A Quantitative Review of Prospective Evidence Linking Psychological Factors With Hypertension Development

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Objective: To quantitatively review and critique evidence from prospective cohort studies (greater than 1 year follow-up) assessing associations between psychological factors (eg, anxiety, anger, depression) and hypertension development. Methods: Keyword searches through the MEDLINE and Psychlit (1970 to present) databases produced in excess of 500 studies, of which only 10 met criteria as a prospective cohort design with a follow-up interval exceeding 1 year. Five additional longitudinal studies were found by tracing references from the above papers. Results: The sample-weighted aggregate effect sizes for hypertension risk were small for continuously measured psychological factors (r = .08), and effect sizes were similar for separate categories of psychological variables (r values = .07–.09). Effect sizes were not associated with reported methodological or sample characteristics, including sample size, racial and sex composition, study duration, or age. Conclusions: Overall, there is moderate support for psychological factors as predictors of hypertension development, with the strongest support for anger, anxiety, and depression variables. Pooled effects for these factors are of sufficient magnitude to suggest potential clinical as well as statistical relevance. Findings regarding potential mechanisms are scarce and the psychometric properties of the scales used to measure psychological variables are often unestablished. Indications for future research are discussed. Key words: hypertension, blood pressure, psychological factors, prospective.

INTRODUCTION

The belief that psychological factors affect long-term blood pressure regulation dates back at least to the early 20th century (1). Past and present theories regarding mechanisms for this potential relationship (Figure 1) center on a) cardiovascular reactivity to stress, in which a recurrent pattern of exaggerated sympathetic nervous system activity is proposed to up-regulate basal blood pressure levels over time; b) neurohormonal models suggesting that psychological characteristics may predispose hypertension development by altering central nervous system control of baroreceptor function, opioid activity, and neurotransmitter levels; and c) high-risk behavioral dispositions associated with psychological characteristics, including poor diet, obesity, exercise habits, smoking, and alcohol abuse, among others (2–6). Although considerable evidence has accrued in favor of these theories, much of the published support has been fairly criticized on methodological grounds (see 7–10 for more thorough reviews of these issues).

The relative absence of prospective data has long been perceived as a critical flaw in the argument that psychological factors play a role in the development of hypertension (2, 9, 11). Although hundreds of cross-sectional and case-control studies have reported that high blood pressure and other CAD risk factors are associated with enduring trait-like psychological characteristics such as hostility, anger expression, defensiveness, and anxiety (eg, 12–16), the findings of these studies are in many cases threatened by an inability to control for competing explanations. For example, the possibility that alternative mechanisms (genetic or environmental) could dispose both psychological characteristics and hypertension risk, that blood pressure increases may precede (rather than follow) hypothesized psychological risk factors, or that psychological factors may similarly serve as a noncausal marker for disease severity are among the most frequently cited shortcomings (2, 5). Prospective studies of psychological effects on blood pressure can offer a means of circumventing certain temporal confounds, but they require sustained funding and follow-up over a period of at least several years. As a result, one of the methodologies best suited to address the impact of psychological factors on hypertension development has contributed less than 1% of the empirical work in this area.

Until recently, the modest size of the prospective literature has not supported a selective review. Over the past decade alone, however, more than 10 longitudinal investigations have released evidence evaluating the effects on psychological factors on hypertension development. Although many of the existing studies report positive findings (eg, 17–25), this conclusion is not universal (eg, 31). The methodological protocols also vary tremendously with regard to the length of follow-up, sample...
size, gender and ethnic composition, psychological characteristics addressed, definition of hypertension (eg, >140/90 vs 165/90 mm Hg), use of clinic-based vs ambulatory blood pressure measurement methods, validity and reliability of the psychological measures, appropriate control for covariates (ie, multivariate vs univariate tests), and estimated effect sizes. Because several studies (eg, 22, 25) showed that demographic variables such as age, sex, and race affected the pattern of psychological factor-hypertension relationships, any attempt to aggregate this literature should likewise take these factors into account.

