Poor self-rated health is not associated with a high total allostatic load in type 2 diabetic patients – But high blood pressure is

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Received 22 November 2010; received in revised form 7 March 2011; accepted 23 March 2011
Available online 18 May 2011

Abstract

Objective. – Allostatic load has been linked to self-rated health (SRH), cardiovascular disease and mortality in non-diabetic individuals. The aim of this study was to construct an allostatic load score and to find any correlations with SRH.

Methods. – The subjects included in the study came from a randomized, controlled trial of type 2 diabetes. Blood samples were drawn, urine was collected for 24 h, and questionnaires, including SRH, were filled out on three occasions: at baseline; after the 10-week intervention; and at a follow-up 3 months after the intervention. Allostatic load was estimated using a wide range of variables, including systolic and diastolic blood pressure, pulse pressure, cortisol, catecholamines, HbA1c, insulin, plasma glucose and waist circumference.

Results. – There was no association between SRH and allostatic load. However, three other components were significantly correlated with allostatic load at the baseline investigation and the two follow-up investigations – namely, systolic blood pressure, diastolic blood pressure and HbA1c.

Conclusion. – The absence of an association between allostatic load and SRH in diabetic individuals contrasts with previous findings in non-diabetic women, and shows that it is hazardous to apply findings in one population to another, especially diabetic and non-diabetic populations.

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Keywords: Allostatic load; Diabetes; Self-rated health; Blood pressure; Cardiovascular prevention

Résumé

La perception d’un état de santé médiocre par auto-évaluation (self-rated health) n’est pas associée chez les diabétiques de type 2 à une augmentation de la charge allostatique totale.

Objectif. – La charge allostatique a été associée à la perception de l’état de santé (self-rated health ou SRH), aux maladies cardiovasculaires et à la mortalité chez les non-diabétiques. L’objectif était de construire un score de charge allostatique et d’étudier ses corrélations avec la perception par les patients de leur état de santé.

Méthodes. – Les patients inclus dans l’étude étaient issus d’un essai randomisé et contrôlé, réalisé dans le diabète de type 2. Des échantillons de sang et les urines de 24 heures ont été recueillis et des questionnaires (dont SRH) ont été complétés à l’inclusion puis après dix semaines et trois mois après intervention. La charge allostatique été évaluée à l’aide d’une gamme étendue de paramètres: rythme cardiaque, pression artérielle systolique et diastolique, pression pulsée, cortisol, catécholamines, HbA1c, insulinémie, glycémie et tour de taille.

Résultats. – Aucune association entre la SRH et la charge allostatique n’a été mise en évidence. Il existait une corrélation significative entre la charge allostatique et trois paramètres (pression artérielle systolique et diastolique et HbA1c) à l’inclusion et aux deux enquêtes de suivi.

Conclusions. – L’absence d’association entre la charge allostatique et la perception de l’état de santé chez les diabétiques contraste avec les résultats précédemment observés chez des non-diabétiques, montrant qu’il est hasardeux d’extrapoler des résultats d’une population à l’autre, en particulier diabétiques et non diabétiques.

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Mots clés : Charge allostatique ; Diabète de type 2 ; Perception de santé ; Pression artérielle ; Prévention cardiovasculaire

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1. Introduction

Allostasis is the healthy response to acute stress that maintains homeostasis, and includes increases in catecholamines and glucocorticoids, and their direct physiological responses [1]. The long-term metabolic effects of stress can be defined as allostatic load, and may include elevated blood pressure, blood lipids, higher levels of catecholamines, poor glycaemic control, increased waist circumference and non-normal cortisol levels [1–3]. A high allostatic load score has also been shown to be associated with incident cardiovascular disease [4] as well as other chronic diseases [5], and may be viewed as a score that represents multisystem biological dysregulation [6].

