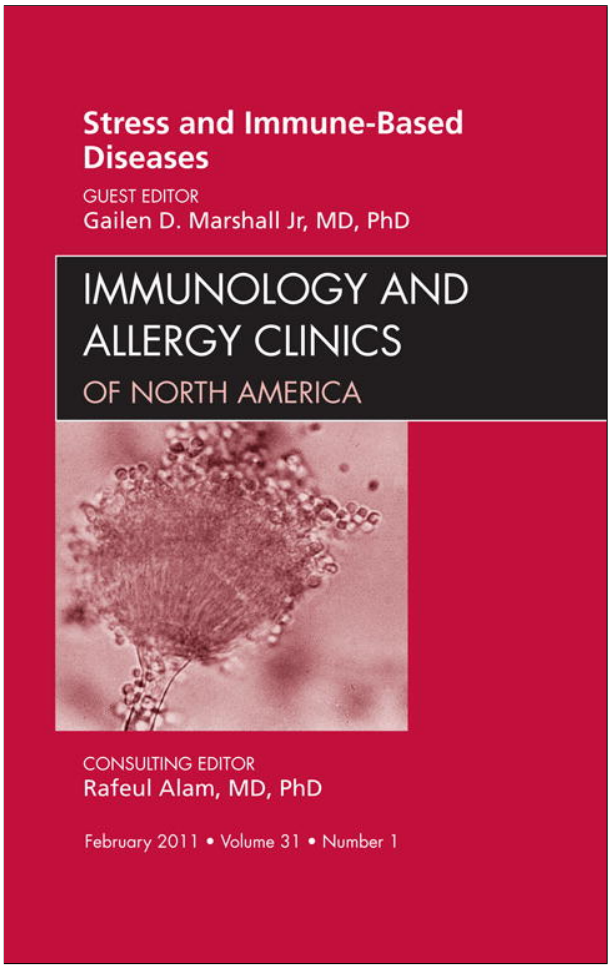

Clinical Potentials for Measuring Stress in Youth with Asthma

Hannah M.C. Schreier, MA*, Gregory E. Miller, PhD, Edith Chen, PhD

KEYWORDS

• Psychological stress • Asthma • Measurement

STRESS AND ASTHMA

It has long been recognized by clinicians and researchers that asthma can be affected by numerous triggers in the physical environment. Among the best understood contributors to asthma are environmental pollutants,[1] such as exposure to traffic-related air pollution[2] and indoor exposure to a variety of allergens[3] and environmental tobacco smoke.[4,5] Similarly, viral infections of the upper and lower respiratory tracts have been linked to asthmatic symptoms.[6]

More recently, increasing attention has focused on the contribution of potential triggers from the social environment, such as stressors.[7] Psychological stress has been increasingly implicated in pediatric asthma[8] and linked to many clinical asthma outcomes, including physician visits and hospitalizations.[9] Several studies provide intriguing evidence of the potential influence that psychosocial stressors can have on asthma outcomes. Several case studies suggest the onset and worsening of asthma symptoms among youth shortly after they themselves or people close to them have experienced negative life events.[10] These negative life events included being the victim of acts of violence or witnessing violent acts, as well as witnessing severe conflict among parents; in all cases, youth experienced significant, acute episodes of asthma. Also of interest is the observation that in some cases the fluctuations in asthma exacerbations changed hand in hand with the presence or absence of psychosocial stressors in the environment, for example the known presence of one's assailant in the neighborhood.

Additional evidence comes from a prospective, longitudinal study which followed 6- to 13-year-old children with asthma for 18 months and involved repeated assessments of life stress through interviews and the collection of daily diary and peak flow

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Department of Psychology, University of British Columbia, 2136 West Mall, Vancouver, BC V6T 1Z4, Canada
* Corresponding author.
E-mail address: hannahs@psych.ubc.ca

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information.[11] In this study, youth were significantly more likely to experience new asthma attacks in the weeks following negative life events, such as the death of a close person. These effects were even more pronounced among youth whom interviews revealed to experience chronic stress in other areas of their lives, for example being bullied at school or coming from a conflictual home environment.

