

Commentary on hostility and physiological responses to laboratory stress in acute coronary syndrome patients

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Hostility is a personality trait associated with higher risk of future cardiac events in both patients with coronary artery disease (CAD) and healthy individuals [1], but information on underlying mechanisms is scarce. Tendencies toward exaggerated physiological reactions to acute stressors predict both accelerated progression of atherosclerosis [2–6] and the likelihood of having a future cardiac event [7–9]. Therefore, testing of relationships between hostility and physiological stress reactivity may provide mechanistic insights. Hitherto, these associations have been investigated in healthy individuals but not in patients who suffered from acute coronary events. This is described in a recent meta-analysis that, in healthy individuals, higher hostility is related to increased cardiovascular stress reactivity [10]. Heightened stress reactivity of intermediate biological risk factors for coronary heart disease (CHD) such as inflammatory activity may also be involved in mediation of elevated risk for acute stress-associated CHD morbidity and mortality [3,8,9,11–15]. However, studies relating hostility with inflammatory stress reactivity are sparse and, to our knowledge, only one study in healthy individuals suggests that hostility is related to higher IL-6 reactivity following a nonconflictual interaction task [16].

The study by Brydon et al. [17] examined for the first time the association between trait hostility and alterations in physiological responses to an acute standardized stress task in diseased patients, namely, 34 men who had survived an

acute coronary syndrome (ACS) approximately a year earlier. Patients were excluded if they were hypertensive or had relevant comorbidities, persisting symptoms, or poor left ventricular function. Participants completed two 5-min behavioral tasks, a computerized color-word interference task and a 5-min speech. The authors measured, in addition to cardiovascular (heart rate and blood pressure), both endocrine (cortisol) and immune (IL-6) measures before and during a 2-h recovery. Hostility was measured using a 39-item abbreviated version of the Cook Medley Hostility Scale. The main study findings are that participants with higher hostility scores had greater systolic and diastolic blood pressure (BP) reactivity to tasks, as well as a more sustained increase in systolic BP at 2 h posttask, independent of age, BMI, smoking status, medication, and baseline BP. Moreover, hostility was also associated with elevated plasma IL-6 levels at 75 min and 2 h poststress, and was negatively correlated with salivary cortisol at 75 min.

As Brydon et al. [17] suggest, these findings may indicate that hostile individuals with advanced cardiovascular disease are particularly susceptible to stress-induced increases in sympathetic activity and inflammation. This may be of clinical relevance as it might contribute to an elevated risk of emotionally triggered cardiac events in such patients. More precisely, heightened stress-induced sympathetic activation may lead to increased peripheral vascular resistance and myocardial ischemia in patients with atherosclerosis as observed in atherosclerotic as compared to healthy coronary vessels [18]. Also, acute elevations in BP may provoke plaque ruptures in vulnerable patients as suggested by Brydon et al. [17]. The findings of the study by Brydon et al. [17] correspond with previous observations pertaining to

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ACSs, such as ACS often occurring within 2 h after emotional triggering [7], and that inflammatory cytokines like IL-6 are linked to the progression of atherosclerosis and stimulate processes that contribute to plaque rupture and thrombosis [19–21]. Thus, IL-6 stress reactivity may play a role in mediation of stress-induced ACS triggering. In this light, it is a particular strength of the study that cytokines were measured up to 2 h after stress cessation since cytokine stress reactivity is known to be observed 90 to 120 min following stress [14]. Notably, although not explicitly tested, the observed negative association between hostility and cortisol stress reactivity at 75 min poststress may be involved in mediation of the positive association between hostility and IL-6 at that time point.

Some caution is needed, however, when interpreting the findings of the study. Since there is no control group it remains unclear whether the observed heightened cardiovascular and inflammatory reactivity associated with increasing hostility is specific to ACS patients. Moreover, the authors referenced several studies that specified “anger” as a potential trigger of cardiac events and then portend to extend these previous findings to those of the present study as attributable to “hostility.” Although anger is a part of trait hostility, trait hostility is not synonymous with acute anger. Therefore, it remains unclear whether the findings of this study reflect mechanisms underlying the previously observed acute anger-induced triggering of ACSs within 1–2 h in CAD patients [22–24].

Future research should verify the findings of this study in a larger cohort including women and control subjects. Moreover, a broader spectrum of mechanisms underlying hostility and the generation of CAD and ACS should be examined. For example, dysregulations of the hypothalamus-pituitary-adrenal axis may play a role [25–27]. Furthermore, the role of additional inflammatory measures related to CAD and ACS beyond the much studied cytokine IL-6 should also be explored. For example, the link between hostility and vascular stress-reactive inflammatory measures associated with CAD and ACS such as P-selectin or ICAM-1 may be of interest [15,28–34]. In addition, it is unclear how hostility relates to the stress reactivity of other intermediate biological CHD risk factors such as lipids or coagulation activity [35]. In sum, the findings of the study by Brydon et al. [17] suggest potential mechanisms that may contribute to an elevated risk of emotionally triggered cardiac events in vulnerable patients and open the door to more studies to further understand this association.

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