It was recently shown that poor self-rated health is associated with an increased allostatic load in a mixed sample of relatively healthy women [7]. Using one simple question, this enabled the identification of individuals with a high allostatic load and, hence, increased cardiovascular risk. The association between allostatic load and self-rated health may also help to explain the well-documented association between self-rated health and morbidity as well as mortality [8].

Diabetes is a major public-health concern, and patients with diabetes are at very high risk of coronary heart disease [9,10]. Global assessment of the prevention of cardiovascular diseases is recommended in guidelines [11,12], and any simple method that identifies individuals at high risk is most welcome. In addition, easily identifiable variables associated with allostatic load in diabetes would be of clinical value. As diabetic individuals are “metabolically ill”, a separate definition of allostatic load has been recommended in guidelines [11,12], and any simple method that identifies those diabetic patients at high risk is most welcome. In addition, easily identifiable variables associated with allostatic load in diabetes would be of clinical value. As diabetic individuals are “metabolically ill”, a separate definition of allostatic load has to be used compared with what has been used for individuals without diabetes.

The present study aimed to construct an allostatic load score for type 2 diabetic individuals from a sample of thoroughly investigated diabetic men and women treated with metformin. The objective was then to study the correlation between self-rated health and this allostatic load score to find the one simple question or measure that identifies those diabetic patients at high cardiovascular risk.

2. Materials and methods

The study sample came from a randomized, controlled, parallel-group trial of weekly tactile massage in type 2 diabetic patients [13]. Tactile massage involves pain-free, deliberate, gentle and superficial manipulation of the skin. The control group received relaxation exercises using a compact disc. Four primary healthcare centres in Stockholm County agreed to participate in the study. Patients with type 2 diabetes and HbA1c of 6–8%, according to the Swedish standard (corresponding to the Diabetes Control and Complications Trial [DCCT], but 1 percentage unit higher), aged 35–75 years of age and taking metformin treatment, were identified based on information in their medical records. To limit the possible effects of genetic differences or of migration seen in diabetes [14] and cardiovascular disease [15,16], the healthcare centres were asked to recruit only Swedish-born subjects with Swedish-born parents for the present study. Exclusion criteria were heart or renal failure and insulin treatment. Three examinations were performed: at baseline; after 10 weeks of intervention; and 12 weeks after completion of the intervention. Altogether, 53 participants (47% women), aged 43–75 years, were included in the study. Treatment for hypertension was reported in 28 of the 53 participants. The study received ethical approval from a regional committee at the Karolinska Institutet. No effect on metabolic control was seen with either tactile massage or relaxation in the original study [13].

2.1 Blood and urine samples, and methods of analysis

The following metabolic and inflammatory markers were analyzed from blood samples: overnight fasting plasma glucose; B-haemoglobin A1c (B-HbA1c), according to the Mono S standard, which is one percentage unit lower than the DCCT standard; and fasting serum insulin. Catecholamine and cortisol levels were analyzed from two separate 24-h urine collections made by each participant, using containers prepared by the laboratory. A certified research laboratory (Laboratory of Clinical Chemistry at Karolinska University Hospital) performed the analyses and prepared the urine containers.

2.2 Waist circumference, heart rate and blood pressure

Waist circumference was measured, with the participant standing, at the midway point between the iliac crest and the lowest rib. Resting heart rate and blood pressure were measured with the subject lying down after a 5-min rest. Pulse pressure was calculated as the difference between the systolic and diastolic blood pressures.

2.3 Allostatic load

An allostatic load score in our diabetic population was constructed, using the following variables and cut-off levels. Cut-off levels were based on the Karolinska Laboratory cut-offs representing normal/non-normal values, and cited if other sources of information were used, or were the upper quartiles of the participating individuals. Each non-normal value added 1 to the individual’s total allostatic score, which was also based on waist circumferences > 102 cm in men and > 88 cm in women [17], systolic blood pressure ≥ 140 mmHg [11], diastolic blood pressure ≥ 90 mmHg [11], pulse pressure ≥ 65 mmHg [18], resting heart rate ≥ 75 beats/min [19], HbA1c ≥ 7%, non-normal insulin levels (< 18 or > 173 pmol/L, Karolinska Laboratory), non-normal cortisol levels (< 40 or > 170 nmol/24 h (Karolinska Laboratory) [20] and, finally, the participants with the highest urinary levels of adrenaline and dopamine (upper quartile due to the lack of normal cut-off levels).

