# Negative Thoughts and Health: Associations Among Rumination, Immunity, and Health Care Utilization in a Young and Elderly Sample

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**Objective:** In the present study, it was tested whether rumination—negative, recurrent thoughts—would be associated with immune parameters and health care utilization. Because rumination has been associated with sadness and subjective sleep quality, it was tested whether these factors mediated the possible effects of rumination. A young sample and an elderly sample were included to test for age differences in the association between rumination and health-related measures. **Methods:** A representative sample of 196 young subjects (20 to 35 years) and 314 elderly subjects (70 to 85 years) completed questionnaire measures of rumination, sadness, and subjective sleep quality. Immune measures included leukocyte counts, lymphocyte subsets, natural killer cell activity, and T-cell proliferation. Contacts with primary care physicians were registered for 1 year through central registers. **Results:** Rumination displayed a positive association with total leukocyte count, total lymphocyte count, and number of B cells among the elderly, and this was not mediated by sadness or subjective sleep quality. Rumination was also positively associated with number of telephone consultations during the follow-up for the elderly, and this was partly mediated by sadness and subjective sleep quality. Although total leukocyte counts correlated with number of telephone consultations at the follow-up, none of the immune parameters mediated the association between rumination and health care utilization. No significant associations were found for the young participants. **Conclusion:** The results suggest that rumination may be associated with health-related measures in the elderly. Thus, negative thoughts may be detrimental to health, independently of negative affect. **Key words:** rumination, immunity, health care, aging.

**NK** = natural killer cell; **GP** = general practitioner; **MMSE** = Mini-Mental State Examination; **PBMC** = peripheral blood mononuclear cell; **FCS** = fetal calf serum; **PHA** = phytohemagglutinin.

## INTRODUCTION

The way a person copes with stress has been suggested to be of importance for both mental and physical health (1). Problem-focused and emotion-focused coping have been suggested as general categories of coping, where problem-focused coping is aimed at changing the situation and emotion-focused coping is used to manage one's emotional response.

Rumination may be considered 1 type of emotion-focused coping (2) and has been defined as conscious, spontaneous, and recurrent thoughts or images or both about past negative information (3). Rumination has been suggested to be related to negative affect by focusing the person's attention on the negative state (4,5) and has in a number of experimental, cross-sectional and longitudinal studies been related to sadness/depression (4–9).

### Rumination and Health

Rumination has been found to be associated with different types of physical pain, dental pain, and pain-related disability in studies using a specific type of pain-focused rumination (10–12). One study exploring the association between rumination and use of analgesia during labor also suggests an association between a more general measure of rumination and pain (13).

Results from studies investigating subjective health also indicate a relation between rumination and health. Several cross-sectional studies have found negative correlations between rumination and various measures of subjective health (14–16), and in a recent prospective study, an association between rumination and self-reported physical health was found when following a young sample over a period of 1 year (17).

These studies imply a connection between rumination and health. However, they all rely on subjective measures of health-related variables, and although subjective health measures are reliable indicators of objective health status (18,19), exploring more objective measures of health would strengthen these findings.

### Rumination and Physiological Responses

One possible pathway between rumination and health may be the cardiovascular system, but studies investigating the association between rumination and cardiovascular measures show mixed results (20–23), and the possibility that rumination affects the cardiovascular system remains open.

Another possible connection between rumination and health is the immune system. Various psychosocial variables, including sleep quality and depression, have been linked with several measures of immunity (24–27). Although different aspects of coping have been shown to be associated with immunity (28), to the best of our knowledge, no previous studies have investigated the relation between rumination and immunity.

### Aim of the Present Study

In the present study, the association among rumination, immunity, and health care utilization was investigated. Be-

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cause rumination has been associated with sadness and subjective sleep quality (29), these were included to test for mediation effects. Because the study included a number of immune parameters at baseline, this opened the possibility to explore whether the possible effect of rumination on health care utilization was mediated by immunity. Because the associations between rumination and immunity and health care utilization have not been investigated before, we consider our study partly exploratory, although we had clear expectations that rumination would be associated with poorer immunity and more health care utilization.

Both a young sample and an elderly sample were included to address possible age differences in the association between rumination and health care utilization. This was done because elderly people have more vulnerable health and higher health care utilization (30) and therefore may show stronger associations between rumination and health care utilization. In addition, it has been suggested that the elderly may be more vulnerable to the adverse effects of psychosocial factors on immunity (31).

