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Associations of Positive Affect and Negative Affect With Allostatic Load: A Lifelines Cohort Study

Hendrika M. Schenk, MSc, Bertus F. Jeronimus, PhD, Lian van der Krieke, PhD, Elisabeth H. Bos, PhD, Peter de Jonge, PhD, and Judith G.M. Rosmalen, PhD

ABSTRACT

Objective: Allostatic load (AL) reflects the deteriorating influences of stress on the body and comprises a selection of biological markers. AL is associated with negative life events, stress, and negative affect (NA), as well as poor health outcomes. However, whether AL is also associated with positive affect (PA) is not clear. The present study therefore explores the association between PA and AL, accounting for age, sex, NA, and health behaviors.

Methods: Data of 45,225 individuals from the first wave of the multidisciplinary prospective population-based cohort study Lifelines were used. AL was operationalized as the sum of 12 inflammatory, cardiovascular, and metabolic markers. The association between PA and AL was tested in a cross-sectional study design using multiple linear regression analysis, adjusting for NA, confounders, and health behaviors. In addition, we explored whether the relation was moderated by age, sex, and NA.

Results: The AL profile was inversely associated with PA ($B = -0.083, p < .001$) when adjusted for NA, age, and sex. The association between AL and PA remained significant after adjusting for health behaviors ($B = -0.076, p < .001$). A significant moderating effect was found for sex (PA by sex: $B = 0.046, p = .001$), indicating that the association between PA and AL was stronger in women than in men.

Conclusions: PA was associated with a more favorable AL profile, especially in women. These results add to the evidence that PA might be of relevance to the etiology of disease.

Key words: positive affect, negative affect, allostatic load, cohort study, biological markers, health.

INTRODUCTION

Mental wear and tear influences physical health (1). Repeated, cumulative psychological and physiological strains on the body require adaptation of multiple interconnected physiological processes, even outside the normal values, a process called “allostasis” (2,3). The allostatic load (AL) model describes dysregulation of homeostatic systems due to prolonged or intense activation of stress systems (3,4). The concept of AL refers to a multisystem view and comprises biological markers of different physiological systems (5). The systems are pertinent to disease, and the markers are parameters wherein activities are associated with disease risk. It has been shown that the different systems have synergistically effect on health outcome. For example, high levels of blood pressure together with high levels of cholesterol will have a more deteriorating effect than high blood pressure on itself. It has been shown that a comprehensive AL profile consisting of several markers is a more valid indication of current health status than the metabolic syndrome or independent markers (4). Elevated AL has been associated with poor health outcomes, including cardiovascular disease, diabetes, depression, and mortality (6,7).

AL is regarded as the outcome of accumulated stress on the body. Indeed, negative life events, stress, and negative affect (NA) are all associated with biomarkers reflecting AL (8–10).

This association may partly be due to harmful health behaviors, which themselves are associated with psychological distress (11,12). Nonetheless, the association between NA and AL may also reflect direct dysregulation of glucocorticoid systems, which leads to dysregulation of downstream systems (13). Assuming that NA and positive affect (PA) can operate independently in a more or less opposite direction, it might be that PA is associated with a decreased AL (14–16).

PA is associated with a reduced risk of cardiovascular disease and mortality (17–19). The influence of PA on health outcomes might be explained by a positive influence on health behaviors. Individuals with higher levels of PA report more beneficial health behaviors, including less smoking, more exercise, and less alcohol intake (20–22). However, positive attributes (such as optimism, self-esteem, and social status) and PA are inversely associated with metabolic syndrome and cardiometabolic risk even after adjusting for health behaviors (23–25). In addition,

AL = allostatic load, CRP = C-reactive protein, HPA = hypothalamic-pituitary-adrenal, MDD/AD = major depressive disorder or anxiety disorder, MINI = Mini-International Neuropsychiatric Interview, NA = negative affect, PA = positive affect, PANAS = Positive and Negative Affect Schedule, SE = standard error

SDC Supplemental Content

From the Interdisciplinary Center Psychopathology and Emotion Regulation (ICPE), University Medical Center Groningen (Schenk, Jeronimus, van der Krieke, Bos, de Jonge, Rosmalen), and Department of Developmental Psychology (Jeronimus, Bos, de Jonge), University of Groningen, Groningen, the Netherlands.