This article describes the first major quantitative review of psychological predictors of blood pressure in which prospective relationships served as the exclusive focus. Using a total of 15 empirical studies gathered from a search of MEDLINE and PSYCHINFO databases and by reviewing the reference lists from the computer-derived articles, we undertook a review assessing the following issues:

- What is the estimated magnitude of psychological associations with hypertension development?
- What is the evidence for specific psychological factors (eg, anger, anxiety, depression)?
- Is there between-study variability in reported relationships? If so, can differences in methodological or sample characteristics such as sex and racial composition, age, study duration, and sample size account for between-study variability in the reported effect sizes?
- Given the moderate size of the prospective literature, how stable (ie, robust to future negative findings) is the evidence for psychological factors as a predictor of incident hypertension?

METHODS

Selection of Studies

In accordance with recommendations by Rosenthal and Rosnow (33), studies were gathered using two strategies. Initially, we completed a computer-assisted search of MEDLINE and PSYCHINFO databases using keyword sets. A series of keyword sets were used, interchanging individual keywords from three categories: 1) time, including prospective and longitudinal; 2) blood pressure, including hypertension, blood pressure, and ABP; and 3) psychological factors, including psychological, hostility, anxiety, depression, defensiveness, job strain, stress, and anger. These searches resulted in several hundred studies, among which an evaluation of abstracts identified 10 reporting findings from a prospective cohort design. The second strategy consisted of a review of the references cited in the above articles. The reference list from each article was reviewed to identify additional sources reporting longitudinal relationships. A total of 15 works were identified using these methods. In all studies, participants were free of a diagnosis of and/or treatment for hypertension at the time of enrollment. All work reported longitudinal relationships exceeding 1 year of follow-up, in which psychological factors served as an independent variable and hypertension development as a dependent variable. Studies varied somewhat in the adjustment for cardiovascular disease covariates, and we included degree of adjustment as a separate variable.

Study Variables

Each article was coded for the following characteristics: sample size, year of publication, sample age, male/female ratio, minority/white ratio, covariate adjustment (1, unadjusted only; 2, age adjusted only; 3, adjusted for multiple risk factors), length of follow-up (years), method of blood pressure measurement (ambulatory vs clinic), criteria for hypertension (eg, >140/90 vs >160/95 mm Hg), annual hypertension incidence rates, and psychological predictor(s).

Study Quality

Although all studies used prospective cohort designs, measurement quality varied widely. We used three of the above criteria to assess the possible effects of measurement quality: 1) degree of covariate adjustment (see above); 2) use of ambulatory vs clinic-based measures of blood pressure; and 3) conservative (>165/95 mm Hg) vs more liberal (>140/90) definitions of hypertension. In addition, although we did not include a formal code due to insufficient numbers, we also performed separate analyses for studies that used psychological measures with established reliability to assess the possible impact of this factor.
Data Analyses

We followed data reduction and analytic procedures discussed by Rosenthal and Rosnow (33) in quantifying psychological effects. The majority of studies reported longitudinal associations between blood pressure levels and several psychological variables. To equalize the impact of each study in computing overall psychological effects, we aggregated (ie, arithmetic mean) effects within studies reporting multiple outcomes to produce a single effect indicator for each study. We calculated effects with and without weighting for sample size due to the large sample-size distribution range reported in these studies. Based on data reported in each paper, we calculated r coefficient values and 95% confidence intervals using published methods (33) as the primary effect size indicator. In calculating the overall mean effect-size estimate, we used a more conservative random-effects model for 95% CI calculation (random-effects estimates create somewhat wider confidence intervals but permit greater generalization). We calculated confidence intervals for individual studies as standard fixed effects models. In cases where the study description indicated only a lack of statistical prediction without data available for an effect-size calculation, we assigned an r value of .00 to the predictor (33). This method is widely used but is admittedly conservative for the construction of aggregated effect sizes. For this reason, reported effect-size values are probably (slight) underestimates of effect sizes calculated under the ideal circumstance of having precise statistical tests or p values reported for all predictors.

After computing overall effect sizes, we divided studies into several outcomes according to category of psychological measure. Anger, anxiety, depression, and other (including single studies using defensiveiness, social networks, personality, and psychopathology as psychological predictors that were of insufficient number to create additional categories) served as the categories for our classification system. One study of hopelessness (20) was classified with depression outcomes for the sake of parsimony. A number of studies reported anger effects, with measures ranging from inhibited power motivation (26) to the Spielberger Anger Expression Scale (19). All studies describing anger-in and suppressed anger or suppressed hostility were categorized as anger-in effects. Anger, anger-out, type A behavior pattern, and hostility expression measures were categorized as anger-out responding. Anger effects were assessed separately as well as collapsed across these categories.

