants with high perceived failure were especially responsive to priming. They manifested a decrease in lytic activity in response to self-congruent priming and an increase in response to self-discrepant priming. The effects on cytotoxicity were partially mediated by priming-induced changes in negative affect. Consistent with the postulate that activating goals would have motivational consequences, it also was observed that priming personal goals elicited an increase in total lymphocyte numbers (in particular, the NK subset, despite the decrease in lytic activity). Strauman et al. speculated that chronic perceived failure could lead to prolonged immune changes that might have a meaningful influence on risk for upper respiratory infection – a question that was addressed in the following studies.

1.3. The role of menstrual cycle dysfunction in stress and illness

Menstrual dysfunction also has been frequently associated with psychological and physical health (Harlow and Ephross, 1995), and linked to alterations in immune responses in several studies (e.g., Cutolo et al., 2006; Groer et al., 1993; Kajantie and Phillips, 2006; Motzer and Hertig, 2004). Matthews and her colleagues (1995) also observed intensified effects of psychological stressors on lymphocyte numbers in young women if they were classified as highly emotionally reactive on the basis of sympathetic nervous system activity. Women who experience premenstrual distress report more intense and prolonged negative affect following stressful life events and everyday hassles, even when not menstruating (Cumming et al., 1995), and report more extreme day-to-day changes in affective state than their peers (Hardie, 1997). Menstrual dysfunction increases women’s susceptibility to chronic negative affect and is often associated with abnormal hormone levels and disturbances in immune function (Benschop et al., 1998). Our pilot research indicated that self-discrepancy was correlated with self-reported menstrual dysfunction, suggesting that studies of the impact of self-regulation on immune-related health also needed to assess menstrual function. In the studies below, it was predicted that menstrual dysfunction would directly influence on immunity and the reporting of URI symptoms and mediate the associations among self-regulation, URIs, and immunity.

1.4. A model for the influence of self-regulation on frequency of URIs

Psychological processes are important determinants of the incidence and severity of URIs (Cohen, 2005), and can create and maintain negative affective states that contribute to vulnerability to viral and bacterial pathogens (Graham et al., 2006). Because chronic perceived failure in goal pursuit is associated with chronic distress, and because goal failure feedback is associated with altered immune function, it was hypothesized that chronic self-regulatory failure would contribute to the emergence of URI symptoms, as follows:

- Chronic perceived failure in goal pursuit leads to chronic distress.
- Sustained distress reduces immune responses involved in protection against infection.
- Distress-associated reductions in immune responses increase the likelihood of URIs.
- Menstrual dysfunction also contributes to incidence of URIs in women via its associations with self-discrepancy, affect, stress reactivity, and immunity.

Study 1: Associations Among Self-Discrepancy, Menstrual Dysfunction, Distress, and Self-Reported Cold/Flu Symptoms

A study was conducted examining the associations among self-discrepancy, emotional symptomatology, menstrual dysfunction, and self-reported frequency of colds and flu in undergraduate women. We predicted that women with chronic self-discrepancy (who therefore experience chronic distress) would report more cold and flu symptoms, and that level of menstrual dysfunction would also predict the reporting of URI symptoms.

2. Methods

2.1. Participants

Two samples of undergraduate women enrolled in psychology courses at a Midwestern university were included. For the first sample (Sample A), all data were collected simultaneously, with participants reporting the frequency of cold and flu symptoms over the past month and year. For the second sample (Sample B), participants completed two measures in a screening session and a third one month later, and then reported weekly about cold and flu symptoms. Sample A had a mean age of 20.02 years; 140 women filled out questionnaires and received course credit. Three participants did not complete all questionnaires and were not included in analyses, resulting in a sample size of 137. Sample B had a mean age of 19.94 years; 58 women were recruited and agreed to provide weekly URI symptom assessments for course credit. Seven participants did not complete at least five weekly symptom assessments and were excluded, resulting in an effective sample size of 51.

2.2. Instruments

1. Selves Questionnaire (SQ; Higgins, Bond, Klein, & Strauman, 1986)—The SQ is a free-response measure which asks subjects to list attributes for three different domains of the self (actual, ideal, ought) from two different standpoints (self and parents) to measure perceived success/failure in personal goal pursuit. Following Higgins et al. (1986), each of the subject's ideal/own, ideal/other, ought/own, and ought/other attributes was classified as to its relation to the subject's actual/own attributes: as a match (synonymous with an actual/own attribute), a mismatch of extent (synonymous with an actual/own attribute but with a difference of extremity rating of > 1), an antonymous mismatch (antonymous with an actual/own attribute), or a nonmatch (neither synonymous nor antonymous with any actual/own attribute). For each self-guide (ideal/own, ideal/other, ought/own, and ought/other), self-discrepancy was quantified as the number of antonymous mismatches (weighted by a factor of 2) plus the number of mismatches of extent minus the number of matches. Discrepancy scores for the four self-guides were averaged to obtain an overall self-discrepancy score (interrater reliability/intraclass correlation = .87). Higher scores indicate greater overall perceived failure in self-regulation.

2. Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961)—The BDI is a widely used 21-item self-report measure of symptoms associated with

depression. Participants rate each item on a scale from 0 (*not at all*) to 3 (*extremely*) on the basis of severity.

3. Menstrual Symptom Questionnaire (MSQ; Stephenson et al., 1983)—The MSQ is a 30-item instrument including questions about symptoms experienced during a typical menstrual cycle and questions regarding typical cycle and length of menses. Answers are rated on an intensity scale of 0 (*does not apply to me*) to 6 (*extremely*). Following Stephenson et al., an overall menstrual dysfunction score was created by summing scores on the following items: irregular cycle length (variation of 7 days or more); pre-menstrual negative affect; menstrual pain/cramps/nausea; and heavy bleeding (> 6 days or >3 days with 2 or more tampons).

4. Survey of Immunological and General Health (SIGH; Kang et al., 1991)—The SIGH is a checklist designed for self-report assessment of symptoms of URIs and other common illnesses in non-medical samples (Lemieux and Coe, 1995). Sample A participants recalled the number of times they had experienced cold and flu symptoms during the past month as well as the past year and completed the SIGH in a single session. For Sample B, participants received weekly emails and were asked to report on cold and flu symptoms they were experiencing that week. Participants were instructed to rate each item on a scale from 0 (*not at all*) to 3 (*severe*). Participants from Sample B completed an average of 75% of the weekly symptom reports.

2.3. Design

Participants volunteered for a study of Personality and Health, receiving course credit for participation. Sample A completed all measures (SQ, MSQ, BDI, SIGH) in the same session. Sample B completed the SQ and MSQ in a screening session; then, four weeks later, participants were recruited via in-class announcements. Those who provided informed consent completed the BDI and agreed to be contacted weekly via e-mail to assess their health for the remaining weeks of the semester. They were given written instructions regarding how to prospectively monitor and self-report the occurrence of cold and flu symptoms. E-mails were sent weekly to all participants containing URI symptom items and brief rating instructions.

2.4. Statistical analysis

Structural equation modeling was conducted using the method of maximum likelihood on the uncorrected covariance matrix, using PROC CALIS in SAS Version 9.1. The model included three measured variables (self-discrepancy, menstrual dysfunction, and distress) plus a latent variable combining four symptoms associated with URIs (*cold, flu [with fever], headache, and fatigue*). For Sample A, scores on the four items represented recalled frequency of symptoms over the past month; for Sample B, scores on the SIGH items were the average across a minimum of five weekly reports. The model hypothesized a partial mediating role for distress: paths from self-discrepancy and menstrual dysfunction to distress, and paths from distress, self-discrepancy, and menstrual dysfunction to the URI latent variable.

3. Results and Discussion

We conducted a multiple group structural equation modeling procedure (Bollen, 1990) using MPLUS (Muthen and Muthen, 2006), to determine whether either the overall model fit or individual path coefficients differed significantly between samples by testing a model that included constraints for equality of coefficients between samples. The multiple group model was an acceptable fit, $X^2(2, N = 188) = 3.41, p = .08$, RMSEA = .05 (90% CI = .00–.11), CFI = .97, GFI = .95. The overall degree of fit for this model indicated that there was no systematic difference in fit between Samples A and B. With the exception of one coefficient (the

correlation between self-discrepancy and menstrual dysfunction), the individual path coefficients for the two samples did not differ by more than .09.

We then tested our hypothesized model on the combined sample data. The model fit the combined data well, $X^2(11, N = 188) = 12.10, p = .35$, RMSEA = .02 (90% CI = .00–.08), CFI = .99, GFI = .98. As shown in Fig. 1, the four symptom items formed a robust latent variable, and all of the hypothesized paths in the model were statistically significant at $p < .01$ or greater. The model indicated that both self-discrepancy and menstrual dysfunction predicted distress and manifested direct as well as mediating influences on self-reported frequency of URI symptoms.

Within and across samples, chronic perceived failure in goal pursuit and menstrual dysfunction predicted self-reported rates of URI symptoms. The association between self-discrepancy and symptoms was both direct and mediated through distress, consistent with previous research suggesting that chronic negative affect was associated with susceptibility to URIs. Menstrual dysfunction likewise showed direct and mediating associations with URI symptoms, suggesting that it could influence health through both mood-based and hormonal mechanisms. The structural equation modeling indicated good model fit across the two samples, despite differences in time frame and assessment of URI symptoms between samples.