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several studies show beneficial associations between high PA and biological profiles (26), and increased levels of PA have been shown to correlate negatively with blood pressure (27) and directly decrease levels of cortisol (28). In addition, positive social experiences are associated with lower AL (29). Surprisingly, the extent to which PA is associated with AL has not been investigated. PA and NA levels are also moderately correlated, both between people and within people over time (15,30). It is therefore crucial to consider both PA and NA together to study their association with AL (31,32). Previous work that used a bipolar measure of affect (PA ↔ NA) was merely able to predict virtually opposing and extreme outcomes (31,33). A nuanced estimation of PA and NA effects on health requires us to consider both their independent effects and their interaction (34) because high PA levels may buffer NA effects.

The relationship between affect and health can be studied using self-report instruments such as symptom scales or disease diagnosis. Self-reported health is strongly associated with reported affect (20). People who report high NA tend to report more physical symptoms, whereas people who report high PA tend to report fewer symptoms, which introduces a bias and an overestimation of the effects of PA and NA. Therefore, for this study, we use AL, a composite of biological markers that represents multiple physiological systems, for example, inflammatory, metabolic, and cardiovascular.

Considering the fact that well-being seems U-shaped through life (35), levels of PA and NA also tend to change with age (36), and their association with AL may therefore also change throughout the life-span. Women typically report slightly more NA and slightly less PA compared with men (37–40), but estimated sex effects on the association between PA and health are scarce (41). Our models were therefore adjusted both for age and sex, but we also tested if age and sex influence the association between PA and AL.

The aim of this article is to study the association between PA and established biological markers for an AL profile, based on inflammatory, cardiovascular, and metabolic markers. We hypothesize an inverse association between PA and AL. Because AL is also associated with age, sex, NA, and health behaviors, we adjust for these covariates. In addition, because the association between PA and AL may be different for people differing in age, sex, and levels of NA, we explored potential moderating effects of these factors. Data were derived from the first wave of the multidisciplinary prospective population-based cohort study Lifelines.

METHODS

Participants

Lifelines is a multidisciplinary prospective population-based cohort study, examining in a unique three-generation design the health and health-related behaviors of 167,729 persons living in the North East region of the Netherlands. It uses a broad range of investigative procedures in assessing the biomedical, sociodemographic, behavioral, physical, and psychological factors that contribute to the health and disease of the general population, with a special focus on multimorbidity and complex genetics (42). Inclusion of study participants began in 2006 via general practitioners (GPs) and self-enrollment. All participants provided written informed consent. The study protocol was carried out in accordance with the Declaration of Helsinki and was approved by the medical ethical review committee of the University Medical Center Groningen. A detailed description of the

Lifelines Cohort Study has been published elsewhere (43). Because each individual is registered with a GP, inclusion was done via the GP's office located in the north of the Netherlands (Groningen, Friesland, and Drenthe). Eligible individuals were between 25 and 50 years of age and were contacted through their GP's office to participate, unless the patient had a severe psychiatric or physical illness, had a limited life expectancy (<5 years), or had insufficient knowledge of the Dutch language to complete a Dutch questionnaire. During the first visit of the participant, the participant was asked if family members would be willing to participate as well. Children could only participate if one of the parents was registered as a participant. Registration could also be done through the Web site of Lifelines (43).

The first wave was conducted between 2006 and 2013. When informed consent forms were received, questionnaires were sent to the participants. During the first wave, participants were invited to a local research site, where the completed questionnaire could be turned in and a physical examination was performed. Participants were invited for a second visit within 2 weeks, when fasting blood samples were drawn (43). The data extraction of the first wave of Lifelines comprises data of 95,413 participants of 18 years and older at the time of visit.

