Using Physiological Dysregulation to Assess Global Health Status

Associations with Self-rated Health and Health Behaviors

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Abstract

Six measures of physiological dysregulation were derived from 11 clinically assessed biomarkers, and related to health outcomes and health behaviors for the Hawaii Personality and Health cohort (N = 470). Measures summing extreme scores at one tail of the biomarker distributions performed better than ones summing both tails, and continuous measures performed better than count scores. Health behaviors predicted men’s dysregulation but not women’s. Dysregulation and health behaviors predicted self-rated health for both men and women, and depressive symptoms predicted self-rated health only for women. These findings provide preliminary guidelines for constructing valid summary measures of global health status for use in health psychology.

Keywords

- biomarkers
- global health status
- physiological dysregulation
- self-rated health

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WITH THE growth of multidisciplinary health research using biological assessments, health psychologists increasingly have access to clinical information in addition to more familiar measures such as self-rated health and quality of life. In contrast to self-ratings, these variables (e.g., clinically assessed height and weight, blood pressure, cholesterol levels) provide objective measures of a person’s physical condition. Individual biomarkers are commonly used in medicine in a dichotomous fashion to determine, for example, whether patients have reached a threshold for medication, or have achieved risk status on a particular indicator. As a result of their training in psychometrics, psychologists typically favor constructs with multiple indicators over single-item measures, but constructs composed of combinations of individual biomarkers are less common in medicine. This report presents a comparative evaluation of several measures of global health status composed of indicators of physiological dysregulation. The data were obtained from the first 470 members of the Hawaii Personality and Health Cohort to complete an extensive clinical examination at middle age (Hampson, Goldberg, Vogt, & Dubanoski, 2006, 2007). Reliable and valid summary variables indicative of global health status will be valuable for investigating psychological mechanisms leading to disease and longevity in this and other prospective studies.

One theoretical starting point for the development of composite measures of global health status is the concept of ‘allostatic load’. Allostasis refers to the flexible response, within the optimal range, of various physiological systems in response to life’s challenges (Sterling & Eyer, 1988), and allostatic load is the cumulative wear and tear caused by physiological responses outside these optimal ranges (McEwen, 1998). Biomarkers of allostatic load provide information about the level of physiological dysregulation before clinically defined disease is diagnosed (Singer, Ryff, & Seeman, 2004). The allostatic load model also includes health behaviors as potential mediators of the effects of environmental challenges. For example, in response to stress, a person may engage in more unhealthy behaviors such as smoking, drinking alcohol and eating a high-fat diet, and these behaviors may have adverse effects on biomarkers.

**Physiological dysregulation**

Measures of allostatic load combine information about the physiological status of two main body systems: hormonal biomarkers for activity in the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system (SNS), and biomarkers of activity in the cardiovascular and metabolic systems. Challenging events in the environment affect the HPA axis and the SNS, which secondarily affect the cardiovascular and metabolic systems, and may eventually result in disease (Seeman, Singer, Rowe, & McEwen, 2001). Biomarkers of activity in the cardiovascular and metabolic systems were assessed for members of the Hawaii Personality and Health cohort and used to develop measures of physiological dysregulation.

Seplaki, Goldman, Glei and Weinstein (2005) evaluated several methods of combining biomarkers of physiological dysregulation, including count scores and continuous summary scores, and concluded that different ways of combining biomarkers had only modest effects on the performance of these composites in predictive models. However, the two-tailed count scores (based on summing the number of biomarkers falling at either the high or low extreme of the distribution) performed somewhat better than the one-tailed count scores (based on summing the number of biomarkers only at the end of the distribution defined medically as high-risk). The best-performing two-tailed measure was a continuous score summing the absolute standardized differences of each biomarker from its respective mean. Other investigators have used only one-tailed summary scores of dysregulation (e.g. Seeman et al., 2004) because it is not always clinically meaningful to combine both tails of the distribution in contrast to the middle. Therefore, we chose to evaluate one-tailed as well as two-tailed summary scores, and both count-based and continuous scores.