Study 1 was exploratory in nature and correlational in design, so therefore no causal inferences could be justified. It relied entirely on self-report (and for Sample A, the study relied upon participants' recollections of the number of times they had experienced URI-related symptoms), and the structural equation model focused on a limited number of URI symptoms. Experimental manipulation and a more detailed assessment of URI symptoms would provide a stricter test of the proposed model. The next two studies used experimental design and *a priori* sampling based on individual differences to provide more stringent tests of our hypotheses.

Study 2: Prospective Experimental Investigation of Self-Regulation, Menstrual Dysfunction, Antibody Response to Flu Vaccine, and Self-Reported Cold/Flu Symptoms

In Study 2, participants were selected for high or low levels of self-discrepancy and menstrual dysfunction and randomly assigned to receive or not receive flu vaccine, then completed weekly reports on URI symptoms. Using this selection strategy and randomization for vaccine, the impact of goal failure and menstrual dysfunction could be determined prospectively for magnitude of antibody response to vaccine and self-reported URI symptoms.

4. Methods

4.1. Design

Four groups of undergraduate women (high vs. low self-discrepancy crossed with high vs. low menstrual dysfunction) were identified at the start of two consecutive fall semesters via the same screening process as in Study 1. Participants were then recruited in November for a follow-up study of Personality and Health and received monetary compensation. After providing informed consent, a blood sample was collected and participants were randomized to receive or not receive flu vaccine. All subjects returned four weeks later to provide a second blood sample (after vaccination), as well as four months later (the following April) to provide a third sample. Beginning in January, they were contacted weekly via e-mail to report whether they had experienced any of a set of URI symptoms during the prior seven days.

4.2. Participants

Participants were undergraduate women (mean age = 20.02 years) in psychology courses at a Southeastern university. A total of 45 women were recruited for the immunization study and gave informed consent to participate. Three participants did not provide the second and third blood samples and one did not complete at least five weekly symptom assessments. Data from these participants were not included in analyses, resulting in an effective sample size of 41.

4.3. Procedure and Instruments

The SQ and MSQ were administered during the screening. Interrater reliability for the overall self-discrepancy score was .88. As in Study 1, a menstrual dysfunction score was created by summing scores on items for irregular cycle length, pre-menstrual negative affect, menstrual pain/cramps/nausea, and menorrhagia.

Approximately three weeks after the screening, participants were recruited via in-class announcements for a study of Personality and Health. Those who provided informed consent agreed to the following: (a) to be randomly assigned to receive or not receive flu vaccine during the period when the University Health Center made vaccine available to students and staff cost-free (the first two weeks of November); (b) to provide a blood sample immediately prior to immunization (or, for those not receiving vaccine, during the two-week vaccination period) as well as a second blood sample approximately one month later and a third sample the following April; and (c) at the start of the spring semester, to be contacted weekly via e-mail for a period of twelve weeks to assess their health. They were given written instructions regarding prospective monitoring for the occurrence of cold and flu symptoms. E-mails were sent weekly to all participants containing twelve URI symptom items and brief rating instructions. Participants were instructed to rate each item on a scale from 0 (*not at all*) to 3 (*severe*). Participants completed an average of 71% of the weekly symptom reports across 12-week reporting period. To quantify URI symptoms, the percentage of weeks during which each participant had reported in which any “cold” or “flu” items were scored greater than zero was computed. This percentage index had a mean of 34.3 and a standard deviation of 10.0.

4.4. Vaccine administration and antibody assessment

Immunized participants received the commercial trivalent influenza vaccine (Fluzone) available in the years of the study. For 2002–2003, it contained 15 µg each of 3 strains: A/Moscow/10/99-like strain [H3N2], A/New Caledonia/20/99 [H1N1], and B/Hong Kong/330/01-like. Antibody responses to the vaccine, both IgM and IgG, were determined by enzyme-linked immunosorbent assay (ELISA). Briefly, 96-well microtiter plates were coated overnight with vaccine diluted in hydroxymethyl methylamine buffer (50 µl vaccine and 4.95 ml Tris buffer per plate). Serum samples were diluted between 1:100 and 1:5000, and 100 µl added to each well. After 2 h incubation at 37 °C, 100 µl of anti-human IgG or IgM (Sigma) were added to each well. After 1 h incubation, Sigma Fast-p-Nitrophenyl was added, and then the reaction stopped with sodium hydroxide. The color intensity was read on a Dynatech plate reader at 405 nM, and the optical density quantified as a reflection of antibody titer.