Hence, although several psychological factors are believed to be related to pediatric asthma outcomes,[12] the influence of psychological stress has been of particular interest, especially because it may exacerbate other psychological problems, including anxiety and depression. One way in which psychological stress may exert its effects is by moderating and potentiating the effects of physical environmental triggers, making individuals more vulnerable to these triggers.

There are numerous ways of measuring stress in people's lives. Researchers use a variety of measures ranging from the administration of self-report questionnaires to the assessment of life events through in-depth interviews. This article differentiates between various conceptualizations of stress and the measurement approaches that are associated with them; provides an overview of the most widely used methods for assessing stress among patients with asthma and discusses their strengths and weaknesses; and reviews evidence for how well different measures of stress can be linked to clinical outcomes and the biologic processes that underlie them.

WHAT IS STRESS?

Stress has been conceptualized in many different ways.[13] Among the most common views of stress are the environmental and the subjective perspectives, which also map onto the different measurement strategies used in today's research. The environmental stress perspective focuses on external demands that individuals encounter as part of their life experience.[14] These demands come in the form of stressors that the individual has to manage, and the assumption is that they will have a fairly uniform effect on people's health,[15] determined by how much change or adaptation is required.

In contrast, there has been an alternative conceptualization of stress that focuses on the interaction of the person and the demands being faced.[16] This view focuses on how people interpret or appraise a stressor, in terms of whether it poses a threat to their goals, and whether they are able to cope with it effectively. The assumption here is that not all events are perceived in the same way by all people, and that only those that are appraised as stressful (ie, threatening and unmanageable) will ultimately prove to be detrimental to health.[17] Thus, although one person may experience a transition to a new work environment as a considerable stressor, it may be unmemorable to another person. This view highlights the importance of assessing subjective perceptions of events and people's beliefs as to whether they think they will be able to successfully cope with the stressor at hand.

The currently used measurement approaches tend to reflect one tradition or the other. Life-event checklists that assess and sum the number of life events a person has experienced within a certain time frame follow from an environmental stress perspective. Other approaches that are more focused on investigating a person's experience of life events, for example by asking people to complete questionnaires about what kind of effect an event has had on their life, are closer to focusing on subjective stress appraisals.

Aside from differentiating the objective occurrence of events from the subjective experience of an event, researchers also make distinctions regarding the nature of the event itself. For example, some stressors are distinct and time limited (acute

stressors), whereas others are long lasting and without definitive endpoints[18] (chronic stress). Acute stressors can be further divided into major life events (eg, being in a car accident) and smaller acute stressors akin to daily hassles (eg, dealing with traffic when commuting to work).[19] There are also stressors that blur the distinction between acute and chronic (eg, a brief event such as a natural disaster, which triggers a string of other challenges such as repairing one's home, finding the money to do so, and so forth). Thus, stressors will vary in both intensity and duration, and it is important to consider these dimensions in measuring stress, because they may have different effects on asthma outcomes.

This article first reviews the evidence for the influence of stress on clinical asthma outcomes and the biologic mechanisms that are believed to mediate these relationships, before addressing the different ways of assessing stress.

EVIDENCE FOR A LINK BETWEEN STRESS AND ASTHMA

Research to date, implementing different methods of stress measurement, suggests a clear relationship between stress and both the onset[20] and course of asthma.[8,21] For example, using a life-event checklist the onset of asthma has been associated with retrospective recall of greater life stressors in the years preceding and concurrent to asthma diagnosis among a sample of university students.[22] Interview-based assessments of adolescents' stress perceptions, including acute and chronic stressors as well as subjective stress interpretations, were found to be associated with patterns of immune response known to be involved in the worsening of asthma, including greater in vitro mitogen-stimulated production of the cytokines interleukin 5 (IL-5) and interferon-γ (IFN-γ).[23] Youth from more stable home environments (ie, youth of parents who reported less parenting stress on a self-report questionnaire) seem to be exposed to more routines at home, which in turn is associated with improved medication adherence.[24]

Other approaches, including experimental manipulations of stress, further underscore the influence of psychosocial stressors on airway functioning. In one study, a group of older children and adolescents asked to relate an embarrassing story to a tape recorder in the presence of an adult experimenter subsequently showed evidence of greater airway resistance.[25] In a small sample of adults with asthma, everyday stressors assessed across a 10-day period using preprogrammed watches, were linked to participants' peak expiratory flow rate (PEFR) as well as asthma symptoms.[26] Hence, connections between psychosocial stress and clinical asthma outcomes have been shown using different research methodologies and study designs.