To compare the validity of these summary measures of physiological dysregulation, they were correlated with two health outcomes: self-rated health and depressive symptoms. We expected higher levels of physiological dysregulation to correlate with poorer self-rated health and more depressive symptoms. We also examined the associations between several health behaviors related to cardiovascular and metabolic health (smoking, alcohol use, eating patterns and levels of physical activity), predicting that less healthy behavior patterns would be associated with greater physiological dysregulation. In addition, because educational attainment (a major component of socioeconomic status) is associated with health status and longevity, we expected that those with higher educational attainment would have less physiological dysregulation (Adler, Marmot, McEwen, & Stewart, 1999).
The effects of gender were examined because, despite living longer, women report more symptoms of poor health, have higher levels of depression and make more use of health care than men (Case & Paxson, 2005; Verbrugge, 1985). However, with respect to chronic disease, previous research has suggested that men have poorer health assessed by cardiovascular and metabolic biomarkers, whereas women have poorer health assessed by biomarkers of sympathetic nervous system and hypothalamic-pituitary-adrenal functioning (Goldman et al., 2004). Accordingly, we expected men to have higher physiological dysregulation scores than women.

Finally, we examined the relative importance of physiological dysregulation and psychosocial variables as predictors of self-rated health. It is well established that self-rated health is a remarkably good predictor of mortality yet it remains unclear what information people use to make these prescient judgments about their own health status (DeSalvo, Bloser, Reynolds, He, & Munfer, 2006). In particular, it would be useful to know the relative importance of psychosocial information versus clinical health status. In sum, this study addressed a number of issues concerning the assessment of global clinical health in a community sample using multiple indicators by comparing the associations of various summary measures of physiological dysregulation with health outcomes and health behaviors.

Method

Participants

Participants were members of the Hawaii Personality and Health cohort, which is a community sample of 2404 individuals from two Hawaiian islands who underwent a personality assessment by their elementary school teachers 40–50 years ago. To date, 83 percent of the original sample has been located, and 69 percent of those have participated in follow-up studies of personality and health. The recruited sample is representative of the original sample in terms of gender, and reflects the ethnic diversity of the Hawaiian population (Hampson et al., 2001). The first 470 members of the Hawaii Personality and Health Cohort to have a medical and psychological examination were included in this study (227 men and 243 women). The largest ethnic subgroups were: 42 percent Japanese Americans; 17 percent Native Hawaiians; and 12 percent European Americans. The remainder included Chinese, Filipino, Okinawan, Latino, Korean and other Pacific Islanders. The mean age of participants at the time of their clinical examination was 50 years (men: $M = 50.3$, $SD = 2.0$ years; women: $M = 50.0$ years, $SD = 2.0$ years). They had somewhat higher levels of educational attainment than the rest of the recruited sample ($M = 6.9$, $SD = 1.83$ vs $M = 6.5$, $SD = 1.93$ on a nine-point scale, $t = 3.35$, d.f. = 1, 237, $p = .001$).

Procedures

Examinations were conducted at the Kaiser Permanente Center for Health Research clinic in Honolulu, during which anthropometric measures were assessed following standard protocols, and blood and urine samples were collected and sent for laboratory analysis. Other data reported here were obtained by questionnaire over the preceding five years.

Physiological dysregulation

Count-based summary scores

The cut-points used for the summary scores were defined using the sample distributions on each variable of interest (Seplak et al., 2005; Singer et al., 2004). Two pairs of count-based summary scores were developed: one pair included both tails of the distribution on some of the biomarkers, and the other pair used only one extreme of the distribution for all biomarkers. The cut-points were the 10th and 90th percentiles (10/90), and the 25th and 75th percentiles (25/75) for the two-tailed scores, and the 90th percentile (> 90) and the 75th percentile (> 75) for the one-tailed scores. The 10/90 or > 90 summary scores represented a greater degree of dysregulation than did the 25/70 or > 75. There is value in comparing the more versus less extreme cut-points because there have been examples in medical research of findings unique to the more extreme ends of distributions such as body mass index (BMI; McTigue et al., 2006).