4.5. Statistical analyses

Because the study was conducted across two years, raw antibody data were converted to percentage change from pre-vaccination baseline (for both post-vaccination blood samples). Analyses were then conducted to assess the effect of vaccination per se, as well as possible effects of level of self-discrepancy and/or level of menstrual dysfunction. To determine whether vaccination, self-regulatory failure, and menstrual dysfunction (all assessed during the fall semester) predicted self-reported URI symptoms from mid-January through mid-April,

analysis of variance were conducted with the cold/flu symptom score as the dependent variable and vaccination, self-discrepancy, and menstrual dysfunction as predictors.

5. Results and Discussion

5.1. Impact of vaccination, self-regulatory failure, and menstrual dysfunction on antibody levels

For IgG, there was a significant effect of vaccination, $F(1, 33) = 20.39, p < .0001$. Immunized participants showed a substantial rise in flu antibody levels over baseline (mean increase = 68.5% after one month and 65.2% after four months). In contrast, non-immunized participants showed almost no change in antibody levels across time (mean change at one month = 3.0% and after four months = -3.7%). No significant effects for level of self-discrepancy or degree of menstrual dysfunction were observed on the IgG response.

For IgM, several significant effects emerged: a main effect for vaccination, $F(1, 33) = 28.11, p < .0001$; a vaccination X self-discrepancy interaction, $F(1, 33) = 5.93, p < .05$; and a vaccination X self-discrepancy X menstrual dysfunction interaction, $F(1, 33) = 5.59, p < .05$. Fig. 2 depicts the mean percent change in IgM at one month by vaccination, self-discrepancy, and menstrual dysfunction. The low-discrepancy/low-menstrual dysfunction participants who received vaccine showed a greater increase (mean = 168%) than did the other three types of participants who received vaccine, all of whom had at least one putative risk factor for URIs (combined mean = 90.5%). A contrast F test indicated that the post-vaccine IgM increase in the low/low subjects was greater than for the other three vaccinated groups, $F(1, 33) = 5.21, p < .05$. As expected, non-immunized participants did not show any significant changes in IgM levels.

5.2. Impact of vaccination, self-regulatory failure, and menstrual dysfunction on URI symptoms

The analysis of reported URI symptoms indicated a significant interaction of vaccination, self-discrepancy and menstrual dysfunction, $F(1, 33) = 4.89, p < .05$. Fig. 3 depicts the mean percentage of weeks in which participants reported URI symptoms. Among the vaccinated participants, there were no substantial differences in URI symptoms. However, within the non-immunized condition, the high-discrepancy/high-menstrual dysfunction participants reported URI symptoms more frequently (mean = 71%) than all other groups (combined mean = 38%). A contrast F test indicated that self-reported URI symptoms among the high/high students was significantly greater than the combined average of all other groups, $F(1, 33) = 4.57, p < .05$.

5.3. Did antibody levels predict self-reported URI symptoms?

To determine whether antibody levels predicted URI symptoms, two hierarchical regression analyses were conducted using the percentage of weeks with URI symptoms as the criterion variable. The first analysis included vaccination status, IgG percent change from baseline at one and four months, and the interactions terms for vaccination X 1-month percent change and vaccination X 4-month percent change. The only step that accounted for a significant portion of variance in URI symptoms was the entry of the vaccination X 4-month percent change interaction term (increment in $R^2 = .18, p < .02$). Probing the interaction indicated that for the vaccinated participants, change in IgG levels from baseline did not predict URI symptoms ($p > .25$); however, for the non-immunized participants, change from baseline in IgG level at the 4-month blood draw was associated with URI symptoms ($\beta = -.54, p < .01$). The greater the increase in IgG, which corresponded to the end of the common season for URI infections, the lower the reported URI symptoms across the prior 12-week period.

The second hierarchical analysis included vaccination status, IgM percent change at 1-month and 4-months, and vaccination X percent change at 1 month and vaccination X 4-month percent change interaction terms. The only step that accounted for a significant portion of variance in URI symptoms was the vaccination X 1-month percent change interaction term (increment in $R^2 = .17, p < .02$). Additional analysis to probe the interaction indicated that for the vaccinated participants, change in IgM levels from baseline did not significantly predict URI symptoms ($p > .20$); however, for the non-immunized participants, change from baseline at the one month significantly predicted URI symptoms ($\beta = -.48, p < .01$). The greater the increase from baseline in IgM level at the one month (in this case, approximately two months prior to the reporting period), the lower the reported URI symptoms.