BIOLOGIC MECHANISMS LINKING STRESS AND ASTHMA

Why would psychological stress be linked to the onset and course of asthma? Asthma is a disease that involves excessive airway inflammatory responses to environmental triggers, such as allergens and pollution.[27] Thus, one model posits that psychological stress accentuates the magnitude of inflammatory responses to these triggers. Specifically, many indoor and outdoor triggers have been linked to asthma exacerbations. For example, living in greater proximity to traffic has been associated with asthma outcomes[28] among youth, likely as a result of the increased exposure to traffic-related pollution that is also known to negatively influence asthma.[29–31] Within their home environments, youth are exposed to other environmental triggers that are associated with worsened asthma. Among the most common triggers are exposure to environmental tobacco smoke, which has been shown to lead to more emergency

department visits among youth,[5] and indoor allergens, such as mouse and cockroach allergens, which result in greater asthma morbidity.[3,32]

The inflammatory pathway that becomes activated in response to these environmental stimuli and leads to asthma involves the activation of T helper cells. On exposure to allergens, pathogens, and some irritants, dendritic cells present fragments of these triggers to T helper cells, which then coordinate downstream immunologic responses that drive the pathophysiology of asthma episodes. Distinctions are often made between 2 classes of T helper cells, Th1 and Th2 cells, which are functionally, but not morphologically, different. Specifically, Th1 cells are involved primarily in cell-mediated immunity and produce cytokines such as IFN-γ. In contrast, Th2 cells coordinate a humoral, or antibody-mediated, response to allergen exposure. Asthma is often believed to be marked by a shift toward Th2-dependent processes, as mediated through 2 main pathways, an early-phase response involving IL-4 and IL-13 and late-phase response involving IL-5.[33]

Th2 cells release IL-4 and IL-13,[34] which promote the proliferation and differentiation of B cells. B cells then synthesize and release immunoglobulin E antibodies that bind to mast cells in the airways, causing them to degranulate and release allergic mediators such as histamines and leukotrienes. These mediators induce smooth muscle constriction, mucus production, and edema, resulting in early-phase asthma symptoms. An alternative pathway involves the release of IL-5 by Th2 cells.[35] IL-5 is partly responsible for the production, maturation, and activation of eosinophils. Once they are recruited to the airways, eosinophils result in both greater inflammation and airway obstruction. Eosinophils release other mediators, for example eosinophil cationic protein, which can damage airway cells, and leukotrienes, which cause edema and further bronchial construction. Hence, this second pathway through IL-5 and eosinophils is believed to be involved in the more chronic, long-term inflammation associated with asthma. For more in-depth discussions of psychological stress and its effects on inflammation and asthma exacerbations, as well as more information on inflammation in asthma in general, see the brief reviews by Chen and Miller[27] and Busse and Lemanske.[36]

Several studies support the importance of assessing these biologic indicators and have linked stress to these processes. Research from our laboratory has shown that, among youth with asthma, greater chronic family stress is associated with greater in vitro stimulated production of cytokines implicated in asthma, including IL-5 and IL-13, as well as in vivo mobilization and activation of eosinophils.[37,38] Similarly, studies have found that examination-related stress potentiates IL-5 production and eosinophil mobilization in sputum following an airway challenge,[39] as well as decreased natural killer cell cytotoxicity[40] among university students with asthma.

MEASURING STRESS

There follows a discussion of the most common approaches to measuring stress, their benefits and disadvantages, and how they relate to asthma-relevant outcomes.

