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Review Article

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Asymmetry In Belief Updating And Carcinogenesis

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Abstract

Accumulating evidence shows that the central nervous system (CNS) regulates the activity of the immune system. Concerning the role of immune system in cancer, psychosocial influences on immune function provide a mechanism of association between psychosocial factors (like interpersonal aggression) and cancer prognosis. Social conflicts between males, involving high aggression stress and threat (psychosocial conflicts) produce both an allostatic state and allostatic load. The costs for aggressors (Hawks) and victims (Doves) tested under semi laboratory conditions are quite different. Testosterone does not cause aggression, only exaggerates the pre-existing pattern and response to environmental triggers of aggression.

Keywords: Aggression Stress, Asymmetry, The Allostatic Load, Testosterone, Type A personality, HPG-Axis, Inflammation, NF k B, IL-6, Stat3, Belief Updating, Carcinogenesis

Introduction

N Power means power-motivated individuals concerned with having impact over others, and they derive reward and reinforcement from having this impact [1]. Power-motivated individuals are more likely to be successful in managerial positions with vibrant careers. They tend to be perceived by others as competent. They also tend to make autocratic decisions [2]. Power-motivated individuals take bigger risk in gambling situations to garner attention. They are also more likely to be violent with their significant others, to abuse alcohol (drugs) and to be sexually promiscuous. Power-motivated individuals are coded to take strong and forceful actions that have impact over others, controlling, influencing others, offering advice, impressing others sexually, they need to achieve fame, prestige and reputation, and actions that elicit a strong emotional response in others [3]. These findings suggest that antisocial and predatory aggression lead to similar stress and are controlled by overlapping neural mechanisms [4,5].

Frustrated n Power: link to immune system impairment

By placing such experiments in a broader context, exploration of changes in real-life outcome behaviors as a function of testosterone or estradiol change in response to dominance contests bolster this research line with greater ecological validity. Exploration of potential relationship between frustrated n Power, cortisol, depression and carcinogenesis is also an important path of this new research. Frustrated n Power has been linked to immune system impairment, inflammation and cancer. The positive link between n Power frustration and cortisol release extend this line of research into exploration of correlations psychopathology with carcinogenesis [6].

In a neuropsychological perspective, fMRI gives a promise for the examination of the neurological basis of individual differences, and researchers in personality neuroscience are beginning to exploit this tool. There are published studies examining the moderating role of n Power on patterns of brain activation. The hypothalamus is active in control of hormone axes (hypothalamic-pituitary-gonadal and hypothalamic-pituitary-adrenal), as well as dominance behavior [7]. Studies of dominance use neuroimaging to measure the relationship between brain activation of the hypothalamus and its connection with other parts of the emotional brain and subsequent hormone release as a function of n Power. The aim is to uncover how the brain orchestrates the complex hormonal responses to dominance challenges, stressors, inflammation, and cancer. Both the striatum and the medial prefrontal cortex (MPFC) receive reward-related dopaminergic inputs from midbrain neurons that encode the reward prediction error (RPE) as the difference between the received and expected reward. The free-energy formulation of false inference can be used to explain positive symptoms in addiction of alcohol, drugs, power and sexuality. The MPFC is reciprocally connected to the posterior cingular cortex (PCC), and both are parts of the brain's default system, which attend to internal body and mental states [8].

Prejudice machine vs. belief updating

In theoretical and computational neuroscience we can focus on Helmholtz's suggestion that the brain is an inference machine. This idea is now a fundamental premise in neurobiology. Above framework assumes that the brain uses internal hierarchical models to predict its sensory input and suggests that neuronal activity (and synaptic connections) try to minimize the ensuing prediction error or free-energy. This free-energy is a measure of surprise and essentially the amount of prediction-error. In both accounts higher cortical areas organize activity of lower-levels through suppression of their freeenergy. In this connection we examined a role of marked

asymmetry in belief updating outgoing from the research previously published by authors from Welcome Trust Centre for Neuroimaging in London [9]. Probably Hawks personalities updated their beliefs more in response to information better than expected, while Doves were not excluding also information that was worse. This selectivity can be mediated by a relative failure to code for errors reducing optimism in Hawks. The prefrontal cortex tracked estimation errors called for positive update, both in subjects scored high (Hawks) or low (Doves) on trait optimism. Optimistic Hawks probably exhibit reduced tracking of estimation errors calling for negative update in right inferior prefrontal gyrus. Optimism tied to a selective update failure and diminished neural coding of undesirable information regarding the future have a positive impact on the health status of Hawks. Pessimism and depressive mode in Doves may have a negative effect on their health status. It is indicating that in brain is activated a basic mechanism such as prejudice machine, influencing the health perspectives of the individuals.