Overall, Study 2 indicated that perceived failure in self-regulation and menstrual dysfunction influenced the magnitude of antibody response to flu vaccine, especially the primary antibody of the IgM class, as well as self-reported URI symptoms over a 12-week period coinciding with peak season of infection over the winter months. Vaccinated students mounted protective antibody responses and thus it was not surprising that no significant effect of psychological status on URI symptoms was observed among them. In contrast, among non-immunized students, the combination of high self-discrepancy/high menstrual dysfunction was associated with the most self-reported URI symptoms. It was of particular interest that among the non-immunized students, those showing the smallest increases in antibody at 1- and 4-months post-immunization reported more URI symptoms across the 12-week observation period.

By assessing flu antibody at two time points after vaccination, it was possible to gauge the effect of self-regulatory failure and menstrual dysfunction on efficacy of immunization. Those two putative risk factors did influence the initial antibody response, although only for the IgM class at one month. Given that flu vaccines are designed to induce protective responses even in those with compromised immunity, it is perhaps not surprising that the longer-term IgG responses were not impaired. One limitation of our assay approach was that we determined the antibody levels to all three flu antigens simultaneously, and thus probably measured more antibody generated in response to the two strains of influenza A. However, the differences found between IgM and IgG do concur with many other studies that showed primary antibody responses are more susceptible to influence than are secondary responses, and further that transitional immune processes, such as class switching from IgM to IgG, are more likely to be impacted than are long-term IgG levels after a potent recall antigenic stimulus like the trivalent flu vaccine (Wetherell and Vedhara, 2007). In contrast to some reports that the sustained duration of the IgG response is a sensitive index (Phillips et al., 2006), we did not see an effect of psychological state on IgG levels at 4 months. However, that simply may reflect that once effectively initiated by immunization, the high production of IgG was then maintained between 1- and 4-months post-vaccination in most students.

To our knowledge, Study 2 provides the first evidence that self-regulation and menstrual dysfunction can influence the primary response to vaccination which, in turn, was associated with frequency of self-reported cold and flu symptoms. Although we did not manipulate either self-discrepancy or menstrual status, participants had been selected on the basis of differences on these attributes. From a clinical perspective, the data suggest the possibility of identifying higher risk students for annual immunization programs. The maximal gains achieved by vaccination were evident in the reduced URI reporting for students with high levels of self-discrepancy. In turn, the findings also raised the possibility that *changing students' perceptions of goal pursuit failure* might lead to fewer cold and flu symptoms – a possibility explored in the final study.

Study 3: The Effect of a Disclosure Writing Manipulation On Antibody Response to Vaccination and URI Symptoms

Writing manipulations have been associated with reliable and even dramatic changes in emotions, immunity, and health. For instance, Petrie et al. (1995) observed that a directed written disclosure of emotional experiences enhanced antibody production following hepatitis B vaccination. Booth et al. (1997) reported differences in numbers of circulating lymphocytes and T subsets after writing about emotional experiences as compared to a control condition (i.e., writing about mundane topics). The therapeutic effects of writing derive from a “cognitive restructuring” of events and subsequent changes in negative affect (Pennebaker, 1997).

If a writing manipulation helped individuals reduce self-perceived failure, such a change might then lead to a decrease in frequency of URIs. Cameron and Nicholls (1998) observed that a self-regulation writing task predicted decreased subsequent health clinic visits. Similarly, King (2001) found that writing about a type of life goal was associated with less subsequent illness versus a control condition. In Study 3, a writing manipulation adapted from Pennebaker and colleagues was used to determine whether changing self-perceived failure in goal pursuit would influence antibody responses to flu vaccination as well as self-reported URI symptoms. In order to focus the study on the potential health impact of altering self-discrepancy, and because we had no *a priori* hypotheses about how the writing manipulation would influence or interact with menstrual dysfunction, that variable was not included in this final study.

6. Methods

6.1. Design

Two groups of undergraduate women (high or low self-discrepancy) were identified at the start of two consecutive fall semesters. Participants were then recruited from this screening sample several weeks later for a study of Personality and Health and received monetary compensation for participation. After providing informed consent, a blood sample was collected and participants agreed to receive flu immunization and enroll in a multi-session prospective study beginning with writing sessions on three days over a five-day period. Participants were randomly assigned to write about personal issues or about mundane details of their lives. All participants returned one month after vaccination to provide a second blood sample, as well as four months later to provide a third blood sample. Beginning in January, they were contacted weekly over a twelve-week period via e-mail and asked to respond to a series of questions regarding whether they had experienced URI symptoms during the prior week.

6.2. Participants

Participants were undergraduate women (mean age = 19.56 years) in psychology courses at a Southeastern university. A total of 41 women from the screening samples were recruited for the prospective study and gave informed consent. Four participants did not provide the second and third blood samples; data from these participants were not included in analyses, resulting in an effective sample size of 37.

6.3. Procedure and Instruments

The Selves Questionnaire (SQ) was administered during a screening battery. Interrater reliability for overall self-discrepancy was .83. Participants for the prospective study were recruited from those scoring in the highest and lowest quartiles for overall self-discrepancy.

