Blood Pressure and Coping with Stressors

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Introduction

One major research tradition in the area investigating the role of psychosocial factors in hypertension focuses on the association between experienced environmental stressors and blood pressure. A wide range of stressors have been studied, sometimes as an independent variable, like the nuclear accident on Three Mile Island (Baum, 1990), sometimes as a dependent variable, like in studies in which hypertensive patients and normotensives were compared on the number of negative life events experienced (e.g., Myers & Miles, 1981; Osti, Trombini, & Magnani, 1980). However, the results have often been contradictory. We feel that not only methodological aspects may be responsible for these discrepancies, but also that the results may have been influenced more systematically by several psychological sample characteristics, which have often been neglected, like awareness of having hypertension. Moreover, there are considerable differences among studies in the amount to which the measurements deal with subjective aspects of stressor exposure, rather than merely focusing on more objective measures. In this contribution, we will argue that these aspects may account for a part of the inconsistent findings.

Therefore, first, a brief review will be provided concerning studies on the relationship between hypertension and objectively derived measures of real-life stressor exposure by comparing exposed with non-exposed groups. Second, studies concerning the relationship between blood pressure and self-reports of exposure to psychosocial stressors will be discussed. Possible confounders in this relationship (e.g., awareness of having hypertension) will be touched upon. Third, a putative underlying psychological mechanism - defensive coping style- for the associations between hypertension and stressor appraisal will be investigated. Finally, conclusions and suggestions for future research will be given.

Blood pressure and objectively assessed stressor exposure

In this section, a selective overview will be offered of investigations on the relationship between blood pressure and objectively established stressor exposure, i.e., studies will be discussed in which stressor exposure has been established by other means than self-reports. Included are studies of individuals exposed to acute traumatic events or to chronic stressors.

For example, Ruskin, Baerd, & Schaffer (1948) studied subjects who witnessed the 1947 Texas City Explosion. Subjects who experienced this disaster
showed elevated blood pressure levels for days after the event. Miasnikov (1961) reported prolonged elevations of blood pressure in Leningrad residents after heavy bombardments of the city in World War II. However, besides the methodological limitations of these early studies, the controversy remains whether such acute disastrous stressor-exposures contribute to the development of hypertension. Another dramatic event that has been studied is the Three Mile Island nuclear accident. This event had also chronic aspects, because the threat of radiation remained for a long time. Baum (1990) has summarized the Three Mile Island studies and has demonstrated that, compared with a control group living near another nuclear power plant, Three Mile Island residents exhibited higher levels of blood pressure and catecholamines up to six years after the accident.

Although methodologically often limited, studies on chronic psychosocial stressors have provided evidence for an association between exposure to environmental stressors and elevated blood pressure. This evidence comes from both local and national studies (e.g., Harburg, Schull, Erfurt, & Schork, 1970; Rofé & Goldberg, 1983) and from cross-cultural studies (e.g., Cassel, 1974; Marmot, 1984). For instance, Rofé and Goldberg found that pregnant women who lived in a Israeli high-stress environment (frequent terrorist attacks) displayed higher blood pressure levels than women living in a low-stress area (no terrorist attacks). Moreover, the beginning of a war was associated with increased blood pressure in all the women, especially in those living in the high-stress area.

Other evidence of psychosocial effects on blood pressure comes from the well-known study on crowding in prisons (D’Atri, Fitzgerald, Kasl, & Ostfeld, 1981) and from research on objectively derived measures of occupational stressors, like the air traffic controllers study by Cobb and Rose (1973) and the longitudinal study on effects of job-loss on blood pressure by Kasl and Cobb (1970). In addition, recently Theorell, de Faire, Johnson, Hall, Perski, & Stewart (1991) found that job strain, assessed by an objective job classification procedure, was significantly positively associated with diastolic blood pressure during both work and at night. These research results thus indicated that persons exposed to stressors had higher blood pressure levels than non-exposed individuals.

Although this brief literature overview concerning the relationship between exposure to real-life stressors and elevated blood pressure is merely illustrative, it certainly suggests that overall the results are in favor of a positive association between objectively established stressor exposure and blood pressure level.
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Confounding variables

When interpreting results of (retrospective) case-control studies based on self-reports, one should always be aware of the possible presence of biasing mechanisms, like search for meaning, socially desirable responding, denial, etc. In this context, two factors, namely awareness of having hypertension and treatment for the disease, which may potentiate the distortion of self-reports of affect-laden matters, are of special interest.