Immunological measures included both quantitative measures, ie, leukocyte and lymphocyte subset counts, and functional measures such as natural killer cell (NK) activity and T-cell proliferation, which are all standard measures within psychoneuroimmunology research (32). Because the primary interest was in health as experienced in the daily lives of people rather than major health problems, health care utilization was operationalized as use of services performed by the general practitioner (GP) and other primary care physicians. Selecting a relatively healthy sample also meant that hospital health care utilization was not expected to be common, and therefore, this variable was not included in the present study.

## METHODS AND MATERIALS

### Participants

A total of 196 (109 women and 87 men) young subjects age 20 to 35 years (mean, 27.29; SD, 4.40) and 314 (169 women and 145 men) elderly subjects age 70 to 85 years (mean, 75.24; SD, 3.95) volunteered to participate in the baseline study. The sample was community-dwelling and representative for these age groups of the Danish population for major sociodemographic variables, including marital status, income, and educational level.

### Recruitment

The participants were recruited from 9 GPs in Aarhus County. From the county's central register of GPs' lists of patients, potential participants in the appropriate age groups were extracted by computer. The extract included all patients age 70 to 85 years and a random selection of patients age 20 to 35 years. Each GP then checked the list of patients and indicated patients fulfilling the following inclusion criteria: a) mobility: the patients had to be able to get to the hospital where the study took place; b) language: the patient had to be able to speak, understand, and read Danish; and c) mental health: the patient could have no history of psychotic episodes, mental debilitation, or dementia. Other exclusions criteria were pregnancy, diagnosed diseases influencing the immune system such as cancer, serious allergy, and autoimmune diseases. Moreover, patients receiving medications with possible effects on the immune system such as systemic hormonal treatment (except the contraceptive pill), systemic antibiotics, antineoplastic and immune modulating agents or drugs, and antirheumatics were also excluded. Thus, the sample recruited for the study was generally in good health.

A total of 1759 patients were selected as described by their GPs and received an invitation to learn more about the study, including an information leaflet and a response slip to be returned to the investigators. A total of 774 patients returned the response slip with a positive indication (resulting in a response rate of 44%) and were contacted by telephone and informed about the project. The patients indicating willingness were enrolled in the study until a total of 510 subjects (196 young and 314 elderly) was reached.

### Questionnaires

All questionnaires had been translated into Danish using a translation/back-translation procedure.

Rumination was measured using the rehearsal subscale of the Emotional Control Questionnaire (33). The scale consists of 14 items, with higher scores indicating more rumination. In the original version, a yes/no answer format was used, but a 5-point Likert scale answer format was adapted (ranging from "does not apply at all" to "applies perfectly"), which has been validated in a previous study (29). The translated scale has been shown to exhibit satisfactory internal reliability (Cronbach á = 0.79) and a 3-month test-retest reliability of 0.71. In the present study, the scale showed a Cronbach á of 0.81. Missing values for totals (35 cases) were replaced using series means.

Sadness was measured using the depression-dejection subscale (8 items) of the short version of the Profile of Moods Scale (34,35). The participant is asked to indicate mood during the previous week on a 5-point Likert scale ranging from "not at all" to "very much." The Danish translation has been shown to have satisfactory internal reliability, with Cronbach á for the different subscales ranging from 0.72 to 0.90. In the present study, the depression-dejection scale showed a Cronbach á of 0.90. Missing values for totals (33 cases) were replaced using series means.

Subjective sleep quality was measured using one 5-point Likert scale question on subjective sleep quality from the Pittsburgh Sleep Quality Index (36). The question correlates highly with the total scale ($\rho = 0.72$; $N = 405$; $p < .0005$) and was selected because it was the item showing the highest correlation with rumination in a previous study (29). Missing values for totals (9 cases) were replaced using series means.

The participants also answered a question on whether they lived alone, and this item was used as an approximation of marital status.

The Mini-Mental State Examination (MMSE; 37) was used to screen for signs of cognitive impairment. The MMSE is conducted as a brief interview in which the participants are asked 19 questions measuring different aspects of cognition like orientation, recall, and naming. The scale yields a total score of 30 if all items are answered correctly. For the present study, a relatively lenient exclusion criterion of 20 was adopted because the testing conditions were not optimal (there was some noise and disturbance).

### Procedure

At the baseline study, participants were mailed a package of questionnaires to be completed at home. This included the rehearsal subscale of the Emotional Control Questionnaire among a number of other measures relevant to other aspects of the study. Between 7 and 14 days later, the participants came to the hospital in groups of 5 to 8 and took part in a session including signing an informed consent and completing questionnaires, among these the Profile of Moods Scale depression-dejection subscale and the item on subjective sleep quality. The participants also had a sample of blood drawn (in Li-Heparine vials), had their hand grip strength measured, and completed the MMSE (none of the participants scored below 20, and therefore, no participants were excluded). After finishing the procedure, the participants were debriefed and thanked for their participation. The participants also received 125 DKK (approximately US $15) to cover transport expenses. The data collection extended from December 2000 to June 2001.