Experimental and Quasi-experimental Approaches

Laboratory manipulations

Some researchers have taken advantage of the controlled laboratory environment to assess the influence of various stressors on asthma-related outcomes that can be closely monitored before, during, and following exposure to psychological stressors. Laboratory manipulations frequently involve participants completing tasks, such as public speaking, engaging in discussions, or watching stressful movies. This approach

has the advantage that researchers can easily compare changes in the outcome variable of interest from before to after stressor exposure, or between groups who have or have not been exposed. Assuming the subjects have been randomly assigned in sufficient numbers to stressor versus control conditions, the researcher can make causal inferences about the influence of the manipulation, without concerns about confounding variables playing a role.

One laboratory manipulation suggests that emotional responsivity may mediate the relationship between psychological stress and asthma outcomes.[41] As part of this study, youth with asthma watched several segments from the movie, *E.T., The Extra-terrestrial*. Youth who had stronger emotional responses to these movie segments exhibited increased airway reactivity and decreased pulmonary functioning, as measured by youth's forced expiratory volume in 1 second (FEV_1). Similarly, youth with asthma who underwent a stressful task in the laboratory, relating an embarrassing moment to a tape recorder in the presence of an adult experimenter, exhibited decreased airway resistance following this task.[25] Furthermore, among adolescents with asthma, exposure to a stressful computer task was sufficient to induce breathlessness, even in the absence of actual airway obstruction.[42]

Research from our own laboratory has also investigated the effects of stress on markers of airway inflammation among healthy youth and youth with asthma using an acute stress task in the laboratory.[43] Youth and their parents were asked to discuss a topic of disagreement for 8 minutes, and youth's airway inflammation was assessed using a measure of exhaled nitric oxide both before and after the acute stress task. Increases in youth's heart rate and blood pressure indicated that youth did experience these discussions as stressful. In addition, youth with asthma, but not healthy youth, also experienced changes in their levels of exhaled nitric oxide, depending on the socioeconomic status (SES) of their background. Youth from low-SES families experienced increases in exhaled nitric oxide about 45 minutes after participating in the acute stress task, whereas youth from high-SES families experienced decreases, indicating that acute psychosocial stressors affect airway inflammation and that this response is moderated by SES.

Naturally occurring stressors

Some studies take advantage of naturally occurring stressors to assess the influence of psychological stress on asthma. Although this does not give experimenters the same amount of experimental control, or the ability to make causal inferences, it has the advantage of greater ecological validity because participants are experiencing stressors outside the artificial laboratory environment.

Commonly used paradigms involving naturally occurring stressors include examination stress among students. Liu and colleagues[39] asked college students with mild allergic asthma to undergo an inhaled antigen challenge at 2 separate time points, once during a low-stress midsemester time point and once during final examination week; that is, during a more stressful time. The inhaled antigen challenge involved the administration of increasingly high doses of allergens to which the participants were sensitized (eg, dust mite or cat dander) until their lung functioning had declined by 20% or more. During the high-stress final examination period, the inhaled antigen challenge resulted in a greater sputum eosinophil response as well as a greater decrease in FEV_1 from before to after the challenge. These results suggest that naturally occurring stressors amplify the inflammatory response to asthma triggers, and therefore have the potential to worsen clinical outcomes.

Some researchers are assessing naturally occurring stressors on an ongoing daily basis; that is, how the small stressors to which people are exposed in their everyday

lives may influence their health. The preferred way for studying stress in everyday life is through a daily diary.[44] By asking participants to briefly report on the stressors they experienced throughout a given day, every evening or multiple times throughout the day, researchers can link the stressors to health outcomes.

One study investigating the effects of daily psychological stress among adults with asthma asked participants to complete 5 daily diary assessments a day, for 10 days.[26] Participants were beeped at random times throughout the day, asked about the occurrence of stressful life events, and asked to complete a peak flow reading. Results suggested that there were diurnal patterns to asthma symptoms and PEFR and that these could be accounted for by psychosocial factors, including stressors. Experiencing more stressors was associated with lower PEFR and more asthma symptoms. Hence, daily diary assessments of stress may prove valuable for understanding the influence of everyday stressors on lung function and asthma outcomes.