For instance, in studies in which aware hypertensives have been compared to normotensives and unaware hypertensives with respect to self-reported well-being and physical and psychological symptoms, the former group often had poorer scores than the latter groups (e.g., Irvine, Garner, Olmstead, & Logan, 1989; Kidson, 1973; Monk, 1980; Müller, Montoya, Schandry, & Hartl, 1994; Zonderman, Leu, & Costa, 1986). On the other hand, unaware hypertensives have been found to have more favorable scores on these measures than normotensives (Davies, 1970; Kidson, 1973). Similar results have been found when treated hypertensives were compared to normotensives and untreated hypertensives on these measures (e.g., Monk, 1980; Goldberg, Comstock, & Graves, 1980; Tibblin & Lindström, 1972). Whether these outcomes are the result of an effect of awareness or treatment per se, or whether a third variable is responsible for the effects -such as help-seeking behavior on the part of complainers/neurotics- is of secondary importance. Because of the statistical relationship of variables as awareness and treatment of hypertension with self-report scores, these variables should always be accounted for in studies concerning the relationship between blood pressure and self-reports of affect-laden matters, including stressor exposure.

In the next sections, the focus will be on the relationship between blood pressure and three categories of self-reported stressor experiences, namely regarding life stressors, occupational stressors, and physical stressors (pain).

Life stressors

The results of studies in which self-reported life changes are the subject of interest, seem rather contradictory.

In their classical study, Reiser et al. (1951) found that the occurrence of stressful life situations was associated both with the onset of hypertension and with medical complications during the course of the disease. Unfortunately, in this study no control group was included. Myers and Miles (1981) found that in a sample of low-income blacks, individuals with borderline hypertension (a part of
them was treated for the disease) reported more negative life events than normotensive blacks. Lal, Ahuja, and Madhukar (1982) demonstrated corresponding results in India; treated hypertensives reported more negative life events than matched normotensives. Also Osti et al. (1980) found more negative life events reported by hypertensive patients, compared with a control group of patients with other cardiovascular disorders. In contrast, results from several other studies strongly suggest a negative association between blood pressure and the number of self-reported life stressors. For instance, Svensson and Theorell (1983) found that 18-year old men with sustained blood pressure elevation reported fewer negative life events than control subjects. Theorell, Svensson, Knox, Waller, and Alvarez (1986) showed that young males with elevated blood pressure reported fewer life stressors than subjects with normal blood pressure readings. Linden and Feuerstein (1983) also showed that untreated hypertensives reported fewer interpersonal stressors and were less depressed than medicated hypertensives and normotensives.

The inconsistencies described here may partly be due to differences between the samples of subjects. Studies in which positive associations were found between blood pressure level and reported life events included hypertensive patients, whereas studies in which the association was negative, the subjects were either unaware of their blood pressure (Svensson & Theorell, 1983) or were primarily untreated hypertensives (Linden & Feuerstein, 1983; Theorell et al., 1986). This may be a relevant difference between the studies in the view of the well-known caveat of retrospective bias. As has been discussed in more detail above, treatment and awareness may have an influence on reporting behavior, resulting in a bias of the results due to phenomena such as a search for meaning. The data suggest that, when treatment and awareness are absent, an inverse association is more likely to be found between blood pressure level and self-reported stressor exposure. This is in line with the results obtained in two large studies on occupational stressors discussed below (Jenkins, Hurst, & Rose, 1985; Winkleby, Ragland, & Syme, 1988). As Theorell (1990) has stated, persons at risk for the development of hypertension or persons being in an early stage of asymptomatic hypertension (and mostly unaware of it) may tend to have a 'non-complaining' life attitude and underreport stressors.

**Occupational stressors**

Inconsistencies with respect to the relationship between blood pressure level and self-reported exposure to stressors have also been found in occupational research.