2.4 Self-rated health

Self-rated health was measured using the item “How would you rate your general health?”, which could be answered as either “very good”, “good”, “neither good nor poor”, “rather
poor” or “very poor”, from the Swedish version of the short-form questionnaire [21].

2.5. Statistical data analysis

For analysis of the data, the STATA statistical software version 10 was used. A non-parametric test had to be used due to the non-normal distribution of the allostatic load score and some of its components. Also, to allow adjustments for gender, partial Spearman coefficients between self-rated health and components of the allostatic load score and the total allostatic load score were calculated [22].

To minimize the risk of mass significance due to multiple testing, all significant findings from the baseline investigation were double-checked at the 10-week and 3-month follow-ups. Each examination was treated as an individual cross-sectional dataset in our study, and only those individuals with complete data from each examination were included in the analysis (eight individuals were missing some data).

3. Results

3.1. Non-normal distribution of self-rated health and allostatic load scores

Figs. 1 and 2 show the distribution of the self-rated health and allostatic load scores in the study population for men and women separately. The non-normal distributions made it essential to analyze the correlations with non-parametric methods.

3.2. Allostatic load cut-off values

Table 1 shows the limits of the allostatic load for each variable included in the allostatic load score. The most common allostatic load components found in diabetic individuals were large waist circumference (66%), high systolic blood pressure (64%), elevated plasma glucose (77%) and non-normal cortisol levels (58%), with only one subject having an above-normal cortisol level. The average waist circumference was 104 cm among men and 98 cm among women, and the average systolic blood pressure was 142 mmHg among men and 145 mmHg among women. The average plasma glucose was 8.9 mmol/L among men and 8.4 mmol/L among women, and the average cortisol level was 50 nmol/24 h among men and 32 nmol/24 h among women.

3.3. Correlations with allostatic load

No significant correlation between self-rated health and allostatic load score was seen (data not shown in tables), and neither was any correlation seen between self-rated health and any of the components of the allostatic load score. There was also no correlation between allostatic load score and age ($P = 0.63$).

Table 2 shows the individual allostatic load components and their correlations with allostatic load. Systolic blood pressure, diastolic blood pressure, pulse pressure, HbA1c and dopamine were all correlated with the total allostatic load score at the baseline investigation. However, only three components were significantly correlated at the baseline investigation and the two follow-up investigations – namely, systolic blood pressure, diastolic blood pressure and HbA1c.

4. Discussion

In this thoroughly investigated sample of type 2 diabetic patients, no correlation was found between self-rated health and allostatic load. This contrasts with previous findings in non-diabetic individuals. However, allostatic load was correlated with high systolic and high diastolic blood pressures as well as HbA1c. In addition, a remarkably high frequency of central obesity, raised blood pressure and plasma glucose, and non-normal cortisol levels was also seen in our group of diabetic patients.