Of particular interest here is the so called 'default-mode network' (DMN), a network of regions that show high metabolic activity and blood flow at rest but which deactivate during goal-directed cognition [10]. We associate failures of top-down control with non-ordinary states of consciousness, such as early and acute psychosis, the temporal-lobe aura, dreaming, hallucinogenic drug states and the Strauss-Kahn syndrome. There is evidence that a loss of top-down control over limbic activity in hierarchically lower systems is equivalent to a loss of the ego's control over conscious process. Failure of system to minimize free-energy (suppress endogenous excitation) results in disturbed affect, cognition and perception, and this is seen in psychosis or in Strauss-Kahn syndrome.

Aggression as psychological stress

In this our study evident that social conflicts including interpersonal difficulties can also have detrimental influences on health. Chronic conflictual interactions foster low-grade systemic inflammation contributes to evolution of psychiatric, infectious, metabolic and cancer [3,4,11,12]. Our study associates with growing evidence about mechanisms converting aggression stress into cellular dysfunction. It is widely accepted that psychological stress affects the immune response, and repeated exposure to a stressor is immunosuppressive. Suppression of immunity is due to anti-inflammatory effects of adrenal glucocorticoid (GC) hormones. Ligation of GC receptors on mononuclear cells suppresses the expression of cytokines, chemokines, and adhesion molecules through a negative regulation of NFkB activation and function. Psychological stress and exposure to the stressor social disruption (SDR) increase cytokine production by monocytes/macrophages and reduce their sensitivity to corticosterone. Splenic monocytes/macrophages from socially stressed mice are primed to be more physiologically active than nonstressed controls. Psychological stress is not always immunospuppressive, if the stressor induces a state of functional GC resistance (for example the murine SDR causes resistance of splenic macrophages) [13]. Repeated social defeat during SDR resulted in a significant increase in spleen mass and the number of splenic monocytes/macrophages and granulocytes. It indicates that repeated social defeat during the SDR stressor enhances innate immunity to E. coli infection and SDR significantly impacts splenic monocytes/macrophages. Several studies demonstrating that macrophages are primed during repeated social defeat. In the nucleus, the translocated GC receptors acts as a ligand-dependent transcription factor to modulate the expression of GC-responsive genes, or to suppress activity of other transcription factors, like NFkB.

Strategy of authoritarian Hawks

In evolutionary terms different organisms adopt different behavioral strategies to cope with stress. For our conceptual framework of the aggression stress is central the strategy of authoritarian Hawks, showing that inefficient management of allostasis mediators may lead to violent behavior, development of impulse control disorders and inflammation [14]. In a competitive situation the Hawk shows aggressive behavior, stopping only if injured or when the opponent submits. The Hawk generally wins the entire resources. If the Hawk is unsuccessful, may have lower fitness because of energy loss, wounds, blood loss and infection, which can lead to the inflammation. This can be also a consequence for Doves as the victims of an aggression stress [1,15]. Authoritarian Hawks show a fight-flight response during which an activation of the hypothalamic-pituitary-gonadal (HPG) axis is increasing the plasma level of the testosterone. Testosterone increases the likelihood of aggression by stimulating vasopressin synthesis. Higher impulsivity may be a consequence of lowered activity of the tonic 5-HT neurotrasmitter system [11,16,17]. Authoritarian Hawks with their high sympathetic reactivity are more vulnerable to developing tachyarhytmias than Doves. Shift of autonomic balance toward sympathetic dominance makes Hawks vulnerable to sudden death once apoptosis has developed in the heart. Sympathetic system hyperactivity affects not only the cardiovascular system but also the immune system. A growing number of animal findings strongly suggest that a hyporeactive HPA axis may be pathologically significant through a shift to Th1 cytokines that increases susceptibility to chronic inflammation [18]. Hawks have an increased risk of wound and infections because they are more aggressive and bolder than Doves [19]. Th1 dominated cellular immune response in Hawks is very adaptive against infections. But this hyperimmune state together with a blunted HPA axis activity incures costs such as the risk of inflammation and autoimmune disease. The lower parasympathetic reactivity of Hawks show that they are less well equipped to inhibit the release of macrophage cytokines via the vagal parasympathetic route. The increased release of cytokines can contribute to the costs of allostatic load of Doves [17].