On several occasions a positive association has been found between blood pressure level and self-reported job stressors (Matthews, Cottington, Talbott, Kuller, & Siegel, 1987; Schnall et al., 1990; Theorell, Ahlberg-Hulten, Jodko,
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Sigala, & de la Torre, 1993; Van Egeren, 1992). For instance, Matthews et al. (1987) examined the relationship between occupational stressors and diastolic blood pressure among 288 male blue collar workers. After controlling for a number of potentially confounding variables, it was shown that diastolic blood pressure level correlated positively with various indices of the stressfulness of work conditions, namely poor contact with co-workers, low decision latitude, and overall job dissatisfaction. Schnall et al. (1990) operationalized job strain as the combination of high work load and low decision latitude. After controlling for confounders, they found that high blood pressure in males from a wide range of occupations was associated with high job strain. Van Egeren (1992) and Theorell et al. (1993) found similar results using the same operationalization of job strain as Schnall et al.

In contrast, in some other studies negative associations were reported, often contrary to the expectations of the researchers. For example, Jenkins et al. (1985) found in their study on 416 air traffic controllers that normotensives who developed borderline or definite hypertension during a three year follow-up reported fewer life stressors, less tension-anxiety, less depression, less burn-out, and more satisfaction with jobs and co-workers than their colleagues who stayed normotensive. In an extensive study (N = 1428), conducted by Winkleby et al. (1988), San Francisco bus drivers were surveyed as part of an occupational health study. An inverse association was obtained between blood pressure level and subjects' self-reports of work-related problems. This association remained significant after adjustment for 12 potentially confounding variables. When the analysis was done using only the data of the 1040 normotensive subjects, again an inverse association was found.

It is difficult to find proper explanations for these inconsistencies. Various sample characteristics, and interactions between them, may have influenced the self-reported rates of stressor exposure. However, we have not been able to identify systematic differences in sample characteristics, such as age, sex, awareness, and treatment for hypertension, between the studies with positive and those with negative findings. On the other hand, an explanation may be offered by taking into account another varying factor: the assessment method used to determine the level of stressor exposure. Occupational questionnaires like the Job Content Questionnaire (used in three of the four studies in which positive associations were found (Schnall et al., 1990; Theorell et al., 1993; Van Egeren, 1992), have a strong objective component as suggested by a large interoccupation variance (Karasek & Theorell, 1990; Schnall et al., 1990). In the previous section, it has been stated that when measures of stressor exposure are derived objectively, positive associations between blood pressure and stressor exposure dominate the results obtained. Therefore, Theorell et al. (1991) suggest that, in order to obtain positive associations between these variables, stressor measurement has to be as
objective as possible. In contrast, as stated by Winkleby et al. (1988), when stressors are assessed via more subjective measures, null or reverse findings are often reported. This explanation is in line with a recent study conducted by Fox, Dwyer, and Ganster (1993). In a sample of 136 nurses they linked objective and subjective measures of job stressors to blood pressure and cortisol levels. The objective measure of job stressors was the head nurse's ratings of individual nurses' work load. Subjective measures were various self-report questionnaires concerning work load, perceived control, the number of stressful events at work, and overall job satisfaction. The intriguing results could be summarized as follows: (a) the objective measure of work load was positively associated with blood pressure level, both at work and at home, (b) job strain (the Karasekian interaction of high work load and low perceived control) was positively associated with blood pressure level (which is in line with the other job strain studies), (c) the subjective measure of work load did not correlate with blood pressure, and (d) the self-reported number of stressful events at work correlated negatively with diastolic blood pressure level at home.

Physical stressors

Evidence for a diminished appraisal of threatening stimuli in hypertensives has also been obtained from pain research. In the past 15 years a solid body of evidence has been accumulated regarding links between blood pressure and diminished sensitivity to painful stimulation (antinociception). It has been demonstrated that individuals with high blood pressure have a higher pain threshold and pain tolerance than individuals with normal blood pressure, indicating a tendency for hypertensives to perceive these stimuli as less aversive. This has been found for electrical (Elbert, Rockstroh, Lutzenberger, Kessler, & Pietrowsky, 1988; Zamir & Shuber, 1980), thermal (Sheps et al., 1992), and finger pressure pain stimulation techniques (Bruehl, Carlson, & McCubbin, 1992). Moreover, also in normotensive samples an inverse relationship between blood pressure levels and perceived painfulness of physical stressors has been found (Bruehl et al., 1992). This inverse relationship has been found in both between-subjects (e.g., Zamir & Shuber, 1980) and within-subjects designs (e.g., Dworkin, Filewich, Miller, Craigmyle, & Pickering, 1979), in animal (e.g., Randich & Maixner, 1984) as well as in human studies (e.g., Sheps et al., 1992).