Finally, because a majority of the prospective findings reported psychological effects based on categorized psychological scores (eg, median split, tertiles, etc.) using risk ratios as the preferred effect-size indicator, we further constructed a chart summarizing these findings as an alternative and supplementary means of determining statistical and clinical significance. In addition, listed risk-ratio values from these articles have been adjusted for age and other biological risk factors and are, therefore, a source of information that cannot be duplicated by extracting r values because information needed to adjust the r value for biological risk variables is not available in the published articles.

Statistical Power and Tolerance for Future Negative Findings

Due to the well-known underreporting of null effects (34, 35), we computed fail-safe n values for the overall and categorized psychological effects to estimate the statistical tolerance for existing “file drawer” or future negative findings (33). The mean Z (32, 33) for each study was estimated using reported p values, with Z = 0.00 used for studies reporting unspecified nonsignificant relationships and Z = 1.65/1.96 for effects reported only as meeting p < .05/.025 criteria.

Effects of Study-Quality Analyses

To assess the potential effects of sample size, study duration, proportion of male and African American participants, degree of covariate adjustment, sample age, and the definition of hypertension on the reported effect sizes, we performed simple correlations between effect sizes and the study-quality variables and regression analyses in which main effect and interactions between the quality variables were tested. All tests were performed using study-quality terms as fixed effects. We also performed exploratory tests to assess potential interactions between study-quality variables and psychological factors used as predictor variables in these studies. Because of the limited sample size (N = 15 articles), the power of these tests to detect small to moderate effects was limited. Furthermore, due to the volume of tests that this exercise generated and the weak evidence for relationships we observed between measured quality variables and psychological factor-hypertension relationships, these results are briefly summarized in the text of the Results section.

Separate quantitative analyses of psychological effects on hypertension among African American and women groups could not be justified based on the small number of studies including sufficient participation from these populations. Effects observed in these populations are summarized in the text.

RESULTS

Table 1 illustrates methodological features of each of the 15 prospective studies. There were a total of 26 longitudinal associations between psychological measures and hypertension development. Sample sizes ranged from 78 to approximately 4650, and most (but not all) studies described effects based on male- and white-dominated cohorts. In a small number of cases, the samples comprising separate articles were not independent. For example, Everson and colleagues (19, 20) report positive associations between anger expression and hopelessness with incident hypertension in separate articles, but each result was based on the same sample of Finnish men. We did not include an additional article reporting findings from the NHANES cohort (36) because the results described relationships between “negative affect” (computed as a sum of anxiety and depression scores) that were separately reported in a previous manuscript (22). With a couple of exceptions (24, 28), studies relied on population-based or college student samples rather than medical patients or groups known to be at elevated hypertension risk.

The mean study duration was 8.4 years, with a range of 2.5 to 21 years, and a mode of just 3 years. Guidelines for defining hypertension varied widely. Six studies (17, 21, 24, 26, 30, 31) used 140/90 mm Hg as the diagnostic criterion, eight (18–20, 22, 23, 25, 27, 28) required blood pressure to exceed 160 systolic or 95 diastolic, and one (29) based hypertension status solely on the participant’s indication of a previous diagnosis of high blood pressure from their physician. Most if not all studies also assessed and included a
participant as hypertensive if they were receiving treatment for high blood pressure. Only one study based hypertension definitions on data from ambulatory monitoring (21, daytime measures only); all others used data collected from readings collected in a physician office setting. Last, the number of office blood pressure measures collected ranged from two to four but were collected and tabulated in a variety of ways, including averaging all scores (eg, 20, 21), using only the final reading (18), and averaging single readings taken from each arm (30), among numerous other methods. We observed no uniform standard in this regard.

Anger variables were by far the most common source of investigation (13/26 reported associations), followed by anxiety (5), depression (4), and others (defensiveness, neuroticism, psychopathology, social networks with one reported association each). Twelve of the 15 studies also described effects that were adjusted for multiple risk factors (18, 26, and 28 reported unadjusted psychological results only). Fourteen of the 15 studies reported at least one positive effect (93%). However, because studies often included multiple psychological measures, the actual ratio of positive to negative findings was less striking (20/26, or 78% positive). Estimated annual hypertension incident rates were modest for most studies, and ranged from less than 1% to 10%.