There was no association found between allostatic load or any of its components and self-rated health. As a consequence, screening for poor metabolic control, cardiovascular risk factors or a high allostatic load cannot be based on self-rated health in this group of patients. The lack of association may be explained by the fact that, although type 2 diabetic patients are metabolically perturbed, their health-related quality of life is relatively high [23]. It is also possible that individuals with a chronic disease such as diabetes type 2 have a different concept of what health is, and this may partly explain our findings. Compared with self-rated health in a population-based sample [24], it appears that our study sample had more individuals with poor self-rated health. However, the small number of individuals in our study limits the possibility of making direct comparisons of the self-rated health distributions. In contrast to our present findings in type 2 diabetic patients, poor self-rated health has been
30% of individuals with diagnosed hypertension have a blood pressure; however, considering that the prevalence of hypertension among 60-year-olds is around 50%[15] and that only around 48% of the men and 68% of the women. This indicates that dysregulation of the hypothalamic–pituitary–adrenal axis is a marker of hypertension control, but also of total allostatic load. High blood pressure may, as a consequence, not only be considered a marker of hypertension among patients with diabetes[20]. The high prevalence of elevated systolic blood pressure may appear to be surprising; however, considering that the prevalence of hypertension among 60-year-olds is around 50% [15] and that only around 30% of individuals with diagnosed hypertension have a blood pressure less than 140/90 mmHg, and that 40% subsequently have the metabolic syndrome and 67% have blood lipid disturbances [28], we see no reason to doubt these numbers. Indeed, the fact that many individuals are unaware of having cardiovascular risk factors may have caused them to rate their health as better than they otherwise would have.

Limitations of the present study include a relatively small sample size; however, the significant findings were verified at the follow-up visits. Blood lipid levels were not measured in our study, although they have previously been included in allostatic load scores in healthy individuals[7]. Nevertheless, blood lipid therapy (statin therapy) is commonly seen among diabetic patients in Sweden, and low blood lipids are more likely to be explained by such effective lipid-lowering therapy than by a low allostatic load. The finding that some components of the allostatic load score correlated with the total score may be criticized in view of the fact that an association is to be expected, given that the component made up part of the total score. However, waist circumference, blood glucose and non-normal cortisol did not correlate with the total allostatic load score. Indeed, the fact that waist circumference was not correlated with the score is puzzling, as it is a component of the metabolic syndrome [29], and has been shown to be strongly associated with newly diagnosed high blood pressure [30] and blood pressure control [28]. In fact, there may be other allostatic load components that we did not have access to that could have resulted in an allostatic load score closer to the true allostatic load in diabetic patients.

The present study has several strengths. The participants were homogeneous due to the fairly strict inclusion criteria, making the results valid for Swedish-born type 2 diabetic patients. Also, although the study design may be regarded as cross-sectional, it is not likely that a chance finding would be repeatedly significant at the follow-ups, and all significant findings were verified on two follow-up investigations. Thus, our findings are not likely to be due to chance. Furthermore, the patients did, to some extent, have changes made to their therapies and they also received 10 sessions of relaxation therapy; however, the fact that the associations persisted indicates that the present findings are robust and repeatable.

### Table 1

<table>
<thead>
<tr>
<th>Variables included in allostatic load score (cut-off levels adding to allostatic load)</th>
<th>Average (standard deviation)</th>
<th>Participants (n/n) having values adding to allostatic score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Waist circumference (≥ 88 cm in women and ≥ 102 cm in men)</td>
<td>Men 104.1 (8.1)</td>
<td>Women 97.7 (9.5)</td>
</tr>
<tr>
<td>Systolic blood pressure (≥ 140 mmHg)</td>
<td>Men 141.9 (16.8)</td>
<td>Women 145.3 (18.3)</td>
</tr>
<tr>
<td>Diastolic blood pressure (≥ 90 mmHg)</td>
<td>Men 83.2 (8.7)</td>
<td>Women 81.7 (7.8)</td>
</tr>
<tr>
<td>Pulse pressure (≥ 65 mmHg)</td>
<td>Men 58.6 (17.7)</td>
<td>Women 63.6 (16.4)</td>
</tr>
<tr>
<td>Heart rate (≥ 75 beats/min)</td>
<td>Men 67 (7.2)</td>
<td>Women 66.7 (7.72)</td>
</tr>
<tr>
<td>HbA1c (≥ 7%)</td>
<td>Men 6.74 (1.22)</td>
<td>Women 6.52 (0.98)</td>
</tr>
<tr>
<td>Fasting plasma glucose (≥ 7 mmol/L)</td>
<td>Men 8.88 (2.44)</td>
<td>Women 8.39 (1.73)</td>
</tr>
<tr>
<td>Non-normal insulin (&lt; 18 or &gt; 173 pmol/L)</td>
<td>Men 82.1 (50.4)</td>
<td>Women 89.7 (45.6)</td>
</tr>
<tr>
<td>Non-normal cortisol (&lt; 40 or &gt; 170 nmol/24 h)</td>
<td>Men 50.2 (40.2)</td>
<td>Women 31.8 (20.8)</td>
</tr>
<tr>
<td>Adrenaline (upper quartile)</td>
<td>Men 22.2 (15.0)</td>
<td>Women 16.1 (11.9)</td>
</tr>
<tr>
<td>Dopamine (upper quartile)</td>
<td>Men 1100 (445)</td>
<td>Women 923 (441)</td>
</tr>
</tbody>
</table>
Table 2