Evidence has been obtained for the mediation of the baroreceptors in this diminished sensitivity to pain; direct baroreceptor stimulation produced antinociception in rats (e.g., Randich, 1986). It has been hypothesized that baroreceptor stimulation could have this effect via cortical inhibition, which has been found to be associated with diminished pain sensitivity in individuals with elevated blood pressure (e.g., Elbert et al., 1988). These authors demonstrated that
in students with elevated blood pressure, baroreceptor stimulation elevated their pain threshold, whereas the same procedure had the opposite effect in normotensives. Additionally, the authors found a positive shift in negative cortical slow waves during baroreceptor stimulation, suggesting cortical inhibition. This positive shift was related to resting blood pressure, indicating differences in cortical activity during pain between normotensives and hypertensives. The findings of France, Ditto, and Adler (1991) suggest that this hyposensitivity to painful stimuli might be associated with a risk for hypertension. They found that healthy, normotensive males with a parental history of hypertension showed reduced pain sensitivity to a constrictive thigh-cuff pressure stimulus compared to males without a parental history of hypertension.

Only Rau et al. (1994) found less clear results. As in earlier studies, hypertensives exhibited higher pain thresholds for thermal pain than normotensives. However, for pressure pain this effect was not found. The authors suggested that this might be due to the fact that unlike in other studies, the pain stimulus was not as inescapable in this study; the subjects could terminate the pain before it became too uncomfortable.

In conclusion, although some inconsistencies have been found regarding results which involved different pain modalities, overall, a good body of evidence exists in support of an association between blood pressure and antinociception, which seems to be mediated by the baroreceptors. Thus, individuals with elevated blood pressure appear to have an altered appraisal of physical aversive stimuli.

Conclusions

The studies using self-reports of stressor exposure in the psychosocial domain show conflicting results. However, when report biasing factors, in particular awareness and/or treatment, are absent and the questionnaires are subjective rather than objective, results are more in favor of an inverse association between blood pressure and perceived stressor exposure. With respect to appraisal of physical stressors, this inverse association seems well established.

This conclusion contrasts with the outcome of the review of the literature based on objectively established stressor exposure in which positive associations predominate. A nice example of the discrepancy between objective and subjective stress measures in relation to blood pressure is, besides the above mentioned investigation of Fox et al. (1993), the study of Harburg et al. (1970). An objectively established index of stressfulness, namely the area in which the subjects lived, was associated with a higher proportion of hypertension. Surprisingly, however, the persons with high blood pressure who were actually living in high stress areas were more satisfied with their neighborhood than their normotensive counterparts in the same tract; consequently, they judged their area
as less stressful than the normotensives.

The discrepancy between results of studies based on objectively established measures of stressor exposure and those of studies using subjective measures needs clarification. Whereas objectively measured psychosocial stressors might contribute to blood pressure elevations, other factors may be responsible for underreporting subjective stress and the higher pain tolerance in hypertensive subjects. One explanation for the underreporting by hypertensives may be a repressive/defensive coping style. In the next section we will discuss whether in literature evidence can be found for an association between repressive/defensive coping styles and hypertension.

**Blood pressure and defensive coping style**

Considerable conceptual confusion has been existing regarding the different defensive coping constructs, such as deception, defensiveness, repression, and emotional inhibition (Paulhus & Reid, 1991; Sackheim, 1988; Tomaka, Blascovich, & Kelsey, 1992). Nevertheless, according to Davies (1971), results from several studies have suggested that high blood pressure may indeed be related to emotional inhibition or related constructs. Also in a more recent review (Sommers-Flanagan & Greenberg, 1989), support was reported in favor of an association between hypertension and the use of psychological inhibiting mechanisms (i.e., denial and repression), both in patient samples and in samples of unaware hypertensives. For example, Sapira, Scheib, Moriarty, and Shapiro (1971) examined hospitalized patients with hypertension, watching two movies about doctor-patient interactions. In one film the doctor was rough and not interested in the patient (the bad doctor), in the other one the doctor was gentle and considerate (the good doctor). It appeared that the hypertensives tended to deny seeing any differences in behavior between the two doctors (which were clearly seen by the normotensive controls). Thus, hypertensive patients seemed to perceive noxious information less clearly. As Lacey and Lacey (1970) have suggested, cardiovascular pressor responses—which are stronger in hypertensives—may go along with rejection of or non-responsiveness to the external environment. It is tempting to speculate about whether this could concern a causal relationship and, if so, in what direction.