Both one- and two-tailed cut-points were examined for systolic and diastolic blood pressure, total cholesterol, triglycerides, fasting blood glucose, BMI and waist/hip ratio, whereas only the high tails of the ratio of total-to-HDL cholesterol (i.e. indicative of unhealthy, low levels of HDL) and urinary protein were used because the low tails are unambiguously healthy. For all four summary count scores, the number of indicators falling at the extremes of the distributions were summed, and an additional point was added for participants taking medications for high blood pressure and/or for cholesterol (maximum possible score = 11, higher scores indicated more dysregulation).
Continuous summary measures The continuous measure corresponding to the two-tailed count scores was the ‘folded z’ score, which was calculated as the sum of the absolute standardized distances of each of the biomarkers from its respective mean (‘folded’ in the sense of treating deviations above and below the mean as the same). As with the count scores, both tails were folded for the distributions of systolic and diastolic blood pressure, total cholesterol, triglycerides, fasting blood glucose, BMI and waist/hip ratio, whereas only deviations above the mean were included for the ratio of total-to-HDL cholesterol and urinary protein. Whether or not the participant was taking medications for high blood pressure and/or cholesterol was included in the folded z score by standardizing these dichotomous variables. The linear z score corresponded to the one-tailed count scores and was the sum of the standard deviations from the mean on all the biomarkers (positive deviations above the mean plus negative deviations below the mean). Higher scores on both continuous variables indicated more dysregulation.

Health outcomes
Self-rated health This was measured with the widely used item from the SF-36 (Ware & Sherbourne, 1992): ‘Compared to others of your same age and gender, would you say that in general your health is (1) Poor, (2) Fair, (3) Good, (4) Very Good, or (5) Excellent?’

Depressive symptoms A modified version of the Center for Epidemiological Studies Depression scale (CESD; Radloff, 1977) was used in which nine culturally appropriate items for Native Hawaiians were added to the original scale (Kanazawa, White, & Hampson, 2007). For each item, participants rated how often they had felt that way in the past month using a five-point scale (1 = ‘Not at all’, 5 = ‘Most or all of the time’). The mean of all 29 items (positive items reversed) was used here (alpha = .92).

Health behaviors
The extent of smoking was measured by 0 = ‘Never smoked’, 1 = ‘Ex-smoker’, 2 = ‘Smokes less than half a pack a day’, 3 = ‘Smokes half a pack or more a day’. Alcohol use combined both frequency and intensity by multiplying the number of days in the past month that alcohol was drunk by the number of drinks typically drunk on one day (non-drinkers scored 0). Eating habits were assessed by a 22-item version of the Food Habits Questionnaire (Kristal, Shattuck, Henry, & Fowler, 1990) and a 24-item Hawaii Food Frequency Questionnaire (Stram et al., 2000). Factor analysis of all 46 items yielded three oblique factors: (a) a high-fiber factor measured consumption of fruit, vegetables and low-fat dairy products (alpha = .83); (b) a high-fat factor measured consumption of meat and high-fat, high-carbohydrate foods (alpha = .80); and (c) a food-preparation factor measured healthy practices such as removing skin from chicken before cooking (alpha = .69). Physical activity measured the total amount of exercise in the past week, with strenuous, moderate and mild activities weighted differently (Godin & Sheperd, 1985).

Educational attainment
Participants selected one of nine levels: 1 = ‘eighth grade or less’, to 9 = ‘postgraduate or professional degree’.

Results
Biomarker distributions and measures of dysregulation for men and women
Men had higher scores than women indicating poorer health status on eight of the 11 individual biomarkers (see Table 1). On the summary measures of dysregulation, men had poorer health status on both the one-tailed count scores and the linear z score, but not on the two-tailed count scores or the folded z score.1 Given these differences, the rest of the analyses were conducted separately for men and women using gender-specific summary scores (i.e. ones based on gender-specific cut-points and gender-specific log-transformed distributions for triglycerides and BMI).