Advantages and disadvantages

Experimental manipulations are beneficial in that they allow researchers to fully control the environment in which stressors occur, thereby ensuring that observed changes in asthma outcomes can be attributed to stressor exposure. In addition, assessing asthma outcomes in response to psychological stressors in the laboratory enables researchers to assess changes via objective markers, rather than having to rely on participant-reported outcomes, such as symptoms, or other clinical outcomes, such as emergency department visits. The primary criticism of laboratory manipulations relates to the questionable extent to which stress responses experienced in the laboratory can be generalized to real-life situations. However, to the extent that experimental manipulations are representative of real-life stressors, the controlled laboratory environments can provide important information regarding how stressors result in physiologic changes that ultimately lead to increased asthma morbidity. Taking advantage of naturally occurring stressors results in greater ecological validity but decreases the amount of control and inferential leverage researchers have.

Furthermore, a daily diary approach allows for more frequent data collection that is less likely to be affected by participants' recall bias. However, daily diaries can be disruptive to people's lives and require a significant amount of effort from participants, and hence information is typically only collected for brief periods of time (eg, 2 weeks) during which participants may not experience many life stressors. However, depending on the study design, it may be possible to integrate several periods of daily diary data collection into a longitudinal study design and ask participants to complete multiple rounds of daily diary, several weeks or months apart.

Environmental Occurrence of Stressors and Life-Event Checklists

An alternative approach is to assess the types of stressors that are occurring in individuals' lives. For example, life-event checklists consist of lists of events that are experienced by the general population and believed to be experienced as stressful by most people, such as moving to a new place, getting divorced, or starting a new job. Participants simply check all the items on a particular life-event checklist that they have experienced within a given time frame, for example, the last 30 days. Researchers can then sum the number of items checked and use the total score as an indicator of the amount of stress in an individual's life. For an overview of existing checklists see Turner and Wheaton.[45]

Turyk and colleagues[9] used a 15-item checklist to assess the effect of stressful life events believed to commonly occur among inner-city youth with and without asthma. Although asthma morbidity was generally high in this sample, the number of stressful

life events youth reported having been exposed to in the past year was associated with asthma symptoms, missed school days, physician contact, and hospitalization for asthma. In addition, the investigators found a dose-response relationship between the number of stressful life experiences and the odds of dry cough at night, number of symptoms, and physician visits for asthma, such that experiencing increasing numbers of negative life events was related to a greater number of symptoms and physician visits. These results remained significant even after several potentially relevant confounding variables were taken into account.

Advantages and disadvantages

Life-event checklists have clear advantages in that they are quick and cheap to administer and do not require any training on the part of the research team. Hence, they may be particularly useful in large samples or when time for stress assessments is limited (eg, in epidemiologic studies). However, although checklists are easy to use, the information that can be collected through them is limited. For example, the events on a checklist may not be a good representation of events experienced by people in the population of interest. Hence, events may be missed entirely if stressful events that participants considered important were not part of a checklist. Alternatively, participants may decline to report an event that has occurred, either because they do not want to disclose them, or they believe they were not of sufficient importance to merit doing so. In addition, these types of self-reports usually do not assess the specific timing or duration of events and fail to capture the participants' appraisal of an event. For example, participants may select items on a checklist because they have experienced them even if they did not consider the occurrence of such an event stressful. As a result, some people consider checklists a better measure of the change occurring in people's lives, rather than negative life events or stress per se.[45]

Assessing Subjective Stress Appraisal

Another common approach to assessing stress in the literature involves self-report questionnaires regarding subjective perceptions of stress in individuals' lives. The Perceived Stress Scale (PSS),[46] for example, is a frequently used 10-item measure that assesses subjective stress experiences by asking participants how stressful they consider their life is in general; for example, how unpredictable they find it to be. Most self-report questionnaires require participants to indicate to what extent they endorse statements assessing their subjective stress experiences on Likert scales; that is, indicating the extent to which they agree or disagree with certain statements on a scale ranging from 5 to 7. These responses can then be summed to create a total score representative of the amount of stress subjectively experienced by participants.