### Immunological Analyses

#### *Leukocyte Counts*

The leukocyte counts were performed immediately after blood was drawn using an automated cell counter (Coulter Counter STKS, Miami, FL).

### *Preparation*

Peripheral blood mononuclear cells (PBMCs) were isolated from lithium-heparinized whole blood samples by Ficoll-Paque (Pharmacia Biotech, Uppsala, Sweden) gradient separation (2), washed twice in RPMI1640 (Gibco BRL, Germany) with 5% fetal calf serum (FCS), and cryopreserved and stored at −135°C until use.

Before analysis for immunophenotype, proliferative capability, and NK activity, the PBMC suspension was quickly thawed at 37°C and washed once before resuspension in RPMI1640 (Gibco BRL) with the addition of 10% FCS (Biochrom KG Merck Eurolab, Berlin, Germany). Cell viability was tested by trypan blue exclusion test (1), and the cell sample was adjusted to obtain a final concentration of $4 \times 10^6$ viable cells/ml.

### *Analyses of Lymphocyte Subsets*

Expression of the cell surface phenotypes was measured by flow cytometry using a Coulter XL-2 flow cytometer (Coulter Electronics, United Kingdom). Data were analyzed using FlowJo software (Treestar, San Carlos, CA). Direct fluorochrome-conjugated antibodies (fluorescein isothiocyanate [FITC] or phycoerythrin [PE]) were purchased from DAKO, Copenhagen, DK (Leucogate cat. no. FR700; anti-CD3FITC cat. no. F0818; anti-CD4FITC cat. no. F0766; anti-CD8FITC cat. no. 0765; anti-CD56RPE cat. no. R7251; anti-CD19RPE cat. no. R0808). The following isotype controls were included in the study: murine $IgG_1$FITC/$IgG2_a$RPE (DAKO cat. no. X0949).

A total of $2 \times 10^5$ cells were incubated with the appropriate antibodies for 15 minutes at room temperature in the dark, washed twice with PBS containing 0.1% sodium azide, and fixed in 0.99% formaldehyde before analysis.

### *Natural Killer Activity*

Cytolytic activity was determined by a standard 4-hour $^{51}$Cr-release assay. The NK-sensitive human chronic myelogenous leukemia cell line K562 (3) was used as target cells, cultured in RPMI 1640 (Gibco BRL); supplemented with 10% FCS, 2% penicillin and streptomycin, and 1% glutamine; and kept in logarithmic growth phase. For radioactive labeling, the target cells (K562) were incubated with 100 $\mu$Ci $Na_2{}^{51}CrO_4$ (NEN Life Science Products, Brussels, Belgium) at 37°C in a humidified atmosphere of 5% $CO_2$ in air for 1 hour under gentle resuspension at 15-minute intervals. After incubation, the target cells were washed twice to remove nonincorporated $^{51}$Cr and adjusted to $1 \times 10^5$ cells/ml.

For nonlabeled feeder cells, K562 cell suspension was adjusted to a final concentration of $5 \times 10^5$ cells/ml.

Target cells were plated in 96-well round-bottomed plates at $10^4$ cells/well. Effectors (PBMCs) were added to the wells at various effector-to-target ratios (10:1, 20:1, and 40:1). Assay plates were incubated at 37°C with 5% $CO_2$ for 4 hours, after which the $^{51}$Cr released from lysed target cells was measured in a ã-counter (Cobra Autogamma Packard, Canberra Company, United Kingdom). The specific release was calculated from the formula

NK cytotoxicity (% kill) = [experimental $^{51}$Cr release − spontaneous $^{51}$Cr release]/[([0.8] max $^{51}$Cr release) − (spontaneous $^{51}$Cr release)] × 100

where max $^{51}$Cr release was obtained by harvesting both cells and supernatant and spontaneous $^{51}$Cr release was obtained by harvesting the supernatant from wells containing target cells alone. The factor 0.8 is a constant, which counterbalances the amount of released $^{51}$Cr, bound by proteins and cell debris. The spontaneous release never exceeded 12% of the maximal release (in most cases, 4% to 8%). To estimate the intraindividual variation of the $^{51}$Cr release assay, PBMCs from the same normal (control) donor were always assayed together with the incubated PBMCs at each assay day (data not shown).