Correlations between physiological dysregulation and health outcomes
To examine their validity the measures of physiological dysregulation were each correlated with the two health outcomes. As can be seen in the first two rows of Table 2, self-rated health was significantly negatively related to all measures of dysregulation except women’s 25/75 count variable. Contrary to prediction, depressive symptoms were not related to dysregulation, except for women’s linear z scores.
Correlations between physiological dysregulation and health behaviors

As shown in Table 2, two health behaviors displayed moderately consistent associations across the dysregulation measures for both men and women: higher levels of smoking and less healthful food preparation were related to more dysregulation. On the > 90 and the linear z, there were some additional correlations with men’s health behaviors. Men who exercised more, ate more fiber and drank more alcohol had less dysregulation. The scatter plot of the correlation with alcohol use indicated that this association was predominately linear. When the separate components of the
Table 2. Correlations Between Gender-specific Measures of Physiological Dysregulation and Health Outcomes and Health Behaviors for Men¹ and Women²

<table>
<thead>
<tr>
<th>Physiological Dysregulation</th>
<th>Count Measures</th>
<th>Continuous Measures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Count 10/90</td>
<td>Count 25/75</td>
</tr>
<tr>
<td></td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>Health Outcomes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Self-rated health</td>
<td>-.23**</td>
<td>-.15*</td>
</tr>
<tr>
<td>Depressive symptoms</td>
<td>.05</td>
<td>-.03</td>
</tr>
<tr>
<td>Health Behaviors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>.16*</td>
<td>.09</td>
</tr>
<tr>
<td>Alcohol use</td>
<td>-.06</td>
<td>-.04</td>
</tr>
<tr>
<td>High-fat diet</td>
<td>-.10</td>
<td>-.00</td>
</tr>
<tr>
<td>Food preparation</td>
<td>-.11</td>
<td>-.16*</td>
</tr>
<tr>
<td>Physical activity</td>
<td>-.04</td>
<td>-.04</td>
</tr>
</tbody>
</table>

¹N ranged from 186–227
²N ranged from 208–243

** p < .01, * p < .05

Count measures of physiological dysregulation summed the number of extreme scores (<10th and >90th percentiles or <25th and >75th percentiles) for systolic and diastolic blood pressure, total cholesterol, triglycerides, fasting blood glucose, BMI, waist/hip ratio; and >90th or >75th for total-to-HDL cholesterol and urinary protein; plus points for medication-taking for high blood pressure and/or cholesterol. Continuous measures summed the standardized deviations from the mean: absolute sum for the folded z and algebraic sum for linear z.
alcohol measure were examined, the number of days per month that alcohol was drunk correlated more highly with the linear z score ($r = -.14, p > .05$) than did the typical number of drinks consumed each day ($r = -.07$), suggesting that the regularity with which alcohol is consumed may be more important than amount for men’s health.

Of the two continuous z scores, the linear z is more theoretically meaningful for this set of biomarkers because the high ends of all the distributions are the clinical indicators of cardiovascular and metabolic risk. Therefore, in the remainder of the analyses, we present results for the linear z summary score only.

### Predicting physiological dysregulation from health behaviors and educational attainment

The allostatic load model predicts that health behaviors will be related to physiological dysregulation. In separate multiple regression analyses for men and women, their linear z scores were predicted from the six health behaviors ($^2$ smoking, alcohol, the three eating factors and physical activity), controlling for educational attainment. Results are summarized in the upper portion of Table 3. Health behaviors were involved in the prediction of men’s dysregulation but not women’s. Less alcohol use (number of days multiplied by typical amount), more smoking and less physical activity predicted