One study has used the PSS to assess stress among caregivers of youth predisposed to atopy throughout early life.[47] Caregivers repeatedly completed the PSS, and results indicated that youth whose parents reported greater perceived stress showed evidence, at the age of 2 to 3 years, of greater IgE expression, a greater allergen-induced proliferative response, as well as changes in cytokine production indicating increased airway inflammation. This study suggests that data gained from questionnaire-based stress assessments among caregivers are relevant regarding the overall immunologic profiles of youth at risk for asthma.

However, another study that assessed the influence of social support among college students with asthma on their immune functioning during low-stress (midsemester) and, presumably, high-stress (final examination period) times found that, although students experienced physiologic changes between midsemester

and the final examination period, they did not report higher levels of stress during the examination period. This suggests that some questionnaire-based assessments of subjective stress experiences may be insensitive to certain types of stressors or among particular populations.[40]

An alternative approach to assessing subjective appraisals involves a controlled laboratory presentation of a life event, from which individual perceptions of that event can then be assessed. The Cognitive Appraisal and Understanding of Social Events (CAUSE) videos[48] were developed to assess people's interpretation of events that have ambiguous outcomes. For example, one of these videos depicts a high school girl browsing in a department store with an overly attentive saleswoman nearby. Participants are asked to imagine themselves in the place of the teenager when watching the video and are subsequently asked about their interpretation of the situation (eg, "Why do you think the saleswoman was paying attention to you while you were browsing?"). By asking participants about their appraisal of this potentially stressful situation, one can code their responses to these ambiguous situations as being more benign (eg, she was trying to make a sale) or hostile (eg, she believed I was about to steal something).

Research from our laboratory using the CAUSE videos indicates that, as with chronic stress, participants' perceived threat in response to an ambiguous social situation also predicts a heightened inflammatory profile (specifically, increased stimulated IL-5 and IL-13 production) as well as higher eosinophil counts among youth with asthma.[37] In addition, other studies found stress interpretations to statistically mediate the relationship between low SES and greater stimulated cytokine production in adolescents with asthma[23] and between low SES and gene transcription control pathways regulating inflammation and catecholamine signaling in adolescents with asthma.[49]

Advantages and disadvantages

Similar to life-event checklists, assessments of subjective stress appraisals are easy to administer and require little time and effort. They also address what some researchers conceptualize as the essence of the stress response: the subjective perception of stress.

However, this reliance on the subjective can create certain measurement problems. For example, people may differ in their subjective assessments of situations and assess stressful life events according to idiosyncratic standards. As a result, it can be difficult to know whether individual differences in responding reflect variations in the occurrence versus the perception of an event. It is also possible that people use scales differently when making ratings, or that they are unwilling to relate details of events that they perceived to be embarrassing, hence rating an event as less severe or important than it may have been. In addition, because different people use different, subjective reference points when making ratings of the effects of stressful life events, meaningful comparisons across individuals may be difficult, if not impossible. Consequently, such an approach may be more useful when investigating within-person changes across several time points.

Interviews

Many studies interested in assessing the influence of psychological stress on asthma also do so through interviews, such as the UCLA Life Stress Interview (LSI)[50] and the Life Events and Difficulties Schedule.[51] These interviews probe both the occurrence of ongoing difficulties (chronic stress) across several life domains, such as family, friends, and school/work, as well as the occurrence of time-limited events that are

typically short in duration (acute events). Ratings of the severity of acute and chronic stress are made by interviewers (rather than by the participants themselves) and typically take into account context. For example, chronic stress may be rated on a 1 to 5 scale for each domain of interest by the interviewer, with higher numbers reflecting more severe difficulties. In addition, acute stressors and their objective effects may be rated by a team of interviewers. Interviewers are briefed on the details about a given event and subsequently agree on a consensus rating, also on a 5-point scale, taking into account the context of a particular situation, such as whether an event was expected and whether a similar event had previously taken place.