### *Phytohemagglutinin-Stimulated T-cell Proliferation*

The effect of polyclonal stimulation with phytohemagglutinin (PHA) on cell proliferation was evaluated by [$^3$H] thymidine incorporation (4). PBMC were resuspended in RPMI 1640 (Gibco BRL) with the addition of 10% FCS to a concentration of 0.2 × 106 cells/ml and cultured in microtiter wells in the presence or absence of PHAp (0.5 $\mu$l/ml; Becton Dickinson) for 42 hours. Cells were pulse-labeled for the last 24 hours with 5 $\mu$Ci/ml of [$^3$H]thymidine (2.0 Ci/mmol; Amersham Pharmacia Biotech, Freiburg, Germany).

Because of error in blood separation procedure, data on NK activity are available for only 271 (86 young and 185 elderly) participants, and data on PHA-stimulated T-cell proliferation are available for only 195 (59 young and 136 elderly) participants.

### Health Care Utilization

Data on health care utilization were extracted from the county's central register. This register is created for payment purposes, because the GPs are partly paid on a fee-for-service basis. The information was retrieved from the register using the unique national identification number for each Danish citizen (the Central Personal Registration number) of the participants in the study. Health care utilization consisted of many different services, with telephone consultations and ordinary face-to-face consultations with the GP the very dominant services.

### *Three-Month Follow-up*

For the short-term follow-up period, data were retrieved for the first 3 months after the participants completed the study. Thus, if a participant completed the study in January, data from February to April were retrieved for the short-term follow-up period. Because the number of health care utilizations was not very large using this relatively short follow-up period, all types of health care utilizations were summarized to yield 1 variable of total health care utilization. Also, because 26 participants had received a letter from the study group that they should contact their GP (eg, because of high depression scores), 1 visit to the GP for each of these participants was subtracted to ensure that data did not reflect visits initiated because of participation in the study.

### *One-Year Follow-up*

For the long-term follow-up period, data were retrieved from October 2001 until October 2002, thus creating a 1-year follow-up period that was equal for all participants (but note that some participants had completed questionnaires 4 months before this period, whereas others had completed questionnaires as long as 10 months before this period). As for the 3-month follow-up, a total health care utilization was calculated. In addition, the longer follow-up period allowed the opportunity to explore the association between rumination and the separate types of health care utilizations. Because preliminary analyses indicated that only 2 types of health care utilization—telephone consultation and face-to-face consultation—had a mean above 1.0, analyses on separate types of health care utilizations were limited to these 2 variables. Participants who had moved to another county or left the country and participants who were deceased during the follow-up period were excluded because these were registered with no health care utilizations (a total of 34 participants). These participants did not differ from the remaining sample with respect to the baseline measures of psychological variables, immunological measures, and health care utilization for the short-term follow-up period ($t$ values from −1.55 to 1.17; $p > .20$).

### Statistical Analyses

Group comparisons were performed using a series of $t$ tests, and associations between rumination, sadness, subjective sleep quality, and selected immune parameters and health care utilizations measures were analyzed by stepwise multiple linear regression. All analyses were conducted using SPSS version 9.0.

## RESULTS

A series of $t$ tests was conducted to investigate age differences in the psychosocial and health-related variables. The results can be seen in Tables 1 to 3. There was an age difference for sadness ($t(475) = 2.04$; $p < .05$), where the young scored higher than the elderly, and for the score on the MMSE, where the young also scored higher than the elderly. The elderly had higher numbers of leukocytes, neutrophils, monocytes, basophils, and $CD4^+$ to $CD8^+$ ratio, whereas the

**TABLE 1. Age Differences in Rumination, Negative Affectivity, Subjective Sleep Quality, and MMSE**

| Variable | Young ($N$ = 196) | Elderly ($N$ = 314) |
|---|---|---|
| Rumination (Emotional Control Questionnaire) | 19.07 (7.61) | 18.14 (7.05) |
| Sadness-depression (BDI-II) | 3.35 (4.62)* | 2.56 (3.64)* |
| Subjective sleep quality | 0.80 (0.66) | 0.73 (0.69) |
| MMSE | 29.24 (0.91)** | 28.24 (1.53)** |