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Predictors</th>
<th>Adj. R</th>
<th>F</th>
<th>df</th>
<th>$\beta$</th>
<th>t</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physiological Dysregulation$^a$</td>
<td>Smoking</td>
<td>.35</td>
<td>7.37***</td>
<td>4,178</td>
<td>.17</td>
<td>2.31*</td>
</tr>
<tr>
<td></td>
<td>Alcohol</td>
<td></td>
<td></td>
<td></td>
<td>-.23</td>
<td>-3.24**</td>
</tr>
<tr>
<td></td>
<td>Physical activity</td>
<td></td>
<td></td>
<td></td>
<td>-.20</td>
<td>-2.82**</td>
</tr>
<tr>
<td></td>
<td>Educational attainment</td>
<td></td>
<td></td>
<td></td>
<td>-.22</td>
<td>-3.02**</td>
</tr>
<tr>
<td>Men</td>
<td>Educational attainment</td>
<td>.20</td>
<td>9.69**</td>
<td>1,202</td>
<td>-.21</td>
<td>-3.11**</td>
</tr>
</tbody>
</table>

| Self-rated Health$^b$ | Dysregulation (linear z) | -.28 | -4.05*** | 4,178 |       |       |
|                       | Smoking                | -.16  | -2.33*   |       |       |       |
|                       | High fiber             | .15   | 2.07*    |       |       |       |
|                       | High fat               | -.17  | -2.55*   |       |       |       |
| Women                  | Educational attainment |       |         |       | .20    | 3.05**|
|                        | Depressive symptoms    | -.34  | -5.31*** |       |       |       |
|                        | Physical activity      | .19   | 3.04**   |       |       |       |
|                        | High fiber             | .15   | 2.50*    |       |       |       |

$^*$ $p < .001$, $^** p < .01$, $^* p < .05$

$^1$ Linear $z = $ algebraic sum of standardized deviations from the mean for 11 biomarkers.

$^a$ Predictors were educational attainment, smoking, alcohol use, high-fat eating, high-fiber eating, healthy food preparation, and physical activity. Only significant predictors are shown.

$^b$ Predictors were educational attainment, physiological dysregulation measured by the linear z summary score, depressive symptoms, smoking, alcohol use, high-fiber eating, high-fat eating, healthy food preparation, and physical activity. Only significant predictors are shown.
worse male dysregulation, whereas only educational attainment predicted women’s dysregulation.

**Predicting self-rated health from physiological dysregulation and other variables**

Regression analyses were conducted to examine the relative importance physiological dysregulation versus psychosocial variables (educational attainment, depressive symptoms, smoking, alcohol use, the three diet factors and physical activity), in predicting judgments of self-rated health. The results are shown in the lower portion of Table 3, and demonstrate notable gender differences. Although dysregulation was a significant predictor for both men and women, eating habits and smoking also determined men’s self-rated health whereas level of depressive symptoms, along with high-fiber eating and physical activity, also determined women’s self-rated health. Educational attainment was a significant predictor for women but not for men.

**Discussion**

Although the differences in performance of the summary scores of physiological dysregulation examined here were not substantial, the one-tailed count scores and the continuous measures proved more valid than the two-tailed count scores. As predicted, they correlated more highly with self-rated health and, to a lesser degree, they correlated more highly with health behaviors. In addition, women’s linear \( z \) was the only dysregulation measure to correlate with depressive symptoms. Based on these comparative analyses, we drew the following conclusions. Count scores using cut-points are likely to be more meaningful when they include only one extreme of the distribution of their indicators. In selecting which extreme, investigators should be guided by the medical significance of high versus low scores, the relations among the individual indicators and by theoretical considerations, such as the allostatic load model. The pattern of correlations for the linear \( z \) score and for the one-tailed count scores were similar indicating that, for the variables studied here, their associations did not alter radically at higher levels of dysregulation. Given that the linear \( z \) makes maximal use of the available variance, thus yielding more power, it is recommended over one-tailed count scores. The numerous gender differences observed here confirmed the importance of conducting gender-specific analyses (Singer et al., 2004).

