Can Affective Processes Influence Cancer Biology?

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Affective Science Perspectives on Cancer Control
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Affect & Cancer: Historical Overview

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• State of the science: Epidemiological, prospective, psychological intervention, & pharmacological intervention studies suggest a link!

Stress & Affect

Affect = Stress
Stress & Affect

Stress

Hans Selye:

**Stressor** = “a change in an organism’s internal or external environment which is perceived by the organism as threatening”.

**Stress** = perceived threat associated with “an alteration in the body’s hormonal and neuronal secretions caused by the central nervous system in response to a perceived threat”.

**Distress** – “negative stress” v/s **Eustress** – “positive stress”

Affective processes in the context of cancer
Environmental & psycho-social factors with an affective dimension

Stress...


Adverse life events (bereavement, divorce, loss of loved one…)

Social support/social isolation

Depression, Anxiety

Emotional distress, poor QOL

Psychological interventions

In animals:
Psychological stress paradigms
Environmental & psycho-social factors with an affective dimension

Affective processes in the context of cancer

Emotion regulation, Coping, & Personality

Type C personality/coping style & emotional suppression

Hopelessness/pessimism

Active coping/avoidance

Denial/minimization

Fighting spirit

Dispositional optimism

No relationship between personality & cancer?

Post-traumatic growth; benefit-finding – adaptive?

Emotional wellbeing

In animals:

Environmental enrichment
At the interface of affect and cancer: From affect & brain to neuroendocrine system

**Affect**

Core limbic structures-
- Amygdala
- Periaqueductal Gray (PAG)
- Hypothalamic activations (Hy)


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Does Stress influence Cancer?

Inconsistent or weak associations have been identified regarding cancer incidence

The association between stressful life events and breast cancer risk: A meta-analysis

Do stress-related psychosocial factors contribute to cancer incidence and survival?
Chida Y et al. (2008) Nature Clinical Practice Oncology 56 (8): 466-475
Does Stress influence Cancer?

Epidemiological and clinical studies document significant evidence for cancer progression.

*Social network, social support, and survival after breast cancer diagnosis*
Kroenke CH et al. (2006) JCO 24 (7): 1105-1111

*Psychological distress and cancer mortality*
How does Stress influence Cancer
The Hallmarks of Cancer

Adapted from Hanahah D and Weinberg RA (2001) Cell 144: 646-674
Neuroendocrine Influences on the Tumor Microenvironment

Antoni MH, McDonald PG et al. 2006 Nat Rev Cancer 6 (3): 240-248
Behavioral Factors and Gene Expression Regulation

Lutgendorf SK et al. (2009) *BBI* 23: 176-183
Social Isolation Alters Mammary Gland Gene Expression and Increases Tumor Growth

Alteration in Lipid Synthesis and Glycolytic Pathway Gene Expression

Chronic Stress promotes Tumor Growth and **Angiogenesis** in Ovarian Carcinoma

Inflammatory Cytokines

- Stress Hormones regulate **IL-6** expression by human ovarian carcinoma cells via a Src-dependent mechanism.
- Stress increases **IL-8** expression associated with ovarian cancer growth and metastasis.
Invasion and Migration

• Stress hormones increase cancer cells production of MMP-2 and MMP-9 through β-adrenergic signaling

• Negative affect and stress associated with higher MMP9 expression from TAMs in ovarian carcinoma
NE and E Protect Human Ovarian Cancer Cells from Anoikis through Adrenergic Pathway

SNS as a novel regulator of Breast Cancer Metastasis

Can Cancer affect Emotion?

• Peripheral Tumors induce Depressive-like Behaviors and Cytokine production and alter HPA axis Regulation

• In Ovarian Cancer Patients IL-6 and Cortisol are related to Depressive Symptoms

Lutgendorf SK et al. (2008) *JCO* 26 (29): 4820-4827
Potential Therapeutic Strategies

- Beta adrenergic receptors blockade
- Dopamine antagonists
- Hypothalamic BDNF stimulation

Cao L et al. (2010) Cell 142 (9): 15-17
Associations between Positive Affect and Health outcomes

Mediating processes:

– Genetic substrate
– Lifestyle Factors
– Neuroendocrine, autonomic, immune and inflammatory pathways
– Psychosocial factors
Opportunities and Challenges

- Health Behaviors
- Affective Processes
- Biological Cancer-Risk Factors
- Neuroendocrine Regulation
- Immune Response
- Tumor Growth
- Metastasis

Adapted from Antoni MH, McDonald PG et al. 2006 Nat Rev Cancer 6 (3): 240-248
DNA damage

Stress Response Pathways Regulate DNA Damage through $\beta_2$-adrenoreceptors and $\beta$-arrestin-1