** $p < .001$. * $p < .05$.

**TABLE 2. Age Differences in Immune Measures**

| Immune Parameters | Young ($N$ = 42–129) | Elderly ($N$ = 99–234) |
|---|---|---|
| Leukocytes[a] | 6.22 (1.68)* | 6.74 (1.86)* |
| Neutrophils[a] | 3.47 (1.33)** | 4.07 (1.55)** |
| Lymphocytes[a] | 1.99 (0.57)* | 1.79 (0.71)* |
| Monocytes[a] | 0.52 (0.18)** | 0.61 (0.21)** |
| Eosinophils[a] | 0.20 (0.13) | 0.21 (0.14) |
| Basophils[a] | 0.004 (0.002)** | 0.005 (0.003)** |
| $CD4^+$ T lymphocytes[a] | 0.54 (0.24) | 0.53 (0.27) |
| $CD19^+$ B lymphocytes[a] | 0.33 (0.17) | 0.30 (0.40) |
| $CD8^+$ T lymphocytes[a] | 0.57 (0.27)* | 0.50 (0.30)* |
| $CD3^-CD56^+$[a] | 0.33 (0.23) | 0.33 (0.20) |
| $CD4^+$:$CD8^+$ ratio | 1.15 (0.83)* | 1.36 (0.98)* |
| NK activity 10:1[b] | 14.06 (12.06) | 12.64 (12.20) |
| NK activity 20:1[b] | 24.21 (17.88) | 22.47 (17.95) |
| NK activity 40:1[b] | 38.97 (23.26) | 36.49 (22.99) |
| T-cell proliferation[c] | 98.54 (91.47)* | 56.38 (78.76)* |

* $p < .05$. ** $p < .0005$.
[a] Number of cells ($10^9$/L).
[b] Percent kill of the NK-sensitive line K562.
[c] T-cell proliferation was determined by [$^3$H]-thymidine incorporation after 42-hour culturing of PBMCs.

**TABLE 3. Age Differences in Health Care Utilization for the Short-Term and Long-Term Follow-Up Periods**

| Health Care Utilization | Young | Elderly |
|---|---|---|
| Total health care utilization for the short-term follow-up period | 1.68 (2.35)** | 3.02 (3.24)** |
| Total health care utilization for the long-term follow-up period | 5.42 (6.21)** | 11.54 (9.96)** |
| Number of consultations during the long-term follow-up period | 3.19 (4.00)** | 6.03 (4.96)** |
| Number of telephone consultations during the long-term follow-up period | 1.90 (2.74)** | 4.73 (5.55)** |

** $p < .0005$.

young had higher numbers of for lymphocytes, $CD8^+$ T lymphocytes, and PHA-stimulated T-cell proliferation. This is in line with other studies on age differences on immunological parameters (38–41). The elderly also exhibited higher means for all the different measures of health care utilization. A series of Spearman correlations were calculated to test whether rumination was significantly related to sadness and subjective sleep quality. The correlations were significant for both the young ($\rho$ values, 0.54 and 0.23; $N = 196$; $p < .005$ for sadness and subjective sleep quality, respectively) and the elderly ($\rho$ values, 0.36 and 0.21; $N = 314$; $p < .0005$ for sadness and subjective sleep quality, respectively). The MMSE was not related to any of the psychosocial variables among the young ($\rho$ range, 0.01 to 0.11; $p > .10$) or the elderly ($\rho$ range, 0.07 to 0.08; $p > .10$). The only correlation between the MMSE and the health measures was a significant association between MMSE and $CD19^+$ B lymphocytes for the elderly ($\rho$, −0.12; $p < .05$).

### Rumination and Immunity

To investigate the relationship between rumination and immunity, a number of stepwise multiple linear regressions were conducted using the different immune measures as the dependent variable. Separate regressions for the 2 age groups were used to explore possible age differences in the relation between rumination and immunity. At the first step, gender, age in years, and whether the participants lived alone were entered; at the second step, rumination was entered; and at the third step, sadness and subjective sleep quality were entered. If the effect of rumination was mediated by sadness, subjective sleep quality, or both, any effects of rumination should have been reduced or should have disappeared when sadness and subjective sleep quality were entered into the regression.

For the elderly, 11 of the 15 regressions resulted in significant models, and 1 model showed a trend toward significance ($F$ values, 2.03 to 3.24; $p < .06$); only number of eosinophils, basophils, and $CD8^+$ T lymphocytes could not be fitted with the regression model ($F$ values, 0.50 to 1.63; $p > .10$). For the young, 10 regressions resulted in significant models ($F$ values, 2.40 to 3.48; $p < .05$), and only lymphocytes, eosinophils, basophils, $CD19^+$ B lymphocytes, and $CD8^+$ T lymphocytes could not be fitted with the regression model ($F$ values, 0.44 to 1.76; $p > .10$). However, rumination emerged as a significant predictor in only 3 of the models for the elderly (number of leukocytes, lymphocytes, and $CD19^+$ B lymphocytes) and showed a trend toward significance for PHA-stimulated T-cell proliferation (Table 4).

Thus, the models for the elderly showed that rumination was a significant predictor of the numbers of leukocytes, lymphocytes, and $CD19^+$ B lymphocytes, and that this was not mediated by sadness or subjective sleep quality. The models for the young did not show any significant effects of rumination.