In contrast, Seplaki et al. (2005) concluded that their continuous score (equivalent to the folded \( z \) used here) was the best summary measure. However, in the present study, the summary scores combined individual biomarkers of cardiovascular and metabolic health for which the unhealthy extreme of the distribution could be defined unambiguously, whereas Seplaki et al. (2005) also included indicators of HPA axis and SNS activity making their summary scores more heterogeneous. Also, unlike Seplaki et al. (2005), we used gender-specific cut-points. Both studies examined biomarkers among older, relatively healthy community populations, but there were cultural and ethnic differences between our sample from Hawaii and Seplaki et al.’s (2005) sample from Taiwan. In both studies, the differences among the various composite scores were not as pronounced as might have been expected, suggesting that the advantages of one summary score over another are relatively subtle.

Consistent with previous findings (Goldman et al., 2004), men had higher levels of physiological dysregulation than women on the one-tailed and linear \( z \) measures, indicating poorer cardiovascular and metabolic health. Women’s dysregulation was only predicted by educational attainment, whereas men with less dysregulation (i.e. better health status) smoked less, drank alcohol and exercised more. Although smoking is an established risk factor for cardiovascular disease, the health benefits of moderate drinking remain controversial (Fillmore, Stockwell, Chikritzhs, Bostrom, & Kerr, 2006).

There were also gender differences in the predictors of self-rated general health. The process by which people arrive at judgments of their general health is not well understood but is presumed to include a self-appraisal of physical health status. Here, physiological dysregulation predicted self-rated health for men and women, although whether they used an intuitive health appraisal or actual knowledge of their levels on indicators like blood pressure and cholesterol could not be determined. Women, but not men, apparently took depressive symptoms into account when judging their general health, suggesting that women, unlike men, may include mental health in their understanding of general health. Alternatively, women who are more depressed may be more prone to perceive their general health more negatively regardless of their actual health status.

The ethnic diversity of the sample, although a strength in comparison with studies of more homogeneous
samples, limited the external validity of the present findings. The effects of ethnicity were not examined because of the relatively small subgroups created by dividing the sample by both gender and several ethnicities. We plan an extensive study of the influence of ethnicity on health when clinical data are available for the entire cohort. Given the sample’s narrow age range ($M = 50, SD = 2$), and the stability of health at middle age, age effects were not studied. However, our goal is to repeat the medical and psychological examination of this cohort approximately every five years, and it will be increasingly important to examine the effects of age differences in the coming decades. Two other limitations may be noted. The lack of HPA and SNS biomarkers restricted comparability with previous studies. A stronger test of the validity of physiological dysregulation measures would be to use them to predict subsequent disease outcomes, which we will do when these data become available for this cohort. The linear $z$ summary measure of physiological dysregulation recommended here may be more useful to health psychologists than composites in medicine, such as the Framingham cardiovascular risk score (e.g. Wilson et al., 1998), that combine demographics, clinical indicators and health behaviors. The combination of risk factors known as the ‘metabolic syndrome’ is based exclusively on biomarkers, some of which overlap with those examined here. A continuous measure of the metabolic syndrome can be interpreted as level of metabolic health (Hillier et al., 2006), and such a measure is another potentially useful clinical outcome based on multiple indicators that is available to health psychologists. The increasing use of biological outcomes in health psychology presents a number of challenges, particularly for studies of relatively healthy community samples. Deriving optimal summary measures of global health status from biomarkers is not straightforward. This report offered a comparative analysis of several composite measures of global health status by examining their cross-sectional associations with health outcomes and health behaviors. Further research is needed to examine pathways leading to health status measured by these and similar composite constructs, and whether these constructs provide early indications of subsequent morbidity and mortality.

Notes

1. To correct for the positive skew in the distributions for triglycerides and BMI, a natural log transformation was used. The transformed distributions for the entire sample were used in the computation of the linear summary scores (folded $z$ and continuous $z$) shown in Table 1.
2. The six health behaviors were only modestly related. For men, the highest correlation was between smoking and high fiber ($r = -.22$), and for women the highest correlation was between physical activity and alcohol use ($r = .25$). Moreover, these health behaviors were only moderately correlated with educational attainment. For men, the highest correlation was $r = .26$ with healthy food preparation, and for women it was $r = -.30$ with smoking. Accordingly, multicollinearity problems were unlikely.

References


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