Approximately three weeks after the screening, participants were recruited for a study of Personality and Health. Those who provided informed consent agreed to the following: (a) to receive flu vaccine during the period when the University Health Center made vaccine available

to students and staff cost-free (the first two weeks of November); (b) to provide a blood sample immediately prior to immunization as well as a second blood sample approximately one month later and a third sample the following April; (c) to participate in a three-session writing exercise, scheduled individually over a five-day period; and (d) at the start of the spring semester, to be contacted weekly via e-mail for 12 weeks to assess their health. E-mails were sent weekly to all participants containing the URI symptom items from the SIGH and brief rating instructions to distinguish colds and flu on a scale from 0 (*not at all*) to 3 (*severe*). Participants completed an average of 67% of the weekly reports across 12-week reporting period. URI symptoms were quantified as to the percentage of weeks in which the “cold” or “flu” items were scored greater than zero. This percentage index had a mean of 39.0 and a standard deviation of 11.1.

6.4. Writing task

Participants were randomly assigned to write either about important personal issues (*unburdening condition*) or about everyday activities (*control condition*). Instructions for the unburdening condition began as follows: “We want you to write down your very deepest emotions and thoughts about those issues that are most troubling for you. This could include who you would like to be or feel you should be, who you have been in the past, and who you are now.” The instructions were phrased to encourage participants to write about their promotion (“who you would like to be”) and prevention (“who you feel you should be”) goals. Instructions for the control condition began as follows: “We want you to describe in detail what you have done since you woke up this morning. Your description should be as objective as possible.” The instructions for the control condition were intended to discourage participants from exploring personal goals and feelings. Participants wrote for approximately 20 minutes. Their responses were scored using the Linguistic Inquiry and Word Count (LIWC) computer program for text analysis (Pennebaker and Francis, 1996). It was hypothesized that during the writing task, the unburdening condition would be associated with greater negative affect content than the control condition (consistent with encouraging participants to confront their perceived failures). We also predicted that participants in the unburdening condition who evidenced some degree of resolution of personal issues (i.e., those who manifested reduced negative affect content by the third day) would subsequently demonstrate larger antibody responses and report fewer URI symptoms than participants in the same condition who did not manifest reduced negative affect content by the third day (i.e., did not give evidence of having resolved personal issues).

6.5. Vaccine administration and antibody assessment

All participants received the trivalent influenza vaccine (Fluzone) used in clinical practice, and IgG responses were quantified via ELISA as in Experiment 3. Because the study was conducted across 2 academic years, raw antibody values were standardized to percentage change from pre-vaccination baseline (for both the second and third blood samples).

6.6. Statistical analyses

To determine the impact of the writing manipulation, a repeated-measures ANOVA was conducted using the LIWC overall negative affect content score for each day of the writing task, with writing condition and level of self-discrepancy as between-subject factors. Repeated-measures ANOVAs then were conducted to determine whether changes in negative affect content over the writing period predicted subsequent antibody levels and URI symptoms.

7. Results and Discussion

7.1. Acute impact of the writing task on negative affect content

Table 1 presents mean negative affect content by writing condition and level of self-discrepancy for each day of the writing task. Main effects were observed for writing condition, $F(1, 33) = 100.11, p < .0001$, and for level of self-discrepancy, $F(1, 33) = 4.17, p < .05$. A statistically significant writing condition X level of self-discrepancy interaction also was observed, $F(1, 33) = 4.25, p < .05$.

Participants in the unburdening condition generated substantially more negative affect content than those in the control condition. Within both writing conditions (but particularly for the unburdening condition), high-discrepant participants expressed more negative affect content than low-discrepant participants. In the unburdening condition, the high-discrepant participants generated the greatest negative affect content, peaking on Day Two. In contrast, the low-discrepant participants showed no significant change in negative affect content.

7.2. Impact of the writing task on antibody levels

To determine the impact of the writing task on IgG responses to vaccination, we classified participants according to a median split on Day One negative affect content as well as whether or not Day Three negative affect content was at least 25% lower than on Day One. This classification resulted in four groups: High Day 1/Low Day 3, High Day 1/High Day 3, Low Day 1/High Day 3, and Low Day 1/Low Day 3. We then analyzed IgG levels at one month and four months post-vaccination as change scores from baseline (Fig. 4). A significant main effect for Time, $F(1, 33) = 4.18, p < .05$, as well as a significant Time X Group interaction, $F(1, 33) = 4.05, p < .05$, were found. At one month post-vaccination, the IgG response was notably greater in the two groups of participants for whom a more robust antibody response would be expected: the High Day 1/Low Day 3 group (i.e., high-discrepant participants who successfully unburdened), and the Low Day 1/Low Day 3 group (low-discrepancy participants for whom the writing task had little affective significance). The IgG response at one month post-vaccination between those two groups (combined mean increase = 241%) and the other two groups (combined mean increase = 163%) was significant in a contrast F test, $F(1, 33) = 4.64, p < .05$. At four months post-vaccination, the differences in IgG levels among the four groups followed the same pattern. In addition, the two groups that had initially manifested greater IgG response maintained those antibody levels while the other two groups manifested slightly decreased antibody levels: contrast F test, $F(1, 33) = 4.98, p < .05$.