To ensure that any associations between rumination and the immune measures among the elderly were not caused by the

**TABLE 4. Regressions for the Elderly Using Number of Leukocytes, Lymphocytes, and CD19$^+$ B Lymphocytes and PHA-Stimulated T-Cell Proliferation as the Dependent Variables[a]**

| Step | Variable | $\beta$ | Significance ($p$) | Adjusted $R^2$ |
|---|---|---|---|---|
| Number of leukocytes | | | | |
| 2 | Rumination | 0.16 | $< .01$ | 0.02 |
| 3 | Rumination | 0.16 | $< .01$ | 0.04 |
| | Sadness | −0.12 | $< .06$ | |
| | Subjective sleep quality | 0.16 | $< .01$ | |
| Number of lymphocytes | | | | |
| 2 | Rumination | 0.15 | $< .01$ | 0.02 |
| 3 | Rumination | 0.18 | $< .01$ | 0.03 |
| | Sadness | −0.15 | $< .03$ | |
| | Subjective sleep quality | 0.11 | $< .08$ | |
| Number of CD19$^+$ B lymphocytes | | | | |
| 2 | Rumination | 0.18 | $< .01$ | 0.02 |
| 3 | Rumination | 0.22 | $< .01$ | 0.04 |
| | Sadness | −0.16 | $< .02$ | |
| | Subjective sleep quality | 0.07 | $< .27$ | |
| PHA-stimulated T-cell proliferation | | | | |
| 2 | Rumination | 0.15 | $< .09$ | 0.003 |
| 3 | Rumination | 0.12 | $< .24$ | 0.07 |
| | Sadness | 0.26 | $< .01$ | |
| | Subjective sleep quality | −0.27 | $< .01$ | |

[a] Note that the first steps of the regressions and the demographic variables are not shown.

elderly's lower scores on the MMSE, all regressions were rerun controlling for the MMSE on the first step. This resulted in an almost identical pattern of results concerning the association between rumination and the immune measures, indicating that the associations were not caused by underlying cognitive impairment. The MMSE, however, did show significant associations with leukocytes and lymphocytes for the elderly ($\beta$ values, $-0.13$ and $-0.14$; $p < .05$, respectively) and with leukocytes for the young ($\beta = -0.17$; $p < .05$).

The analyses were also conducted separately on young and elderly women and men, and although some gender differences were found (ie, elderly men appeared to show a stronger effects than elderly women), the regression models were generally not significant because of the reduced number of participants in each group; therefore, further data are not reported.

### Rumination and Health Care Utilization

To investigate the relationship between rumination and health care utilization, a number of stepwise multiple linear regressions were conducted using the different health care utilization variables as dependent variables. Separate regressions for the 2 age groups were used to explore possible age differences in the relation between rumination and health care utilization. At the first step, gender, age in years, and whether the participants lived alone were entered; at the second step, rumination was entered; and at the third step, sadness and subjective sleep quality were entered. If the effect of rumination was mediated by sadness, subjective sleep quality, or both, any effects of rumination should have been reduced or should have disappeared when sadness and subjective sleep quality were entered into the regression.

The regressions resulted in significant models for all health care utilization variables for both the young and elderly ($F$ values, 2.32 to 7.75; $p < .05$). Among the elderly, rumination was a significant predictor of health care utilization for telephone consultation in the long-term follow-up and, moreover, showed a trend of being a significant predictor for total health care utilization at the long-term follow-up. The models for total and telephone consultations at the long-term follow-up are shown for both young and elderly in Table 5.

The results generally show that rumination predicts total and telephone consultation health care at the long-term follow-up among the elderly, and this appears to be partly mediated by sadness and subjective sleep quality. For the young, rumination shows a similar although weaker and nonsignificant pattern.

Again, we reran all analyses, controlling for the MMSE at the first step to test whether the associations between rumination and the health care utilization measures were caused by cognitive impairment. The regressions showed a pattern of results almost identical with the results shown in Table 5, and the MMSE showed no significant associations with the health care utilization measures, implying that the associations between rumination and the health care utilization measures are not explained by cognitive impairment in the elderly.

As above, the analyses were also conducted separately on young and elderly women and men, and although there were some gender differences (ie, elderly women appeared to show a stronger effects than elderly men), the regression models generally were not significant because of the reduced number of participants in each group; therefore, further data are not reported.