Tibblin and Lindström (1972) found that untreated hypertensives reported less physical and psychological symptoms compared with normotensive controls and treated hypertensives. Moreover, for most symptoms a gradient was found: the higher the blood pressure the lower the reported frequency of symptoms. These authors therefore concluded that hypertensives "are denying or suppressing their
feelings" (Tibblin & Lindström, 1972, p. 139).

In contrast with the studies discussed above, in several investigations blood pressure level was the dependent variable (see Table 15.1). However, the direction of the associations found was not different from those obtained in the former studies. For instance, in an epidemiological study in Michigan (Cottington, Brock, House, & Hawthorne, 1985), suppressed emotion was associated with higher blood pressure in both males and females undiagnosed and untreated for hypertension. Finally, several recent studies (King, Taylor, Albright, & Haskell, 1990; Warrenburg et al., 1989) have demonstrated that repressive individuals had higher resting systolic blood pressure levels and higher systolic blood pressure reactivity in response to a mental challenge than non-repressive individuals.
<table>
<thead>
<tr>
<th>Studies</th>
<th>N(^a)</th>
<th>Independent variables(^b)</th>
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<tr>
<td><strong>Blood pressure as independent variable</strong></td>
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<tr>
<td>Davis, 1971</td>
<td>Review</td>
<td>HTs vs. NTs</td>
<td>BP, self-report, interview</td>
<td>HTs: emotional inhibition ↑</td>
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<tr>
<td>Sapira et al., 1971</td>
<td>34 (m+f)</td>
<td>HT patients vs. NT patients</td>
<td>BP, interview</td>
<td>HTS, emotional denial ↑</td>
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<td>Tibblin &amp; Lindström, 1972</td>
<td>622 (m)</td>
<td>Untreated HTs vs. NTs</td>
<td>BP, a ten-iten scale</td>
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<td>Sommers-Flanagan &amp; Greenberg, 1989</td>
<td>Review</td>
<td>HTs vs. NTs</td>
<td>BP, self-report, interview</td>
<td>HTS: repression ↑</td>
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<tr>
<td><strong>Blood pressure as dependent variable</strong></td>
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<tr>
<td>Cottington et al., 1985</td>
<td>402 (m+f)</td>
<td>Emotional suppression</td>
<td>BP, a eight-item scale</td>
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<td>Jammer &amp; Schwartz, 1986</td>
<td>534 ( )</td>
<td>Repression</td>
<td>BP, MC-SDS, TMAS</td>
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<tr>
<td>Jorgensen &amp; Houston, 1986</td>
<td>122 (m+f)</td>
<td>Denial + FH +</td>
<td>BP, MMPI-DS</td>
<td>BP-reactivity ↑</td>
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<tr>
<td>King et al., 1990</td>
<td>120 (m+f)</td>
<td>Repression</td>
<td>BP, MC-SDS, TMAS</td>
<td>SBP + SBP-reactivity ↑</td>
</tr>
<tr>
<td>Warrenburg et al., 1989</td>
<td>45 (m)</td>
<td>Defensiveness</td>
<td>BP, MC-SDS</td>
<td>SBP + SBP-reactivity ↑</td>
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</table>
Results from the studies concerning the relationship between blood pressure and coping/reporting style reviewed here thus generally suggest that individuals with elevated blood pressure tend to minimize aversiveness, in particular concerning their negative emotions and experiences or, to put it differently, tend to be defensive. The issue of causality cannot be resolved from the cross-sectional studies reviewed here. However, apart from the question, whether the association is a causal one and, if so, what the direction of this causality might be, the importance of the association between blood pressure and defensiveness is that it may explain the observed diminished stressor report rates by an altered appraisal of threatening stimuli or by hiding negative information. To what extent the underreporting may be attributed to one or more of the defensive constructs mentioned in this review (repression, self-deception, denial, etc.) remains unclear, partly due to the definitional confusion. Therefore, elucidating the theoretical and statistical relationship between these constructs, in addition to directly examining the association of these constructs with self-reported stressor exposure, seems desirable in order to be able to construct experiments that could discriminate between the various possible hypotheses regarding the role of defensive coping in the underreporting tendency of hypertensives (Nykliček, Vingerhoets, & Van Heck, in press).\(^1\)