The biomarkers that compose the AL profile were only measured in the first 60,000 Lifelines participants. Measurement of albumin and high-sensitive C-reactive protein (hsCRP) was terminated after this number was reached. The current article selected the 56,476 participants with at least one value for albumin or hsCRP, which were unavailable for 3524 participants (5.9%). This group with valid biomarker measurements did not differ from the other Lifelines participants in terms of sex ($t_{(92,613)} = -0.95, p = .34$), but was on average a few months older (mean [standard deviation {SD}] = 44.96 [12.66] versus 44.69 [11.98]; $t_{(92,613)} = 3.28, p < .001$).

The sample of 56,476 participants selected based on biomarker availability still showed some missing data for affect ($n = 1513$), smoking ($n = 861$), alcohol use ($n = 21$), exercise levels ($n = 3166$), and specific biomarkers that were part of our AL index ($n = 2888$). We excluded participants who did not revisit the research facility within 100 days after the first visit ($n = 2134$) or showed CRP levels higher than 10 mg/l ($n = 2027$), which may indicate an acute inflammatory response. These exclusion criteria led to a sample of 45,225 participants with complete data (see Table 1).

To avoid the loss of the 13.6% of the participants in a complete-case analyses, we used multiple imputed data sets. Multiple imputations were done in the subgroup of 56,476 participants with at least one value for albumin or hsCRP. Variables that showed skewness or kurtosis (CRP, glucose, triglycerides, hemoglobin A1c [HbA1c]) were transformed to improve the imputation model. The number of imputed data sets was 25. The maximum number of iterations was 20. The two exclusion criteria, namely, a second visit more than 100 days later and CRP levels higher than 10 mg/l, were applied after the imputation process, resulting in slightly different sample sizes for each of the 25 imputed data sets (range, 52,320–52,342). The results we present reflect pooled results of 25 data sets of 52,331 participants on average.

PA and NA

Levels of PA and NA were measured with the Positive and Negative Affect Schedule (PANAS), with 20 items answered on a 5-point Likert scale (never–very often) (44,45). Participants were asked to report their PA and NA over the last 4 weeks. Sum scores of the 10 PA items (feeling interested, excited, strong, enthusiastic, proud, alert, inspired, determined, attentive, active) and 10 NA items (feeling distressed, upset, guilty, scared, hostile, irritable, ashamed, nervous, jittery, afraid) were calculated.

Allostatic Load

The concept of AL comprises biological markers that reflect dynamic, physiological systems (10). The AL profile was composed of a) inflammatory

TABLE 1. Sample Characteristics of the Complete-Cases Data Set ($N = 45,225$)

| | |
|--|---------------|
| Female, n (%) | 26,408 (58.4) |
| Age, M (SD), y | 45.0 (11.9) |
| PA sum score, M (SD) | 35.4 (4.2) |
| NA sum score, M (SD) | 20.8 (5.2) |
| Current smoker, n (%) | 10,145 (22.4) |
| Alcohol use ^a , M (SD) | 3.8 (2.0) |
| Physical activity ^b , M (SD) | 4.4 (2.2) |
| AL risk profile | |
| C-reactive protein, median (IQR), mg/l | 1.1 (1.8) |
| Systolic blood pressure, M (SD), $mm\ Hg$ | 126.1 (15.1) |
| Diastolic blood pressure, M (SD), $mm\ Hg$ | 74.1 (9.2) |
| Heart rate, M (SD), $beats/min$ | 67.8 (11.2) |
| Total cholesterol, M (SD), $mmol/l$ | 5.1 (1.0) |
| Triglycerides, median (IQR), $mmol/l$ | 1.0 (0.7) |
| Low-density lipids, M (SD), $mmol/l$ | 3.2 (0.9) |
| High density lipids, M (SD), $mmol/l$ | 1.5 (0.4) |
| Albumin, M (SD), g/l | 45.1 (2.4) |
| Glucose, median (IQR), $mmol/l$ | 4.9 (0.7) |
| HbA1c, median (IQR), % | 5.5 (0.5) |
| Waist circumference, M (SD), cm | 90.6 (12.0) |

M = mean; SD = standard deviation; PA = positive affect; NA = negative affect; AL = allostatic load; IQR = interquartile range; HbA1c = hemoglobin A1c.