**TABLE 5. Regressions for the Young and Elderly Using the Total Health Care Utilization and Telephone Consultation for the Long-Term Follow-Up Period as the Dependent Variables[a]**

| Step Age | Variable | $\beta$ | Significance ($p$) | $R^2$ |
|---|---|---|---|---|
| Total health care utilization at the long-term follow-up | | | | |
| 2 Young | Rumination | 0.10 | .17 | 0.12 |
| 3 Young | Rumination | 0.03 | .74 | 0.12 |
| | Sadness | 0.15 | .08 | |
| | Subjective sleep quality | −0.03 | .69 | |
| 2 Elderly | Rumination | 0.11 | .06 | 0.07 |
| 3 Elderly | Rumination | 0.04 | .55 | 0.11 |
| | Sadness | 0.13 | .05 | |
| | Subjective sleep quality | 0.14 | .03 | |
| Telephone consultations at the long-term follow-up | | | | |
| 2 Young | Rumination | 0.12 | .12 | 0.13 |
| 3 Young | Rumination | 0.08 | .35 | 0.13 |
| | Sadness | 0.08 | .37 | |
| | Subjective sleep quality | −0.03 | .66 | |
| 2 Elderly | Rumination | 0.17 | .01 | 0.11 |
| 3 Elderly | Rumination | 0.11 | .06 | 0.12 |
| | Sadness | 0.12 | .06 | |
| | Subjective sleep quality | 0.08 | .22 | |

[a] Note that the first steps of the regressions and the demographic variables are not shown.

### Rumination, Immunity, and Health Care Utilization

To test whether immunity mediated the association between rumination and health care utilization, the immune parameters that showed an association with rumination (ie, the numbers of leukocytes, lymphocytes, and $CD19^+$ B lymphocytes and PHA-stimulated T-cell proliferation) were correlated with health care utilization variables for the elderly. The number of leukocytes correlated significantly with the total and telephone consultations for the long-term follow-up ($\rho$ values, 0.15 and 0.16; $N = 295$; $p < .01$ for total and telephone consultation at the long-term follow-up, respectively). Thus, 2 stepwise multiple linear regressions for the elderly were conducted using the health care utilization variables as dependent variables and entering gender, age in years, and whether the participants lived alone at the first step; rumination at the second step; and number of leukocytes at the third step. Sadness and subjective sleep quality were not entered into these regressions, because the primary interest was in the mediating effects of the immune parameters. If the effect of rumination was mediated by number of leukocytes, any effects of rumination should have been reduced or should have disappeared when this was entered.

The regressions showed that entering number of leukocytes at the third step reduced the â values for rumination only marginally (0.02 at most), and thus, number of leukocytes does not appear to mediate the association between rumination and health care utilization. Furthermore, number of leukocytes did not reach significance as a predictor of the 2 health care utilization variables (â values, 0.08; $p > .10$).

## DISCUSSION

Our results confirm an association between rumination and objective health measures, showing that rumination was significantly positively related to immune measures and health care utilization in the elderly sample. The results furthermore suggest that sadness and subjective sleep quality did not mediate the association with immunity and only partially mediated the association with health care utilization. In addition, controlling for scores on the MMSE did not alter the pattern of results, indicating that the associations between rumination and the health-related measures were not caused by underlying cognitive impairment among the elderly. These results are in agreement with studies that find an inverse association between rumination and subjective health (14–17), although the present findings also extend these findings to objective measures of health.

### Rumination and Immunity

The present study is the first to report an association between rumination and immunity in an elderly sample. Interestingly, this association did not appear in the young sample. This age difference supports the hypothesis that psychosocial variables may be more strongly associated with immunity in elderly people (31). However, it is possible that if other immune parameters were addressed, a different pattern regarding age differences would emerge. Rumination was positively associated with the immune measures; thus, highly ruminating people had higher numbers of leukocytes, lymphocytes, and $CD19^+$ B lymphocytes and higher polyclonal T-cell activation. These positive associations may indicate that rumination is related to an activation of the specific immune system; this would be in agreement with findings from studies using cardiovascular measures suggesting that rumination is associated with prolonged cardiac activation (20,21). Thus, it has been suggested that rumination is associated with a general disinhibition of physiological systems (42), but further studies are needed to address this notion. Previous studies have found that high leukocyte counts within the normal range

are associated with an increased risk of ischemic disease (for reviews, see 43,44), thus indicating that leukocyte counts even within the normal range, as in the present study, may be associated with specific clinical outcomes.

