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Examining psychosocial factors related to cancer incidence and progression: In search of the silver lining

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The possibility of links between psychosocial factors and cancer incidence and progression have generated considerable scientific and public interest. As early as the mid-1920's, psychologists were speculating about psychogenic influences on cancer (Evans, 1926), and, for decades, personality and individual differences have been hypothesized as both etiologic and prognostic determinants of cancer development (Brown, 1966; Eysenck, 2000; Fox, 1983).

With advances in psychoneuroimmunology have come challenges to earlier theories addressing these links (Fox, 1983; Kiecolt-Glaser & Chee, 1991). Biopsychooncological researchers now emphasize the crucial role of both the endocrine and immune systems in cancer outcomes, and stress-associated dysregulation of biological and physiological processes have been highlighted. Unfortunately, this inquiry has been fraught with methodological and conceptual hurdles that cloud any concrete understanding about these potentially important linkages. We believe there is a silver lining behind this cloud. As Segerstrom (this issue) and others (Brown, 1966; Garssen & Goodkin, 1999) have indicated, heterogeneous sampling and measurement have produced divergent findings concerning the psychosocial-cancer link. Notably, the relevance and validity of the immunological and psychological assessments used within cancer contexts have received little attention. These are remediable weaknesses. Here, we highlight some methodological points related to contextual specificity that should be considered seriously in psychoneuroimmunological studies of individual differences and cancer outcomes.

Psychoneuroimmunology research on psychosocial modifiers of stress responses and cancer processes have primarily focused on nonspecific immune responses, including NK cell function, mitogen stimulation of peripheral blood lymphocytes, and subsequent cytokine production (Kiecolt-Glaser & Glaser, 1999).The rapid methodological advancements in immunological, cellular and molecular assaying techniques permit psychoneuroimmunological researchers to examine extraordinarily micro-level physiological and biological processes. Importantly, this technology affords examination of specific, cancer-related mechanisms.

A potentially productive research focus for psychosocial oncology is the study of stress effects on cellular processes. Many carcinogens appear to induce tumors by damaging cellular DNA and producing abnormal cells (Fox, 1978; Setlow, 1978; Tomei, Kiecolt-Glaser, Kennedy, & Glaser, 1990). The body's defenses against this process include enzymes that destroy chemical carcinogens, processes for repairing damaged cellular DNA, and the destruction of abnormal cells via apoptosis, a process of genetically programmed alterations in cell structure that leads to failure of proliferation and differentiation, and eventual cell suicide (Fox, 1978; Tomei et al., 1990). Stress can alter each line of defense. First, levels of methyltransferase, an important DNA repair enzyme induced in response to carcinogen damage, were significantly lower in stressed rats' spleenic lymphocytes compared to nonstressed controls (Glaser,

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Thorn, Tarr, Kiecolt-Glaser, & D'Ambrosio, 1985). Second, more depressed nonpsychotic, nonmedicated new psychiatric admissions showed significantly poorer repair of damaged DNA than their less depressed counterparts. Finally, examination stress enhanced the ability of low concentrations of tumor-promoting phorbol ester to block apoptosis (Tomei et al., 1990), potentially resulting in immune function suppression. Perhaps individual differences, such as optimism or loneliness, mediate the effects of stress on cellular damage and apoptosis.

In addition to these cancer-related cellular processes, an important future direction for individual differences and cancer research is the exploration of tumor-specific immune responses, using, for instance, tumor specific antigens such as epithelial mucin for breast, pancreas, colon, lung, prostate, and ovarian tumors or melanoma antigen for melanomas (Andersen, 2002). Examining psychosocial-cancer links within the context of immunogenic tumors should be strongly emphasized as well (Finn, 2001). There is substantial evidence from both healthy populations as well as individuals with cancer linking psychological stress with immune dysregulation. Cancers that are inherently tied to immune system compromise should be advantageous for revealing relationships between individual differences, stress-associated physiological responses, and cancer processes; indeed, some of the notable null relationships may be a consequence of studying tumors that are relatively insensitive to modulation by the immune response.

The contextual specificity in the study of psychosocial processes and cancer not only pertains to immune processes, but is pertinent to the measurement of individual differences and personality. First, relationships between individual differences and physiological responses to stress should be assessed within contexts where the state or trait characteristic is afforded expression (Mischel & Shoda, 1995). For example, associations between hostility and cardiovascular responses are more reliably detected when the situation is one in which the individual is provoked (Suls & Wan, 1993). Examining, say, loneliness within the context of cancer may be more productive when it is measured prior to and following a cancer diagnosis, when individuals may be seeking support and, hence, becoming more acutely aware of their social environment.

Second, the reliability and validity of psychological measures for cancer populations should be a priority. Existing measures validated in nonmedical samples should be routinely cross-validated with diverse cancer patient samples (Hann, Winter, & Jacobsen, 1999); doing so provides valuable information for researchers. For instance, general measures of psychological distress may be less sensitive in detecting distress in women at-risk for breast cancer than cancer-specific distress measures (Croyle, Smith, Botkin, & Baty, 1997; Lerman et al., 1996; Thewes, Meiser, & Hickie, 2001). This finding also highlights the need for careful attention to the face validity of measures used in psychosocial oncology research. Alternatively, however, it is also very helpful to know how distress within a given cancer population compares with population-based norms.