^a Number of times drinking alcoholic beverages in the past month.

^b On average, how many days per week are you more than 30 minutes physically active (biking, gardening, etc)?

markers: CRP; b) cardiovascular markers: systolic blood pressure, diastolic blood pressure, and heart rate; and c) metabolic markers: total cholesterol, triglycerides, low-density lipids, high-density lipids, albumin, glucose, HbA1c, and waist circumference (7). High-density lipid and albumin scores were recoded such that high scores reflect a poorer outcome. All items were standardized (z score). A continuous measure was derived to represent an AL risk profile (46). A sum score of each category (inflammatory, cardiovascular, and metabolic) was calculated and divided by the number of items in the category, to ensure that each category received the same weight. Sum scores of the three categories were summed and formed the outcome measure AL. Higher scores indicated an elevated AL profile. It has been shown that several of aforementioned biomarkers load on a common latent factor, which supports the construct of AL (47).

Covariates and Health Behaviors

Analyses were adjusted for NA, age (36), sex (40) (women, 0; men, 1), and the health behaviors “current smoking status” (yes, 1; no, 0), “alcohol use” (defined as the frequency of alcohol use in the past month), and “physical activity” (defined as days per week with at least half an hour physical activity, such as biking, sports, and gardening). Information on health behaviors was collected using a self-report questionnaire. Because the association between PA and AL may be different for people differing in age, sex, and levels of NA, we explored potential moderating effects of these factors, by adding interaction terms (PA by age, PA by sex, PA by NA).

Statistical Analyses

A series of multiple linear regression analyses were conducted on the imputed, cross-sectional data. The outcome measure and predictor variables were standardized (z scores), except the binary variables smoking and sex, to facilitate comparison of estimates across measures. The first model

tested the association between PA and AL, adjusted for age and sex. In Model 2, NA was added. Model 3 tested the association between PA and AL, adjusted for NA, age, and sex and the interaction terms PA by age, PA by sex, and PA by NA. In Model 4, current smoking status, alcohol use, and physical activity were included. We classified correlations (r) and β values as small if between 0.10 and 0.20, moderate if between 0.20 and 0.30, and large if greater than 0.30, based on the effect sizes commonly found in psychology (48,49).

Additional sensitivity analyses were performed in participants with major depressive disorder or anxiety disorders (MDD/ADs), somatic disease, and healthy individuals. The presence of a current (past 2 weeks) depression (major depressive episode) and ADs (panic disorder, agoraphobia, social AD, and generalized AD) was assessed according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria. Posttraumatic stress disorder and specific phobia were not assessed in Lifelines. A systematic diagnostic interview, the Mini-International Neuropsychiatric Interview (MINI 5.0.0), was performed by trained research assistants. Previous studies suggested acceptable validity and reliability of the MINI (50). Individuals who met the criteria for MDD or who met criteria for an AD on the MINI, were included in the MDD/AD group. Somatic disease was defined as a positive response to the question whether a participant had a somatic disease diagnosed by a medical doctor, or to 1 or more of 18 items about specific endocrine, pulmonary, cardiac, gastrointestinal, and autoimmune diseases. Individuals who did not meet the criteria for MDD/AD or somatic disease were assumed to be healthy. In the aforementioned models, outcome measure and predictor variables were standardized.

Because Lifelines is a three-generation study, some participants were related to each other, which violates the independent-observations assumption in linear regression models. The information on the relationships was derived from the municipal personal record database, which did not distinguish between biological and nonbiological relationships (such as adopted people or stepfamily). Moreover, when the parents of an adult participant were not participating in the study, siblings were not identified. To check whether biological dependencies influenced our results, we reran our analyses with the subgroup of participants without family connections in Lifelines. As an additional sensitivity analysis, we reran the analyses on the subgroup of participants who revisited the research site within 14 days, to check whether the time delay between PANAS assessments and biological assays influenced the results of the analyses.