**Conclusions**

Rather than to provide an exhaustive review of the literature, the primary objective of this chapter is to search for possible psychological mechanisms (e.g., appraisal and coping styles) underlying discrepancies found in the literature concerning the relationship between blood pressure and stressor exposure. Studies concerning this relationship have been reviewed and possible explanations for the discrepancies found have been offered. Especially the results of studies based on

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1 Notes Table 15.1

a The number of subjects in the study, m= male, f= female, review= review article, based on several studies with unknown total number of subjects.

b HTs= hypertensives (systolic pressure $\geq 140$ mmHg and/or diastolic blood pressure $\geq 90$ mmHg), NTs= normotensives (systolic blood pressure $< 140$ mmHg and diastolic blood pressure $< 90$ mmHg), FH+= normotensives with a family history of hypertension.

c BP= blood pressure, MC-SDS= Marlowe Crowne Social Desirability Scale, MMPI-DS= Denial Scale of the Minnesota Multiphasic Personality Inventory, TMAS= Taylor Manifest Anxiety Scale.

d When groups were compared: scores of the first group (mentioned under 'Independent variables') compared to the second group (HTs= hypertensives, SBP= systolic blood pressure, DBP= diastolic blood pressure, BP= blood pressure [systolic and diastolic], HR= heart rate, ↑= higher.
self-reported stressor exposure have often been contradictory, partly because of differences in operationalizations of the concepts studied, partly because of the confounding effect of awareness of having hypertension and being treated for the disease. Therefore, it has been argued that these variables should always be accounted for in studies concerning the relationship between blood pressure and psychosocial variables. Nevertheless, overall, some striking tendencies in the results were observed.

A discrepancy has been found between the results of studies based on objectively established measures of stressor exposure and those of studies using more subjective measures. Whereas the former studies often showed a positive association between stressor exposure and blood pressure, the results of research based on self-reported psychosocial stressors with a low objectivity level tended to yield more often negative associations between reported stressors and blood pressure level. These negative associations have also been frequently demonstrated in studies on self-reported pain as a result of exposure to laboratory physical stressors. A possible explanation is that whereas objectively measured psychosocial stressors might contribute to blood pressure elevations, other factors related to hypertension may be responsible for the negative associations between blood pressure and self-reported stressor exposure and distress. For the possible role of defensive coping styles (e.g., repression) in the inverse associations described above, support has been obtained in recent literature.

The association of high blood pressure with antinociception has been frequently found to be mediated by the activation of the baroreceptors. It might be speculated that Central Nervous System (CNS) inhibition, brought about by baroreceptor activation and possibly opioid mediated, is linked to defensive coping styles. Indirect support for this notion has been offered by studies, in which repression has been found to be related to antinociception (e.g., Jamner & Schwartz, 1986). The baroreceptor stimulation mediated antinociception has been suggested to play a role in the development of hypertension by a conditioning mechanism. Blood pressure elevation in potentially stressful situations may be learned, because it results in baroreceptor activity mediated CNS-inhibition and subsequently an altered appraisal of the stressor (which becomes less aversive). In this way, frequent exposure to stressors may potentiate the development of sustained blood pressure elevation in individuals sensitive to the baroreceptor mediated antinociception (Dworkin et al., 1979; Elbert et al., 1988; Randich & Maixner, 1984). It would be of interest to examine the potential relationship between this mechanism and defensiveness.

In future research it would be desirable to perform research in which blood pressure level is studied in relation to: (a) simultaneously established objective as well as self-reported stressor exposure, appraisal of and coping with the stressor, and (b) simultaneously obtained measures of different defensive coping styles.
Furthermore, studies are necessary in which self-reported stressor exposure is directly related to appraisal, defensive coping styles, pain sensitivity, baroreceptor activity, and CNS-inhibition. Preferably subjects who have not yet elevated blood pressure, but who are at risk for hypertension-like persons having a family history of hypertension should be included in future investigations. Needless to say that particularly in all such cross-sectional research potential confounders, like awareness of having elevated blood pressure, should be controlled for. Finally, besides cross-sectional studies, prospective studies should receive much attention in order to be able to obtain more insight into causal associations.

References