Quantitative Effect Summary

Table 2 provides effect-size values and respective 95% confidence intervals for psychological predictors of hypertension by study for primary endpoints reported in the prospective studies. Pearson r values ranged from .00 to .38, with a mean sample-weighted effect size of .08 (95% CI, .04–.13). Broken down by category of psychological variables, sample-weighted effect sizes for anger (r = .09, 95% CI, .06–.11) and depression (r = .09, 95% CI, .07–.11) each differed significantly from zero (all p values < .001). The overall test of variability among the observed effect sizes was not significant at the .05 level (F = 2.4, p > .10). Comparisons of effect sizes by category of psychological variable also failed to suggest significant differences (F = 0.61, p > .6), indicating that observed effect sizes within the categories of anger, anxiety,
effects of psychological variables on hypertension development. A number of studies, including those by Carpenter et al. (6), have indicated a 8% increase in prospective hypertension risk among adults high on one or more of the psychological variables reviewed here in comparison with a low-scoring group. Given the prevalence, clinical repercussions, and medical costs associated with hypertension, a fac-

depression, and other were similar. Finally, observed effect sizes showed few statistical relationships with design aspects, including year of publication, hypertension incidence rate, control for biological covariates, proportion of male or African participants, study duration, or mean age of the sample (r values $-0.17$ to $0.15$, $p$ values $>0.05$). The single reliable association was a negative relationship between effect size and sample size ($r = -0.57$, $p < 0.01$). Because smaller studies require larger effects to obtain statistical significance—and probably to generate the interest to be published—the latter result may be an artifact of the publication process itself.

Figure 2 illustrates covariate-adjusted results (risk-ratio point estimates and 95% confidence intervals) from studies reporting psychological variable-hypertension development associations based on categorical standing on the psychological instruments. Figure 2 values represent comparisons between highest and lowest scoring categories of participants. Six studies assessed psychological effects exclusively as continuous variables and could not be included in Figure 2. Risk-ratio point estimates for the latter effects ranged from 1.6 to 7.5, with most exceeding 2.0. Although the apparent magnitude of effect appears larger based solely on the results of the categorical analyses, this result is not necessarily surprising because the effects reflect comparisons of extreme groups. Relationships with anger variables accounted for 3 of the 10 significant relationships, followed by depression (3, including one measure of hopelessness), anxiety (2), social network size (1), and defensiveness (1). The confidence intervals associated with the risk-ratio estimates, not surprisingly, show a pattern similar to those for the associated $r$ values in Table 2. Because the reported risk-ratio estimates shown in Figure 2 are adjusted for age and other covariates—unlike the $r$ values we extracted for each study—they may be a more stable effect-size indicator for these studies.

Data summaries for combined psychological variables and by categories of psychological variables indicated statistical significance irrespective of continuous or categorized measurement strategies. Because the magnitude of overall effect ($r = 0.08$, see above) is relatively small by traditional behavioral science standards, however, one may be tempted to downplay the clinical importance of the relationships. As described extensively by Rosenthal and colleagues (32, 33), such an interpretation could be seriously in error. The use of the $r$ statistic as an effect-size indicator carries the advantage of an easy conversion to binomial effect-size display (BESD) language. From a BESD model of effects (32), an $r$ value of .08 would be associated with an 8% increase in prospective hypertension risk among adults high on one or more of the psychological variables reviewed here in comparison with a low-scoring group. Given the prevalence, clinical repercussions, and medical costs associated with hypertension, a fac-