Allostatic load score distributions in type 2 diabetic men and women, with gender-adjusted correlations between the individual factors included in the allostatic load score and the score itself.

<table>
<thead>
<tr>
<th>Variables included in allostatic load score</th>
<th>Correlations at baseline investigation</th>
<th>Verification of findings from baseline investigation at follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameters of allostatic load</td>
<td>Correlations with dichotomous variables</td>
<td>Correlations with continuous variables</td>
</tr>
<tr>
<td></td>
<td>P value</td>
<td>P value</td>
</tr>
<tr>
<td>Waist circumference (≥ 88 cm in women and ≥ 102 cm in men)</td>
<td>0.20</td>
<td>0.24</td>
</tr>
<tr>
<td>Systolic blood pressure (≥ 140 mmHg)</td>
<td>0.49</td>
<td>0.002</td>
</tr>
<tr>
<td>Diastolic blood pressure (≥ 90 mmHg)</td>
<td>0.44</td>
<td>0.005</td>
</tr>
<tr>
<td>Pulse pressure (≥ 65 mmHg)</td>
<td>0.39</td>
<td>0.015</td>
</tr>
<tr>
<td>Heart rate (≥ 75 beats/min)</td>
<td>0.54</td>
<td>0.001</td>
</tr>
<tr>
<td>HbA1c (≥ 7%)</td>
<td>0.39</td>
<td>0.015</td>
</tr>
<tr>
<td>Fasting plasma glucose (≥ 7 mmol/L)</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Non-normal insulin&lt;sup&gt;a&lt;/sup&gt; (&lt; 18 or &gt; 173 pmol/L)</td>
<td>0.097</td>
<td>0.56</td>
</tr>
<tr>
<td>Non-normal cortisol&lt;sup&gt;a&lt;/sup&gt; (&lt; 40 or &gt; 170 nmol/24 h)</td>
<td>0.23</td>
<td>0.16</td>
</tr>
<tr>
<td>Adrenaline (upper quartile)</td>
<td>0.18</td>
<td>0.29</td>
</tr>
<tr>
<td>Dopamine (upper quartile)</td>
<td>0.42</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Significant findings (shown in boldface) in men and women from the baseline investigation were verified at the two follow-up investigations; elevated or non-normal levels of each score component added 1 percentage unit to the allostatic load score.

<sup>a</sup> Karolinska Laboratory.
5. Conclusion

Contrary to previous findings in non-diabetic individuals, self-rated health cannot be used to identify diabetic individuals with a high allostatic load. This shows that it is hazardous to apply findings from one population to another, a fact that may be especially the case for diabetic and non-diabetic populations. Blood pressure and HbA1c were correlated with the total allostatic load score and may, with more evidence, be used as proxies for a high score. This may partly explain why blood pressure is such an important cardiovascular risk marker in diabetic patients, and suggests that diabetics with high blood pressure, in addition to receiving intensified antihypertensive therapy, should also be monitored for other non-normal allostatic load components.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

Acknowledgments

This study was supported by grants from Stockholm County Council. We would also like to thank the participants of the study, the nurses who performed the tactile massage and the participating healthcare centres in Stockholm County.

References