7.3. Impact of the writing task on weekly reporting of URI symptoms

To determine the impact of the writing task on URI symptoms, we conducted an ANOVA using the same participant classification as in the previous analysis. A statistically significant effect of Group was observed, $F(1, 33) = 3.36, p < .05$. Participants in the High Day 1/High Day 3 group (i.e., those who wrote about emotionally significant issues but apparently were unable to “process” them successfully) reported URI symptoms more often (mean = 54.5%) than the other groups (combined mean = 32.8%, range = 30.3% to 35.3%). The difference between the High Day 1/High Day 3 group and the other groups was significant in a contrast F test, $F(1, 33) = 4.28, p < .05$.

7.4. Did antibody levels predict URI symptoms?

To determine whether antibody levels predicted the weekly reporting of URI symptoms, a hierarchical regression analysis was conducted using percent weeks with URI symptoms as the criterion variable and percent change in IgG at one and four months post-immunization plus their interaction as predictors. The interaction term, entered last, accounted for a

marginally significant increment in variance (increment in $R^2 = .08$, $p < .10$). Additional analysis to probe the marginal interaction indicated that among participants with large increase in IgG at one month, the percent change in IgG at four months did not predict URI symptoms. However, among participants with smaller IgG responses at one month, the IgG levels at four months were negatively associated with URI symptoms ($\beta = -.31$, $p < .10$).

8. General Discussion

Previous research examining the acute effects of priming personal goals (Strauman et al., 1993, 2004) revealed a psychobiological pathway whereby perceptions of success or failure in goal pursuit influenced motivation and affect, which in turn led to alterations in NK cell numbers and activity. Those studies suggested that self-regulatory failure could influence health, but they had not been designed to assess the chronic impact of perceived failure in goal pursuit on either immunity or illness. The studies presented here indicated that individual differences in self-regulation predict the reporting of cold and flu symptoms in otherwise healthy young adult women, both alone and in combination with menstrual dysfunction.

The three studies varied in terms of time frame (cross-sectional as well as prospective), design (correlational as well as experimental), and assessment of health-relevant outcomes (self-reported URI symptoms alone versus self-reported URI symptoms in conjunction with antibody responses to flu vaccine). As such, the general finding that self-discrepancy influences both retrospective self-reporting of URI symptoms as well as their prospective occurrence and the associated antibody biology provides robust support for the hypothesis that individual differences in self-regulation can affect the likelihood that healthy adults will experience URIs.

RFT proposes that promotion and prevention goals operate as general social-perceptual styles or “world views” that exert a continuous influence on self-evaluation. Such individual differences are not inherently adaptive or maladaptive; rather, they have costs and benefits depending on one’s perceived success or failure in attaining goals. Individual differences in regulatory focus can be identified as early as age six (Manian et al., 2006). Moreover, although the kinds of goals that people prefer to pursue are relatively stable (Strauman, 1996), perceived success or failure can vary according to life circumstances and can be modified via psychotherapy (Strauman et al., 2006). The findings from Study 3, in which high-discrepancy participants who successfully “unburdened” subsequently reported fewer URI symptoms (and manifested stronger antibody responses to flu vaccine) than high-discrepancy participants who did not, are particularly noteworthy from the perspectives of both vulnerability and intervention.

The results from the present studies (as well as the priming studies by Strauman et al. [1993, 2004] on which these studies were based) are consistent with prior research linking chronic negative affect with greater vulnerability to URIs, but there are several key distinctions that deserve comment. Participants in the present studies were not dealing with discrete life events that were objectively positive or negative; rather, they were reacting to their own perceptions that they either were or were not attaining personal goals. In this regard, Studies 2 and 3 are particularly informative. All participants, as students, faced the same basic set of challenges across the academic year; but in both studies, their perceptions of success or failure in goal pursuit influenced their self-reported URI symptoms as well as the initial magnitude and persistence of antibody responses to flu vaccine.

