

The High Prevalence of Depression Among Adolescents With Asthma in Iran

A recent study in *Psychosomatic Medicine* by Smith and colleagues (1) showed the effectiveness of expressive writing on lung function, quality of life, medication use, and symptoms in individuals with asthma. These findings suggest that cognitive and emotional processes might be involved in physiological demands associated with asthma. Therefore, behavioral and pharmacological interventions targeting psychological disorders could result in improved asthma control. Asthma and depression are two major health problems particularly in adolescence, with several impacts such as negative and poor school performance, and impaired social, work, and family functioning (2,3). The prevalence of major depressive disorder is increased significantly across adolescence (3). Regarding the high prevalence of asthma and mood disorders in adolescents in our area (3–6), we evaluated the frequency of depression in adolescents with asthma in comparison to adolescents without asthma in the city of Zanjan, Iran.

Our study consisted of 1500 children aged 13 to 14 years who had been randomly selected by multivariate cluster sampling from 20 guidance schools of the city of Zanjan from March to July 2013. After written informed consent was provided by participants and their parents, the children completed the International Study of Asthma and Allergies in Childhood (7) questionnaire modified for face-to-face interview. Asthma was defined as present if the participant reported the presence of a physician-based diagnosis of asthma, or if the International Study of Asthma and Allergies in Childhood revealed a) symptoms of dry cough with a duration of longer than two weeks, b) symptoms also occurring at night; and c) symptoms of wheezing or whistling sounds in the chest that were not attributable to the common cold or other diseases. The severity of asthma was assessed and classified into mild ("as waking up at night less than one night per week and no limitation in activity") and moderate to severe asthma ("as having wheezing attack in the last 12 months, sleep disturbance more than one night per week and limitation in speaking and activity.") The control group consisted of randomly selected classmates who did not suffer from atopy and asthma. The depression status and its severity in students with asthma and controls were measured by using the Beck Depression Inventory.

Two hundred twenty-five (15%) students had asthma symptoms, with a prevalence of 13.7% and 16.2% in boys and girls, respectively. One hundred ninety-four (86%) adolescents had mild and 31 (13.7%) had moderate asthma. The frequency of depression among adolescents with asthma

and controls was 61.8% and 36%, respectively ($p < .001$). Major depression was found in 20% and 7.6% of asthmatic patients and controls ($p < .001$). There was a significant correlation between severity of asthma and depression ($p < .001$). The odds ratio (OR) for depression associated with asthma was 2.82 (95% confidence interval [CI] = 1.96–4.21), which was higher in girls (OR = 4.55, 95% CI = 2.54–7.44) than in boys (OR = 1.82, 95% CI = 1.04–1.32).

Inflammatory processes may play a role in the relationship between asthma and depression in adolescents. Some evidence indicates altered levels of interleukin-4, interleukin-6, and tumor necrosis factor α in depressed individuals (8). Furthermore, in a study by Ritz et al. (9), the amount of exhaled nitric oxide was used as a marker of inflammation in individuals with asthma. Depressive mood was associated with a reduced mobilization of airway nitric oxide in acute stress. However, the nitric oxide-based index was largely unrelated to asthma status and inhaled corticosteroid use.

In our study of an Iranian sample of adolescents, we found a high prevalence of depression in youth with asthma. There was a significant correlation between asthma severity and depression. Female asthmatic adolescents were at particular high risk for depression. Considering the burden of these disorders on cognitive function and quality of life in this age group, special attention for screening and treatment of youth with asthma should be encouraged.

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Closing the Border on a New Frontier: the Problem With Salivary Nerve Growth Factor

In 2013, a study appeared in *Psychosomatic Medicine* showing that salivary levels of nerve growth factor (sNGF) rapidly increase (to +45% of baseline levels) in response to an acute psychosocial stress task that involved discussing

an unresolved conflict with a romantic partner (1). NGF, also referred to as mature NGF- β , is a neurotrophic factor that, among other functions, mediates neuronal growth and differentiation, although it may also drive cell death (2). The study presented a genuinely novel finding, which was emphasized by the authors' branding of sNGF as a “new frontier for stress research” that could “represent a resilience factor protecting individuals from adverse effects of stress” (1,3). Secondary analyses of these seminal data were in line with these speculations, showing, for example, that greater sNGF reactivity to conflict was related to stronger appraisals of coping ability and agency, lower anticipatory stress appraisals, and higher well-being (1,3). However, there is one problem, which is substantial: saliva appears to contain little, if any, NGF. Therefore, on grounds that the findings are biologically implausible, we think that the validity of these data (and related data published in other journals) need to be reconsidered.

While our main concern pertains to the validity of measuring NGF- β in saliva (discussed further below), there are two other issues that we would like to comment on—namely, the interpretation of stress-induced changes in salivary NGF- β and statistical/design issues of the aforementioned study (1,3).

First, we noticed that speculations regarding the role of human salivary NGF- β as presented by Laurent et al (1), and in subsequent articles (3–6), seemed inconsistent with current knowledge in this area and were based, in part, on extrapolations from studies in mice. In these animals, the submaxillary salivary gland produces high concentrations of NGF- β , thought to have important local and endocrine functions (7). However, there are no human data to suggest a biological role for salivary NGF- β in any other part of the body, and there is also no evidence that NGF- β levels in human saliva correspond with the levels in other compartments (e.g., blood, brain). Likewise, speculations about the protective roles of salivary NGF- β did not seem to be well supported. An example is the statement that “a neurotrophic response to acute stress—found at both central and peripheral levels—may have evolved as a resilience mechanism to protect the brain and other tissues against cortisol release” (1). The biological effects of NGF- β (e.g., cell growth versus cell death) are highly contextual and depend on NGF- β concentration, differential activation of its receptors (Trka and p75NTR), and signals from other growth factors and progrowth or antiprogrowth receptors (2).

Second, the aforementioned article (1) raises statistical and methodological concerns. For example, the observation that salivary NGF- β increases in the stress group ($n = 40$) but not in the control group ($n = 20$) would be more convincing if a significant time by condition interaction was demonstrated (i.e., to indicate that the two groups differ). Such control group comparisons were, however, not presented in the *Psychosomatic Medicine* article or in subsequent stress