<table>
<thead>
<tr>
<th>Study</th>
<th>Predictor</th>
<th>$r$ Value</th>
<th>CI</th>
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<tbody>
<tr>
<td>Davidson et al. (27)</td>
<td>Depression</td>
<td>0.09</td>
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</tr>
<tr>
<td>Ewerson et al. (19)</td>
<td>Anger-in</td>
<td>0.19</td>
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<tr>
<td>Ewerson et al. (20)</td>
<td>Anger-out</td>
<td>0.25</td>
<td>0.17–33</td>
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<td>Anger control</td>
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<td>0.01–15</td>
</tr>
<tr>
<td>Ewerson et al. (20)</td>
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<td>0.32</td>
<td>0.25–39</td>
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<td>Ewerson et al. (20)</td>
<td>Depression</td>
<td>0.06</td>
<td>0.02–14</td>
</tr>
<tr>
<td>Jenkins (28)</td>
<td>Anger</td>
<td>0.10</td>
<td>0.03–23</td>
</tr>
<tr>
<td>Jonas et al. (22)</td>
<td>Anxiety</td>
<td>0.07</td>
<td>0.03–11</td>
</tr>
<tr>
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<td>Anger-in</td>
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<td>0.01–07</td>
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<tr>
<td>Kahn et al. (18)</td>
<td>Social network</td>
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<td>-0.02–0.08</td>
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<td>Markowitz et al. (25)</td>
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<td>-0.09–0.09</td>
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<tr>
<td>Markowitz et al. (17)</td>
<td>Anger-out</td>
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<td>-0.09–0.09</td>
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<td>McClelland (26)</td>
<td>Anger-in</td>
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<td>-0.09–0.17</td>
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<td>Anger</td>
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<td>0.20–54</td>
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<td>Rutledge and Linden (21)</td>
<td>Defensiveness</td>
<td>0.24</td>
<td>0.07–40</td>
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<tr>
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<td>Anger-in</td>
<td>0.10</td>
<td>0.01–18</td>
</tr>
<tr>
<td>Siegler et al. (29)</td>
<td>Hostility</td>
<td>0.00</td>
<td>-0.09–0.09</td>
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<tr>
<td>Spiro et al. (30)</td>
<td>Neuroticism</td>
<td>0.13</td>
<td>0.06–20</td>
</tr>
<tr>
<td>Valliant and Gerber (31)</td>
<td>Psychopathology</td>
<td>0.00</td>
<td>-0.04–24</td>
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</table>
tor disposing a risk increase of this magnitude could be considered highly important to clinical health experts.

Effects Among African American and Women Participants

As indicated, white men frequently made up the majority or even entirety of the study samples reported in this review. Separate effects among African American samples were, however, reported in four studies (17, 22, 23, 27) and effects among women (or gender-interaction effects) in four studies (17, 22, 25, 27). All four studies assessing effects among African Americans, with a combined sample of approximately 2100, reported increased temporal hypertension risk among participants with elevated psychological distress, including factors such as depression, anxiety, and suppressed anger. Notably, only the CARDIA cohort described by Davidson and colleagues (27) reported effects with an African American sample size impressive by epidemiological standards (N = 11538). The next largest cohort (13), consisting of black African university students, numbered only 300.

Effects reported among women were less consistent, with limited evidence for gender differences (ie, psychological variables were significant predictors of hypertension development among both women and men) in a pair of large cohort studies (22, 27), no effects for anxiety or anger among women in another study (25) that did observe effects among the subgroup of men, and finally, positive associations between anxiety symptoms at baseline and hypertension development in a cohort of black and white women (17). Participation by women in these studies was higher in comparison with African American or black populations, however, with a combined representation exceeding 4000 cases and several cohorts (22, 25, 27) with women subgroups ranging in size from 500 to more than 1500.

Effects of Measurement Quality

Effect sizes were generally robust to differences on coded measurement quality variables. Adjustment for multiple covariates actually strengthened associations in most studies (eg, 19–22), and hypertension cutoff criteria showed no relationship with reported effects. One study (27) described depression effects on incident hypertension using conservative (ie, >165/90 mm Hg) and liberal (ie, >140/90 mm Hg) diagnostic criteria, showing positive associations under both definitions. We also observed a pattern in recent large-scale studies for more consistent effects to be present based on validated psychological measures such as the Spielberger anger scales (19), the General Well-Being Scale (22), and the Center for Epidemiological Studies Depression Scale (27). Because many studies used scales with unknown reliability and validity properties, however, this potentially important relationship is impossible to quantify.

Fail-Safe N Values

Fail-safe N values were estimated by deriving a single Z value (and respective p value) corresponding to the size of the reported association for each study. To maintain statistical independence, only a single Z value—created by averaging across effects within studies reporting multiple associations—for each study was used (32, 33).