Several studies have successfully implemented interview-based approaches to measuring stress and linked them to outcomes relevant to asthma. Studies from our own research group have repeatedly used the LSI.[52] Using this approach, we have linked stress in the lives of youth with asthma to various biologic outcomes. Specifically, we have investigated the effects of stress in vitro by culturing peripheral mononuclear blood cells with a mitogen cocktail consisting of phorbol myristate acetate and ionomycin and subsequently measuring the amount of cytokines being produced. We have found that, among youth with asthma between the ages of 9 and 18 years, greater chronic home and family stress was associated with an increased production of IL-5, IL-13, and higher levels of circulating eosinophils, whereas the opposite was true for a healthy comparison group.[37] We have also linked greater home life stress among youth with asthma to a decreased output of salivary α-amylase across the day,[53] indicating lower sympathetic activity. This finding suggests another possible mechanism through which stress in the lives of youth with asthma may lead to asthma exacerbations.

Chen and colleagues[54] also found interactions of interview-based stress measures with physical environment measures of air pollution in predicting asthma outcomes. Specifically, higher levels of chronic family stress were associated with higher IL-5 production, IgE levels, and eosinophil counts among youth with asthma living in neighborhoods with modest levels of traffic-related air pollution. In contrast, among youth living in neighborhoods with high traffic-related pollution, psychological stress was not associated with inflammatory profiles. These interaction effects also extended to clinical changes over 6 months, such that, among youth with asthma living in neighborhoods with modest levels of traffic-related air pollution, higher levels of chronic family stress predicted increases in asthma symptoms and declines in pulmonary function in a 6-month follow-up period. These findings suggest that, when physical environment exposures are modest, social environment exposures may exert their greatest effects, whereas high levels of physical environment exposures may overwhelm effects of the social environment.

Other research groups have also evaluated the effects of interview-based stress on clinical asthma outcomes among youth. As part of a prospective 18-month longitudinal study, Sandberg and colleagues[55] used the Psychosocial Assessment of Childhood Experiences (PACE) interview[56] to repeatedly assess the occurrence of life events across the study period.[57] Sandberg and colleagues[55] found that the likelihood of youth experiencing a new asthma attack increased shortly after the experience of a stressful life event, and again roughly 5 to 7 weeks later.

Some measures are also beginning to circumvent the problems inherent in questionnaire and checklist approaches by supplementing the traditional checklist approach with additional questions that allow for the collection of more in-depth data. One such measure, the Crisis in Family Systems (CRISYS)[58] instrument, successfully combines quantitative and qualitative approaches. Participants first indicate, using a checklist format, whether they have experienced a particular set of stressful life events. In addition, they answer questions for items they endorsed, either on a Likert

scale or in response to open-ended questions from an interviewer, and provide more detailed information about the event in question. Hence, this represents a successful combination of different approaches to stress measurement. Shalowitz and colleagues[59] used this measure to assess stress among caregivers of youth with asthma and found that children of mothers who experienced more negative life stressors were more likely to have high, rather than low or moderate, asthma morbidity.

There is also mounting evidence that chronic and acute stress need to be considered together to allow for a coherent assessment of the effects of stress on asthma outcomes. For example, Sandberg and colleagues[11] investigated the effects of chronic and acute stress among children between the ages of 6 and 13 years as part of an 18-month prospective study. Although youth who experienced an acute stress event had an increased likelihood of an asthma attack in the weeks following the event, youth who were also exposed to chronic stress showed a shortened latency to asthma exacerbations following the acute stressor.

Similarly, Marin and colleagues[60] found that youth with asthma who experienced acute stressors in the context of high chronic stress showed increased inflammatory profiles in response to stress. Youth participated in 5 study visits across 5 years (ie, once every 6 months) and, among youth living in a home environment marked by increased chronic family stress, at times when they had recently experienced an acute stressor they exhibited heightened stimulated production of asthma-relevant cytokines such as IL-4 and IL-5 compared with times when they had not recently experienced an acute stressor. In addition, youth provided information on their asthma symptoms for 2 weeks following each laboratory visit. Among those with more severe asthma, at times when participants exhibited higher levels of stimulated cytokine production, they also reported more asthma symptoms, pointing to the clinical significance of the observed changes in stimulated cytokine production.