A p value of .05 was used to indicate statistical significance. All statistical analyses were done using SPSS 22.0 (IBM Corp, Armonk, NY).

RESULTS

Descriptives

Of the 45,225 participants of the complete-cases data set, 58.4% ($n = 26,408$) were female. Mean (SD) age was 45.0 (11.9) years, mean (SD) PA score was 35.4 (4.2), and mean (SD) NA score was 20.8 (5.2). Descriptive statistics of the separate biomarkers are shown in Table 1. Correlations between PA, NA, the demographic variables, and the elements of AL are provided in Table S1, Supplemental Digital Content 1, <http://links.lww.com/PSYMED/A429>. Almost all variables showed significant associations, but the magnitudes did not suggest multicollinearity.

Multiple Linear Regression

The regression analyses were performed on the imputed data sets, which had a mean sample size of $n = 52,331$ participants. A significant inverse relationship was found in the first model between PA and AL ($B = -0.096$, standard error [SE] = 0.007, $p < .001$).

The full model tested the association between PA and AL, adjusted for NA, age, and sex and the interaction terms PA by age,

TABLE 2. Multiple Regression Models of PA, NA, Confounding Measures, and Health Behaviors Predicting Levels of AL

| Predictors | Model 1 | | | Model 2 | | | Model 3 | | | Model 4 | | |
|-------------------|----------|-------|----------|----------|-------|----------|----------|-------|----------|----------|-------|----------|
| | <i>B</i> | SE | <i>p</i> |
| PA | -0.096 | 0.007 | <.001 | -0.083 | 0.007 | <.001 | -0.104 | 0.009 | <.001 | -0.076 | 0.009 | <.001 |
| Age | | | | 0.384 | 0.007 | <.001 | 0.386 | 0.007 | <.001 | 0.440 | 0.007 | <.001 |
| Sex | | | | 0.290 | 0.014 | <.001 | 0.289 | 0.014 | <.001 | 0.343 | 0.014 | <.001 |
| NA | | | | -0.004 | 0.007 | .546 | -0.008 | 0.007 | .246 | -0.015 | 0.007 | .040 |
| PA by NA | | | | | | | -0.014 | 0.006 | .018 | -0.010 | 0.006 | .072 |
| PA by age | | | | | | | 0.005 | 0.007 | .478 | 0.004 | 0.007 | .580 |
| PA by sex | | | | | | | 0.052 | 0.014 | <.001 | 0.046 | 0.014 | .001 |
| Physical activity | | | | | | | | | | -0.150 | 0.007 | <.001 |
| Current smoker | | | | | | | | | | 0.383 | 0.016 | <.001 |
| Alcohol use | | | | | | | | | | -0.140 | 0.007 | <.001 |

CRP cutoff ≤ 10 .

PA = positive affect; NA = negative affect; AL = allostatic load; CRP = C-reactive protein; SE = standard error.

Outcome measure: AL risk profile. Number of imputations = 25, $N_{\text{pooled}} = 52,331$. Bold *p* values indicate significance. Standardized predictor variables: PA, NA, age, physical activity, and alcohol use. Sex: 0, women; 1, men; smoking: 0, nonsmoking; 1, smoking.

PA by sex, and PA by NA (Table 2). The model showed a significant inverse association between PA and AL ($B = -0.076$, $SE = 0.009$, $p < .001$). The interaction PA by sex was also significant (PA by sex: $B = 0.046$, $SE = 0.014$, $p = .001$). This indicates a stronger association between PA and AL in women than in men. When analyzing simple slopes for men and women PA, the following was found for men: $B = -0.075$, $SE = 0.010$, $p < .001$, $N_{\text{pooled}} = 21,744$, and for women: $B = -0.112$, $SE = 0.010$, $p < .001$, $N_{\text{pooled}} = 30,587$. The interactions PA by NA and PA by age did not reach significance ($B = 0.010$, $SE = 0.006$, $p = .072$; $B = 0.004$, $SE = 0.007$, $p = .580$). The main effect of NA showed a significant inverse association as well ($B = -0.015$, $SE = 0.007$, $p = .040$).