The mean Z value for all studies reporting relationships with hypertension development was 1.3. Broken down across categories (anger, depression, anxiety, and other), corresponding mean Z values were 1.1, 2.1, 2.0, and 1.3, respectively. As shown in Table 3, the number of studies averaging null effects (ie, Z = 0.0) required to reduce these results to nonsignificance (p < .05) is 125 (for all psychological effects), 27 (anger variables), 33 (anxiety variables), 11 (depression variables), and 7 (other variables).

<table>
<thead>
<tr>
<th>Psychological Measurea,b</th>
<th>Pooled</th>
<th>Anger</th>
<th>Anxiety</th>
<th>Depression</th>
<th>Other</th>
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<tbody>
<tr>
<td>Number of reported findings (k)</td>
<td>15</td>
<td>9</td>
<td>5</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>Mean Z</td>
<td>1.3</td>
<td>1.1</td>
<td>2.02</td>
<td>2.05</td>
<td>1.3</td>
</tr>
<tr>
<td>Fail safe N</td>
<td>125</td>
<td>27</td>
<td>33</td>
<td>11</td>
<td>7</td>
</tr>
</tbody>
</table>

a Values in the table are based on the number of projected studies with an effect size of exactly 0 (or an odds ratio of 1.0) required to lower the mean Z to nonsignificance.
b Fail-safe values give an indication of the strength of a set of findings on the grounds of statistical significance and do not in themselves suggest a potential or a lack of potential clinical relevance.
SUMMARY

To summarize, a sizable body of published prospective findings provides collective, although far from unanimous, support for proposed relationships between psychological factors and hypertension development. The effect sizes reported across 15 studies—although showing some variability in magnitude—could not be explained on the basis of the methodological characteristics examined here. The interpretation of clinical significance is more difficult to assess. Our calculations suggest a hypertension risk difference of approximately 8% among high psychological distress vs low psychological distress groups. When aggregated across studies, the effect sizes for all four measured categories of psychological variables were statistically significant and appear robust to any reasonable estimate of unpublished null findings. Anger, anxiety, and depression variables continue to be the most common focus for behavioral medicine investigators, and each area is supported by a number of positive longitudinal relationships with hypertension development.

DISCUSSION

Using standardized methods for quantitative literature reviews (32, 33), this article presented the first empirical review of the psychological-hypertension literature that assessed only prospective cohort studies. Fifteen articles described results varying widely in sample size, duration of follow-up, and ethnic and gender composition, among other differences. Estimations of effect also showed some variability in magnitude, although the aggregated results offered robust support for relationships between psychological factors and hypertension development.

A wide range of psychological tools was used in these respective studies, many containing few items and possessing little if any independent validation. This was especially true for measures of anger characteristics, for which more than a dozen separate instruments were employed. Despite the consistent pattern of effect observed, this represents a serious flaw in the literature. Psychological scales, in some instances, were as brief as two items and often were backed by no independent psychometric data. Some of the most recent publications in this area, however, have used more established measures (eg, the Speilberger Anger Expression Scale (19) and General Well-Being Schedule (22)) and have shown some of the strongest predictive associations. The latter trend must be the norm of future research if knowledge in this field is to advance.

The importance of including psychological scales with proven reliability and validity cannot be overemphasized in the investigation of possible hypertension effects. The frequent reliance on psychological tools chosen more for convenience than demonstrated merit may be an important factor in understanding many of the inconsistent results observed across studies.

We noted several additional conclusions worthy of recognition. First, the meta-analytic calculations indicated reliable support for psychological effects on hypertension not only when combined across all studies but also for a number of relatively distinct areas of research. Anger (including measures of anger-in, anger-out, and hostility), anxiety, and depression, are each supported by effects demonstrated in multiple studies. Fail-safe N values, a measure of tolerance to unpublished null findings, reinforced this finding. Although it is conceivable that a body of prospective data exists showing no relationship between psychological factors and hypertension development, it is unlikely that this number exceeds the fail-safe N values of 50 to more than 100 studies necessary to unbalance the effects of anxiety, depression, anger, or overall psychological effect drawn from published data. Tolerance values for less-studied factors such as defensiveness and social networks are more modest but nevertheless appear robust to reasonable estimates of file-drawer papers.