Because sadness and subjective sleep quality did not mediate the association between rumination and immunity, the question arises how the association is manifested. One possibility is that other negative emotional states, eg, anxiety and anger/hostility, could mediate the relation. However, the association between anxiety and anger/hostility and immunity is much less well-researched than the association between sadness/depression and immunity; thus, knowledge about possible mediating effects of anxiety and anger/hostility is limited (for an exception, see 45). Another possibility is that other health behaviors, like physical exercise and smoking, play a mediating role between rumination and immunity, but to the best of our knowledge, no research has attempted to explore this. Exploratory analyses of our own data found no associations between rumination and smoking, but a weak negative correlation between rumination and hand grip measure was found (Spearman's rho values [189 and 282] = $-0.21$ and $-0.14$; $p < .02$ for the young and elderly, respectively) indicating that highly ruminating people may be less physically fit. Future studies should explore this possibility in more depth. In addition, the association between rumination and health could be direct, possibly in the form of increased neuronal sensitization or disinhibition of neural networks controlling physiological responses (43,46).

### Rumination and Health Care Utilization

In addition to the association between rumination and immunity, the present study is also the first to report an association between rumination and health care utilization. The results showed that the elderly displayed positive associations with total and telephone consultations at the long-term follow-up, and this was partly mediated by sadness and subjective sleep quality. It appears that the association between rumination and total health care utilization at the long-term follow-up was primarily a result of the association between rumination and telephone consultation, because face-to-face consultations did not show a significant relationship with rumination. This raises the question why rumination predicts only telephone consultations and not face-to-face consultation use. Possibly, telephone consultations are used for less severe health problems, such as colds, influenza, and milder pains, and these ailments may be associated with rumination, whereas more severe health problems as presented in face-to-face consultations do not show an association with rumination, at least not within this relatively short follow-up period. Alternatively, the association between rumination and telephone consultation may be explained not by objective health problems but by ruminating about health. Thus, ruminating about whether one's health is poor and whether a headache is a sign of something serious may cause people to call the GP, who then may convince the patients that no serious illness is indicated.

The finding that the young did not show a significant relation between rumination and health care utilization may indicate that rumination is more strongly associated with health in vulnerable groups, like the elderly. The young did show a pattern similar to the elderly with respect to rumination, but the effects were smaller and did not reach conventional levels of significance, indicating that a weak relationship may be present.

Sadness and subjective sleep quality appeared to mediate only partially the association between rumination and health care utilization. As mentioned, other negative emotional states or health behaviors may play a role. Furthermore, the mediators were measured at baseline, and it may be that rumination as a stable coping tendency relates to the later development of sadness and sleep problems. Thus, the reason that these factors did not appear as mediators in the present analyses may be that they were not measured in the same period as the health care utilization was assessed.

Finally, the immune measures did not mediate the association between rumination and health care utilization. It may be argued that these immune parameters were assessed at baseline and therefore did not show a relation with health care utilization consumed one and a half years later, but the correlations indicated that the number of leukocytes was related to both total and telephone consultation at the long-term follow-up. Possibly other immune parameters play a mediating role in the connection between rumination and health care utilization. Other health problems not directly related to immunity, eg, pain, could also explain the association between rumination and health care utilization. Alternatively, as suggested, ruminating people may not have objectively verifiable health problems but may have recurrent, negative thoughts about their health, and this may cause them to contact their GPs.

### Limitations of the Present Study and Future Directions

The present study has several strengths: using both a young and an elderly representative group, sampling several immune and health care utilization variables, and testing for mediation effects. However, the study also has some limitations. First, mediating variables were measured at baseline; a stronger design would include multiple assessments of mediating variables across the follow-up period. Second, specific knowledge about the reasons for contacting the GP would also illuminate the association between rumination and health care utilization further. One last problem is clarification of the cause-effect relationship. Although the prospective design allows for tentative conclusions that rumination may influence health care utilization, it is possible that underlying variables like health status cause the person to both ruminate and see the GP, although it is less clear why this should be the case only for the elderly sample. In relation to the immune parameters, the cross-sectional design opens the possibility that immune parameters, via communication with the central nervous system, may influence rumination. Experimental designs manipulating rumination and measuring immunity may clarify this question.

It should also be mentioned that the variance explained by the variables entered into the regression was relatively small ($R^2$, 0.03 to 0.12), and as such, rumination may be considered a minor variable in health contexts. The present study, however, was conducted as a baseline study; recruiting relatively healthy people and sampling people in a more vulnerable position (eg, chronic stress or facing health strains) may yield stronger effects.

## CONCLUSION

In the present study, it was shown that elderly display positive associations between rumination and numbers of leukocytes, lymphocytes, and $CD19^+$ B lymphocytes and health care utilization. These associations appeared to be mediated by sadness-depression and subjective sleep quality only to some extent. None of the immune parameters mediated the association between rumination and health care utilization. The findings indicate that rumination may influence health-related measures, at least in elderly people. Thus, not only negative affect but also negative thoughts may have detrimental effects on health.

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