Also, health behaviors linked to PA were included, namely, physical activity, smoking, and alcohol consumption. All health behaviors showed significant associations with AL (physical activity: $B = -0.150$, $SE = 0.007$, $p < .001$; smoking: $B = 0.383$, $SE = 0.016$, $p < .001$; alcohol use: $B = -0.140$, $SE = 0.007$, $p < .001$).

Sensitivity Analyses

To check whether biological dependencies influenced our results, we reran our analyses with the subgroup of participants without family connections in Lifelines ($N_{\text{pooled}} = 34,394.6$). The models yielded virtually identical results (Table S2, Supplemental Digital Content 2, <http://links.lww.com/PSYMED/A430>).

Additional analyses in three subgroups, namely, MDD/AD ($n = 4098$), somatic disease ($n = 14,167$), and healthy individuals ($n = 29,986$), showed significant inverse associations between PA and AL in the full model ($B = -0.072$, $SE = 0.017$, $p = .010$; $B = -0.072$, $SE = 0.017$, $p < .001$; $B = -0.069$, $SE = 0.012$, $p < .001$). In contrast to the somatic disease and the healthy individual subgroups, the MDD/AD subgroup showed no significant association between the interaction term PA by sex and AL, nor was the association between NA and AL significant in the MDD/AD subgroup (Table S3, Supplemental Digital Content 3, <http://links.lww.com/PSYMED/A431>). Sensitivity analyses in the subgroup of participants who revisited the research site within

14 days were essentially the same as those obtained in the group of participants who revisited the research site within 100 days (see Table S4, Supplemental Digital Content 4, <http://links.lww.com/PSYMED/A432>).

DISCUSSION

Participants with higher levels of PA had a more favorable AL profile than did participants reporting lower levels of PA. The effect size of PA was small; however, the association between PA and AL remained significant, even after adjusting for NA, sex, age, life-style factors, and moderation effects of sex, age and NA. Additional sensitivity analyses in different subgroups yield approximately the same results. This strengthens our hypothesis that individuals with higher levels of PA have a more favorable biological profile, in contrast to individuals with lower levels of PA, independent of the presence of somatic disease or mental health problems. These associations remained present when adjusting for NA and health behaviors. Although the small size of the association between PA and health may not directly seem clinically meaningful, the positive association between PA and health behavior, including more physical activity and smoking abstinence, at the price of slightly higher alcohol consumption is noteworthy. Conversely, people with more NA also smoked more but consumed less alcohol. The accumulating effects of these health behaviors are undoubtedly important factors in the association between affect and health (51,52), key to the idea of AL, and a substantial economic burden (1).

The positive association between PA and health remained robust after additional adjustment for health behavior, next to NA, age, and sex. Although additional analyses showed significant inverse associations between PA and AL in both men and women, the association proved slightly stronger in women than in men, which is interesting from a prevention perspective. In previous studies, women reported slightly lower PA levels than did men (53), which we did not observe, but this stronger effect of PA on health in women is new in the literature. One mechanistic explanation for the observed association between PA and health may

involve the hypothalamic-pituitary-adrenal (HPA) axis, which can provide a direct link between affect and inflammatory, metabolic, and cardiovascular markers. Cortisol is known to influence many processes, and sex differences in HPA-axis reactivity might explain the slightly stronger association between PA and AL in women (54,55). Further research is required to explain the differential effects of affect on physiology in women and men.