The interpretation of clinical significance remains a critical and as yet unanswered component of this literature. A number of effect-size indicators—including r values, odds and risk ratios, and risk differences, among others—can be used to describe relationships with dichotomous outcome criteria such as hypertension development, but no measure of effect size by itself can determine importance in the public health domain. We reported both r value, due to their ready conversion to BESD language, and covariate-adjusted risk ratios for a subset of studies as a means of assessing the size of the psychological effects in real-world terms. Although the aggregated r values were small by conventional psychological research standards, the interpretation of these values as estimates of risk differences (32, 33) suggests that high standing on anger, anxiety, and depression scales is linked in these studies to an appreciable increase in prospective risk of hypertension development, a level of risk that compares favorably with better established predictors of hypertension such as obesity and physical inactivity (37).
ISSUES FOR FUTURE RESEARCH

Much like clinical significance, the argument for biological plausibility remains an important but as yet unattained standard for interpreting psychological effects on high blood pressure risk. The argument for psychological factors as potential causes of hypertension is that these factors are stable, dispositional variables that may adversely affect behavior and biological functioning over long periods of time. As seen earlier in Figure 1, a variety of biological pathways has been proposed, including chronic sympathetic nervous system activation, catecholamine release, serotonergic disregulation, and endothelial dysfunction (2, 6), as well as equally relevant behavior factors such as obesity and inactivity. In much of the existing work to date, the objective has been to demonstrate that psychological factors could impact hypertension risk independent of known risk factors. Although this approach offers valuable information, future research must go further by actively proposing and testing mediational relationships that will better allow us to assess potential mechanisms in these relationships.

Nearly all studies to date derived their estimates of psychological effects on hypertension from a single point estimate of psychological functioning. Although there is evidence to indicate that many personality characteristics are relatively stable over long intervals, other psychological characteristics such as depression are known to fluctuate even among individuals with diagnosed mood disorders (8). The inclusion of multiple samplings adds yet another layer of difficulty to prospective studies, but the probable benefits of improved reliability and a better understanding of the temporal relationship between psychological factors with blood pressure may be important enough to motivate us to overcome this obstacle. The use of a single measure or relatively small number of samples not only fails to demonstrate the temporal stability of the psychological measures but may also affect the quality of the definitions of hypertension used in many existing studies. For example, the probability of white coat hypertension cases is quite high in many of the studies summarized in this review due to an absence of baseline blood pressure measures or a criterion of hypertension based on a small number of clinic blood pressure samples. A convincing demonstration of the relationship between psychological factors and hypertension development in prospective designs will only result from studies that not only use unbiased sampling methods but also reliable measures of both the predictor and outcome variables. The use of ambulatory monitoring may be the most effective means of dealing with white coat hypertension risk, but to date, only one, comparatively small, prospective study (29) has reported results based on ambulatory blood pressure measures, and none have used 24-hour data.

The question of differences in psychological effects based on gender and ethnicity remains unanswered as well. Combined results shown here failed to show moderator effects; however, because only a handful of studies included sufficiently sized samples of women and African American groups, our analyses were poorly equipped to detect such differences. Notably, four of the prospective studies reviewed were able to compare black and white samples (17, 22, 23, 27), with results from each suggesting stronger effects among black or African American participants. Given these findings, the inclusion of African American groups in future cohort studies should probably be the norm rather than the exception.

Finally, intervention trials, in which participants are selected on the basis of high standing on one or more psychological characteristics, represent an additional avenue for possible future research. Empirical findings suggesting that a reduction in psychological distress was associated with a decreased prospective risk of hypertension would strengthen the argument for a relationship between these factors. Even within existing databases, explorations of changes in psychological standing over time in relation to blood pressure could offer indirect support on this issue. In some ways, the proposed relationship between psychological factors and hypertension parallels recent findings in the depression and cardiovascular disease field, in which a series of positive prospective findings generated support for a pair of large-scale intervention trials (38, 39).

In summary, the results of this review provide additional statistical support for the proposed relationship between psychological factors and an increased risk of future hypertension development. Mechanisms explaining this potential relationship remain speculative and should continue to be a focus of research among behavioral medicine investigators. The status of psychological factors as a clinically important risk factor for high blood pressure development appears promising, but additional research—potentially including intervention trials—will be necessary to further clarify this issue.

REFERENCES