The co-occurrence of chronic and acute life stress events among youth with asthma has been linked to gene expression profiles relevant to asthma inflammation.[61] Youth with asthma experiencing chronic stress in their homes and who also experienced a major acute life event within the previous 6 months exhibited reduced expression of glucocorticoid receptor mRNA and β2-adrenergic receptor mRNA. This reduction could potentially lead to a decreased sensitivity to the antiinflammatory properties of glucocorticoids, resulting in greater airway inflammation, as well as to a decreased efficacy of asthma medications that target these receptors. Together, these studies suggest that, when studying acute stress in particular, chronic stress should also be assessed because it may significantly moderate people's response to acute stressors.

Advantages and disadvantages

Using semistructured interviews allows researchers to use a repertoire of follow-up questions to probe for additional detail regarding stressful life events. This greater flexibility makes it possible to obtain information regarding the circumstances surrounding an event, exacerbating and mitigating factors, details about the timing and duration of the event, and the participant's appraisal of an event. In addition, semistructured interviews, as opposed to structured interviews, provide the advantage of allowing the interviewer to ask whatever questions are most relevant to a certain event and participants, instead of working with a fixed set of questions that are answered by all participants.

Other advantages of using an interview-based approach are the assessment of contextual information that can aid in making severity ratings, and having interviewers, rather than participants, making ratings of stress. Specifically, within the context of a semistructured interview, an interviewer will be able to obtain additional information on events that would not have been available through a checklist approach, for

example a participant's perceived sense of ability to control an event. This information can then be used to make a more objective rating of an event by rating the normative stress levels that would commonly be associated with it. This in turn allows the researcher to distinguish between normative events (eg, child transitioned from middle to high school and is adjusting well to their new school), and more stressful events (eg, child got expelled from old school because of behavioral problems and was forced to attend a new school midsemester). Note that in both cases children may have endorsed a "Switched schools in the past half year" item on a checklist even though the exact circumstances between these situations vary widely. Although the former situation represents a normative transition, the latter does not and is likely to be associated with significantly greater stress. Within the framework of contextual interviews, researchers can make more objective ratings of the stress associated with the particular life events that participants report, rather than having to rely on participants' ratings. Having obtained all this additional information, researchers will be able to make well-informed and objective ratings of stressful life events.

Interview-based assessments that capture stress across a variety of domains also allow for comparisons of the relative effects from domain to domain. For example, across several studies from our laboratory we find that chronic stress in the family domain has robust associations with asthma inflammatory measures, but that chronic stress in other domains, such as friendship and school, are not associated with inflammatory profiles in asthma.[60–62]

Using an interview-based approach has its costs, primarily in terms of the greater burden on both the participants and researchers. Interview-based assessments of stress require training of interviewers, regular checks on inter-rater reliability, and take longer to administer than questionnaire-based assessments. Hence these approaches are more costly, labor-intensive, and may not be feasible in larger samples.

SUMMARY

This article reviews different methods of assessing stress that are most commonly being used in current research. Quicker ways of measuring stress, for example, through self-report questionnaires and event checklists, may be the necessary tools for large-scale studies and can be easily implemented. However, there are concerns regarding the quality of information that can be gained from these measures and they may not always be sensitive enough. An alternative to these measures is interview-based assessments of an individual's stress. Although they are more resource intensive, we believe that the flexibility and resulting in-depth information that can be gained from interview-based approaches are worth the increased costs in terms of time and labor, because research suggests robust associations of interview-based stress measures with both asthma biologic and clinical outcomes. Research on stress and asthma should also take into account subjective appraisals of stress, as well as dimensions such as duration and intensity in characterizing stress. Through a more sophisticated understanding of the dimensions of stress that are associated with asthma pathophysiologic processes and functional impairment, researchers and clinicians will be able to identify the components of stress that would be important to target, together with medication compliance and environmental exposures in multipronged behavioral interventions intended to reduce asthma morbidity.

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