It should be noted that the self-reports of URIs included a range of symptoms, from fatigue and headache to muscle aches, nasal congestion, and fever. We did not attempt to determine whether the pattern of reported symptoms would have met strict diagnostic criteria for influenza, although the predictive associations obtained in our studies were found both for

more mild cold-like symptoms and more severe flu-like symptoms that included the occurrence of fever. In Study 2, the high-discrepancy/high-menstrual dysfunction participants reported having cold or flu symptoms during a full 70% of the weeks for which they provided data, which were collected during the high infection season of the winter months. The findings for self-reported URI symptoms were supported by the quantification of antibody in Studies 2 and 3, in which the high rate of illness was markedly attenuated in the immunized women. Although the effects of self-discrepancy and menstrual dysfunction in Study 2 were more evident for the IgM levels during the primary response at one month post-vaccination, we also observed that participants in Study 3 who failed to benefit from the unburdening condition tended to have lower IgG at both one and four months post-vaccination.

Whereas the self-regulation literature has emphasized the acute impact of priming manipulations on affect and physiology (e.g., Strauman et al., 1993), emotional disclosure writing manipulations are often reported to have a longer-term impact on health (Smyth, 1998; Smyth et al., 1999). Indeed, Study 3 provided qualified support for the health benefits of the unburdening writing condition. However, it should be noted that the high-discrepant women whose writings continued to include high levels of negative affect content on the final writing day actually showed a substantially *weaker* antibody response to vaccination, with relatively lower IgG levels at both one month and four months post-vaccination. In contrast, the high-discrepant women whose writings contained high levels of negative affect content initially but lower levels by the third writing day showed stronger antibody responses and did not report the strikingly high occurrence of URI symptoms reported by their high-discrepant counterparts.

The three studies focused on women both because of previous reports of small but reliable gender differences in the magnitude and variability of self-discrepancy. In addition, our pilot research indicated reliable associations between self-discrepancy and menstrual dysfunction, and therefore assessing menstrual dysfunction provided a second means to probe the relationships between chronic negative affect and health status. The alternative hypothesis that arose in our pilot data was that self-regulation might not be an independent influence on immunobiology and health; as such, it was important to measure both self-discrepancy and menstrual dysfunction in order to determine the nature of their predictive associations with antibody response to vaccine as well as self-reported cold/flu symptoms. In fact, the highest levels of URI symptoms was reported by high-discrepant women who also experienced menstrual dysfunction. Would the same association between self-discrepancy and self-reported frequency of URI symptoms be evident among males? We believe so, although it would likely be less pronounced.

In summary, the three studies contribute to the growing literature indicating that psychological processes are important determinants of the incidence and severity of URIs (Cohen, 2005). Individual differences in perceived success/failure of self-regulation may influence health by creating and maintaining negative affective states that, in turn, contribute to a vulnerability to pathogens. Certainly there were some limitations of the studies, including sample sizes and reliance on self-report of URI symptoms. As always, replication is in order, and additional studies of the health consequences of self-discrepancy and self-regulation should focus on other mediating and moderating processes that link psychological states with illness susceptibility, as well as on identifying which individuals are most likely to benefit from established immune-enhancing interventions, such as immunization.

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Fig. 1.

Path model linking self-discrepancy and menstrual dysfunction with distress and frequency of self-reported cold and flu symptoms over the past year. Path coefficients are listed separately for Sample A (cross-sectional data collection, $N = 137$) and Sample B (prospective data collection, $N = 51$). Total $N = 188$. $X^2(11) = 12.10$, $p = .35$. RMSEA = .02 (90% CI = .00–.08). CFI = .99. GFI = .98. $*p < .01$. $**p < .001$.

Fig. 2.

Mean percent change in IgM levels at one month by vaccination status, level of self-discrepancy, and level of menstrual dysfunction. SD = self-discrepancy. MD = menstrual dysfunction.

Fig. 3.

Mean percentage of weeks during which participants reported URI symptoms, by vaccine status, level of self-discrepancy, and degree of menstrual dysfunction.

Fig. 4. Mean percent change in IgG at one and four months post-vaccination by level of negative affect content on Day 1 of the writing task and change in negative affect content by Day 3 (the final day of the manipulation).

Table 1
Mean negative affect content for each day of the writing task by writing condition and level of self-discrepancy

Writing Condition	Level of Self-Discrepancy	N	Day 1	Day 2	Day 3
Unburdening Unburdening Control Control	High	10	3.18 (0.8)	3.68 (1.1)	2.29 (0.9)
	Low	9	2.09 (0.7)	2.11 (0.6)	2.11 (0.7)
	High	12	0.45 (0.5)	0.20 (0.4)	0.27 (0.4)
	Low	6	0.36 (0.4)	0.16 (0.3)	0.40 (0.3)

Note. Standard deviations are presented in parentheses.