The lack of replication of an association between NA and AL is also striking. Because we studied the general population, it would be reasonable that the lack of variability in NA would be the obvious explanation. However, the SD for NA (5.2) is larger than the SD for PA (4.2) in this sample. There are studies that did notice an association between NA in nonpathological ranges and AL (56,57), but those studies did not adjust for positive states or traits. This is a substantial issue in most literature presented on the association between affect and health measures. Adjusting for PA might in this case be the reason that we did not find an association between NA and AL.

The counterintuitive association between NA and AL is in contrast to most studies, which show a positive association between those constructs. Not only the association between NA and AL, but also the correlations between the separate items of AL and the NA construct were predominantly negative. This was an unexpected finding, and unfortunately, no clear or satisfying explanation was found for this unusual pattern. It might be that not only valence but also arousal and perhaps persistence of affect play a role in the relationship between affect and health.

In the present study, several life-style factors were associated with AL. Besides sex and age, smoking had the most pronounced association with the AL profile. Also, physical activity showed a significant negative association with AL. This association was expected, considering the widespread paradigm that exercise is healthy (58,59). More striking was the significant negative association between alcohol use and AL. Although heavy drinking and alcohol abuse have been shown to have a deteriorating effect on health (60), we did not expect a strong association between alcohol and AL because most of our study population were social drinkers. Although inconsistent, the literature shows some evidence about potential health benefits from moderate alcohol intake (61). One explanation for our finding may be that the alleged health benefits of moderate drinking are confounded by abstainer and formal drinker biases, as has been suggested by Stockwell et al. (62). Our data set did not allow for checking this bias. We also have to take into account that the items about physical activity and alcohol use were self-report items, which may imply that subjects underreport alcohol intake and are heavier drinkers than they report.

A major strength of our study is that it was performed in a large sample from the general population. Previous studies had a smaller sample or studied the effect of PA on health in a subgroup such as elderly or cardiac patients (32,63). Also, that we took into account both dimensions of affect in our analyses is a strong point of this study. The many studies of the effect of affect on health outcome focused solely on only one dimension of affect (64), used bipolar measures to determine levels of affect, or used one or several individual biomarkers (31,65). The broad spectrum of available markers enabled us to form an adequate and comprehensive AL profile (7), which is probably a more valid indication of current health status than metabolic syndrome or independent markers alone (4). Finally, the AL profile comprises an objective measurement, instead of

self-reported symptoms or diagnoses, preventing bias (such as shared method variance) and an overestimation of the effects of PA and NA.

Nonetheless, we acknowledge the following limitations. The cross-sectional design of this study impedes causal conclusions. It therefore remains unknown whether an increase in PA leads to an increase in AL or vice versa and whether it plays a role in the etiology of disease. Furthermore, our models were not adjusted for the presence of chronic disease. However, sensitivity analyses in a subgroup with chronic somatic diseases yielded approximately the same results. Although a comprehensive AL profile is used as an outcome measure, preferably one would also like to include measures of physiological stress. Primary measures of stress would be markers of the activation of the HPA axis and the sympathetic nervous system, for example, cortisol and catecholamines (8). Measuring glucocorticoids and catecholamines in blood is challenging, because levels are highly dependent on the circadian rhythm (66). Present developments might handle this problem for future studies, for example, by measuring cortisol in other samples than blood (67,68). Lastly, the PANAS does not assess what is traditionally thought of as PA (e.g., happy), but merely affect items associated with high arousal. Therefore, it was unfortunately not possible to study the influence of high and low arousal on health. Several studies show that there is a different physiological response in high and low arousal affect (69–71); however, the long-term consequences are not studied thoroughly yet. Future studies may include affect items representing both PA and NA and the different dimensions of arousal, to study the effect of arousal on health.

CONCLUSIONS

In this study, we found an association between PA and AL using a broad panel of biomarkers measured in blood and despite adjustment for several covariates. The association between PA and AL was more pronounced in women than in men. The question remains how PA influences biomarkers and improves health. Further research could focus on mechanisms explaining this link between affect and physiological markers.

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(research@Lifelines.nl). The Lifelines system allows for access for reproducibility of the study results.

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