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Visceral pain and public speaking stress: Neuroendocrine and immune cell responses in healthy subjects

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Abstract

Whereas responses to psychological stressors are well-characterized, little is known regarding responses to painful visceral stimuli. We analyzed the emotional, cardiovascular, neuroendocrine, and cellular immune responses to painful rectal stimulation and psychological stress in healthy individuals. Eleven healthy subjects were studied in three conditions on separate days: painful rectal distension, public speaking stress, and rest. Blood was drawn for endocrinological and immunological analyses; heart rate and blood pressure were measured continuously; state anxiety was assessed with a questionnaire (STAI-S). Anxiety scores were highest in the rectal distension condition. This was evident following rectal distension (mean STAI-S scores: 44.2 ± 3.5 post-distension vs. 36.6 ± 3.8 post-speech, $p < .05$), but anxiety was also elevated at baseline (41.6 ± 3.9 vs. 32 ± 3.2 recovery, $p < .01$). This anticipatory effect was reflected by elevated baseline cortisol ($p < .05$) and baseline ACTH ($p < .01$) levels, as well as circulating lymphocytes and lymphocyte subsets, including decreased basal $CD3^+CD4^+$ cells ($p < .05$) and increased $CD16^+CD56^+$ cells ($p = .06$) compared to rest. Both public speech and rectal distension induced cardiovascular activation, but the effect was more pronounced following rectal distension ($+63.8 \pm 9.4$ mmHg in response to distension vs. $+36.4 \pm 6.2$ mmHg in response to speech for systolic BP, $p < .05$). Different response patterns were also observed in the distribution of circulating leukocytes and lymphocyte subsets, including $CD16^+CD56^+$ cells ($p < .05$). An acute visceral pain stimulus causes profound emotional, neuroendocrine, and immune cell responses, which are markedly affected by anticipatory anxiety. These findings may have implications for conditions associated with visceral hyperalgesia.

Keywords: Public speaking stress; Rectal distension; Psychological stress; Visceral pain; Gastrointestinal pain

1. Introduction

Stress-induced modulation of immune functions by hypothalamic–pituitary–adrenal (HPA)-axis mediators and autonomic nervous system (ANS) mechanisms is one of the most intriguing examples of neuroendocrine-immune communication. Various types of stressors have been characterized with regard to their ability to induce changes in HPA-axis and autonomic functions, associated with immune system alterations (Padgett and Glaser, 2003). Public speaking stress is one of the

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best-characterized acute laboratory psychosocial stressors, which has been consistently found to affect neuroendocrine and cellular immune functions in healthy controls (Bosch et al., 2003; Caggiula et al., 1995; Goebel and Mills, 2000; Hennig et al., 2001 Landmann et al., 1984; Mills et al., 1995; Redwine et al., 2003; Sgoutas-Emch et al., 1994) and various patient groups (Buske-Kirschbaum et al., 2002; Jacobs et al., 2001; Pawlak et al., 1999; Schmid-Ott et al., 2001).

Public speaking stress can be considered a "purely" psychological or psychosocial stressor, characterized by the absence of any real threat of physical danger or harm. In contrast, pain is a stimulus that signals the danger of physical harm, and as such can be considered a physical stressor. However, given the emotional responses evoked by pain, it clearly has psychological components. As a model of somatic pain stress, the cold pressor test has been utilized in several studies within the context of psychoneuroimmunology. It has consistently been found to induce emotional responses (e.g., distress, anxiety) and cardiovascular activation, and to affect various immune parameters (Chi et al., 1993; Delahanty et al., 1996; Santos et al., 1998). *Somatic* pain stimuli thus represent stressors which evoke complex neuroendocrine and immune responses. In contrast, little is known about the effects of painful visceral stimuli, although knowledge about this would have important clinical implications for conditions involving recurrent abdominal pain, such as present in patients with functional gastrointestinal disorders. Indeed, existing data strongly suggest that painful visceral sensations are centrally processed as stressors, and represent salient stimuli which evoke emotional responses not only in patients with heightened visceral pain sensitivity, but also in healthy subjects. For example, Hamaguchi et al. recently demonstrated in healthy subjects that distension of the colon induced visceral perception and pain associated with emotional responses, particularly with anxiety, which correlated with activation of specific brain regions, including the limbic system and the association cortex, especially the prefrontal cortex (Hamaguchi et al., 2004) . These data are substantiated by our own recent animal data which showed that repeated rectal distensions led to significant increases in corticosterone levels, indicating HPA-axis activation consistent with a stress response in these animals (Elsenbruch et al., 2004b). For the upper gastrointestinal tract, we further reported that gastric distension by food intake induced cardiovascular activation, cortisol and catecholamine release, associated with cellular immune changes in healthy women and in patients with irritable bowel syndrome (IBS) (Elsenbruch et al., 2004a; Elsenbruch and Orr, 2001). Hence, visceral stimuli may represent stressors which evoke neuroendocrine and immune cell responses. Based on these findings, the long-term purpose of this project is to study stress responses to visceral and non-visceral stress stimuli in patients with disturbed visceral perception. Therefore, the goal of the present, initial study was to establish an experimental model which would allow to characterize responses to a series of painful rectal sensations, compared to public speaking stress, in healthy individuals. We hypothesized that in healthy subjects rectal pain would elicit a stress response, and chose public speech a well-characterized and reproducible psychological stress model as a comparison condition to evaluate the magnitude of the stress responses.

2. Methods

2.1. Recruitment and screening procedure

Exclusion criteria for participation were age <18 or >65 years, any evidence of gastrointestinal diseases or chronic gastrointestinal symptoms, immunological, endocrinological, cardiovascular, or psychiatric conditions. The screening process included a personal interview with routine physical examination. Out of a total of 18 individuals who contacted us, 14 met the criteria, and 11 agreed to participate. All subjects were informed about the study protocols. For the public speaking condition, subjects were informed that they were going to be asked to hold a speech, but no further detail was given with regard to content, duration or circumstances of the task. Procedures included in the rectal distension protocol were fully disclosed. The study protocol was approved by the Local Ethics Committee, all participants signed informed consent and were paid for their participation.

2.2. Study design

All participants were studied in two conditions, rectal distension and public speech. The study conditions were accomplished on separate days, in counterbalanced order. In each condition, three blood samples (baseline, post-stress/post-distension, and recovery) were drawn, heart rate and blood pressure were measured continuously, and state anxiety was assessed. To provide additional data, hormones and leukocytes, and lymphocyte subsets were analyzed on a separate occasion (rest condition), which was always scheduled following completion of the other study conditions.

2.3. Study protocols

2.3.1. Rectal distensions

Rectal distensions were carried out with a pressure-controlled barostat system (modified ISOBAR 3 device, G&J Electronics, Ontario, Canada) following preparation of the rectum with physiological saline solution (Clyssie, B. Braun Medical AG, Melsungen, Germany).