A discussion of personality and individual differences and their relationship to cancer incidence and progression cannot neglect mention of health behaviors. Minimal attention has been given to the role of individual differences in health behaviors that put people at risk for cancer initiation, progression, and recurrence (Garssen & Goodkin, 1999); however, more recent studies are characterizing these associations. Personality attributes, such as extraversion, neuroticism, and mastery, are associated with smoking initiation among women (van Loon, Tijhuis, Surtees, & Ormel, 2001). Among low conscientiousness women, higher psychological distress is associated with lower mammography utilization (Schwartz et al., 1999); high conscientiousness individuals who perceive high risk from radon in conjunction with smoking report a reduction over time in the proportion of cigarettes smoked in the home (Hampson, Andrews, Barckley, Lichtenstein, & Lee, 2000). Psychosocial oncology could benefit from more explicit examination of these processes.

The unique immunological and psychosocial phenomena concomitant with cancer initiation and progression should shape empirical study of psychosocial oncology. As both Segerstrom and Hawkley point out in their articles (this issue), psychosocial factors, as mediators of psychoneuroimmunological and physiological pathways, are likely important for cancer. We, too, believe there is a silver lining, even amidst divergent findings and continuous debate. It is likely the effects of individual differences have more bearing upon cancer progression, rather than development (Butow et al., 2000; Fox, 1983). However, only careful methodological attention to the cancer context will clarify who gets, and who survives, cancer.

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References

Andersen, B. L. (2002). Biobehavioral outcomes following psychological interventions for cancer patients. *J. Consult. Clin. Psychol., 70*(3), 590–610.

Brown, F. (1966). The relationship between cancer and personality. *Ann. N Y Acad. Sci., 125*(3), 865–873.

Butow, P. N., Hiller, J. E., Price, M. A., Thackway, S. V., Kricker, A., & Tennant, C. C. (2000). Epidemiological evidence for a relationship between life events, coping style, and personality factors in the development of breast cancer. *J. Psychosom. Res., 49*(3), 169–181.

Croyle, R. T., Smith, K. R., Botkin, J. R., & Baty, B., et al. (1997). Psychological responses to BRCA1 mutation testing: Preliminary findings. *Health Psychol., 16*(1), 63–72.

Evans, E. (1926). *A psychological study of cancer*. Oxford, England: Dodd Mead.

Eysenck, H. J. (2000). Personality as a risk factor in cancer and coronary heart disease. In D. T. Kenny & J. G. Carlson et al. (Eds.), *Stress and health research and clinical applications* (pp. 291–318). Amsterdam, Netherlands: Harwood Academic Publishers.

Finn, O. J. (2001). Assessing the important effector mechanisms in the immune response against cancer. In A. Baum & B. L. Andersen (Eds.), *Psychosocial interventions for cancer* (pp. 175–191). Washington, DC: American Psychological Association.

Fox, B. H. (1978). Cancer death risk in hospitalized mental patients. *Science, 20l*, 966–967.

Fox, B. H. (1983). Current theory of psychogenic effects on cancer incidence and prognosis. *J. Psychosoc. Oncol., 1*(1), 17–31.

Garssen, B., & Goodkin, K. (1999). On the role of immunological factors as mediators between psychosocial factors and cancer progression. *Psychiatry Res., 85*(1), 51–61.

Glaser, R., Thorn, B. E., Tarr, K. L., Kiecolt-Glaser, J. K., & D'Ambrosio, S. M. (1985). Effects of stress on methyltransferase synthesis: An important DNA repair enzyme. *Health Psychol., 4*, 403–412.

Hampson, S. E., Andrews, J. A., Barckley, M., Lichtenstein, E., & Lee, M. E. (2000). Conscientiousness, perceived risk, and risk-reduction behaviors: A preliminary study. *Health Psychol., 19*(5), 496–500.

Hann, D., Winter, K., & Jacobsen, P. (1999). Measurement of depressive symptoms in cancer patients: Evaluation of the center for epidemiological studies depression scale (CES-D). *J. Psychosom. Res., 46*(5), 437–443.

Kiecolt-Glaser, J. K., & Chee, M. (1991). Personality, stress, and cancer: A re-examination. *Psychol. Inquiry, 2*(3), 249–251.

Kiecolt-Glaser, J. K., & Glaser, R. (1999). Psychoneuroimmunology and cancer: Fact or fiction? *Eur. J. Cancer, 11*, 1603–1607.

Lerman, C., Schwartz, M. D., Miller, S. M., Daly, M., Sands, C., & Rimer, B. K. (1996). A randomized trial of breast cancer risk counseling: Interacting effects of counseling, educational level, and coping style. *Health Psychol., 15*(2), 75–83.

Mischel, W., & Shoda, Y. (1995). A cognitive-affective system theory of personality: Reconceptualizing situations, dispositions, dynamics, and invariance in personality structure. *Psychol. Rev., 102*(2), 246–268.

Schwartz, M. D., Taylor, K. L., Willard, K. S., Siegel, J. E., Lamdan, R. M., & Moran, K. (1999). Distress, personality, and mammography utilization among women with a family history of breast cancer. *Health Psychol., 18*(4), 327–332.

Setlow, R. B. (1978). Repair deficient human disorders and human cancer. *Nature, 271*, 713–717.

Suls, J., & Wan, C. K. (1993). The relationship between trait hostility and cardiovascular reactivity: A quantitative review and analysis. *Psychophysiology, 30*(6), 615–626.

Thewes, B., Meiser, B., & Hickie, I. B. (2001). Psychometric properties of the Impact of Event Scale amongst women at increased risk for hereditary breast cancer. *Psycho-Oncology, 10*(6), 459–468.

Tomei, L. D., Kiecolt-Glaser, J. K., Kennedy, S., & Glaser, R. (1990). Psychological stress and phorbol ester inhibition of radiation-induced apoptosis in human PBLs. *Psychiatry Res., 33*, 59–71.

van Loon, A. J. M., Tijhuis, M., Surtees, P. G., & Ormel, J. (2001). Personality and coping: Their relationship with lifestyle risk factors for cancer. *Pers. Individ. Diff., 31*(4), 541–553.