NF- B and Stat3 integrate interpersonal stress signals

Nuclear factor- kB (NF- kB) and Stat3 proteins are transcriptional factors, which integrate stress signals and orchestrate immune responses also linked to carcinogenesis [20-22]. Cancer development in Doves include: self-sufficiency in growth signals, insensitivity to growth inhibitors, evasion of apoptosis, limitless replicative potential, tissue invasion, metastasis and sustained angiogenesis. NF-kB signaling is involved in all these hallmarks. Recent experimental studies showing the mechanistic pathways by which NF-kB signaling contributes to carcinogenesis. Inflammation promotes carcinogenesis, NF- kB and Stat3 signaling integrate interpersonal stress signals during this process [2,14,23]. NF- kB and Stat3 control the expression of anti-apoptotic, pro-proliferative and immune response genes. These genes overlap and show transcriptional cooperation and inhibition between the two factors. Activation and interaction between NF- kB and Stat3 plays a key role in control of the dialog between the malignant cell and its microenvironment, with inflammatory/immune cells that infiltrate tumors [7,19]. Cytokines induced in response to NF- kB in immune cells of the tumor microenvironment lead to Stat3 activation in both malignant

and immune cells. Within malignant and pre-malignant cells Stat3 activates oncogenic functions, within inflammatory cells it may also suppress tumor promotion through its anti-inflammatory effects.

An unstable hierarchy produces robust changes in allostatic state depending on the social status of the primates [24]. A relationship exists between stress-related diseases and behavioral strategy of Doves. It was observed that humans with type A personality are more aggressive and hostile, extremely competitive, impatient and always in a hurry. Authoritarian personality type A closely resembles the Hawk type.

Conclusion

Psychoneuroimmune interactions could be one of the biologic mechanism underlying correlations between psychologic factors and cancer. A possible mechanism suggested by recent studies are factors secreted by leucocytes (cytokines) which can influence both immune and CNS processes. The evidence for physiologic pathways linking the CNS and the immune system suggests that "hardwiring" is in place for regulation of the immune system by the CNS. The association between times of psychologic distress (aggression) and reductions in proliferative response of lymphocytes cultured with mitogens, are mitogens that activate T-cells. This in vitro measure of lymphocytes activation, sensitive to psychosocial influences is linked to any disease outcome. There are studies that have explored the relationships between psychosocial variables and natural killer (NK) cell activity. This studies support the link between psychosocial factors (aggression) and alterations in immune function in Doves personalities.

In conclusion, the research related to possible psychoneuroimmunologic processes in Doves'cancer provides support for the following hypotheses: (1) the outcome of some cancers can be influenced by psychosocial factors, (2) the activities of the immune system can influence the outcome of some cancers, (3) immune responses such NK-cell activity play role in defenses against cancer, appears be influenced by psychosocial factors (aggression). Alterations in immune defenses can be investigated as a possible mechanism by which psychosocial factors could influence cancer. Chronic inflammation in Doves promotes tumor development and is not the one response but instead represents a dynamic, continuously changing microenvironmental process with various effects at subsequent stages of tumorigenesis. Multiple factors in both the host and the malignant cells, the malignancy has impact on the inflammatory response in Doves and vice versa [17]. Once the locus coeruleus (LC) become hyperactive due a positive correlation between hypercortisolism and increased cerebrospinalfluid (norepinephrine - NE), this core system in Doves may enter a vicious circle, because the LC can inhibit the prefrontal cortex. The allostatic load in Doves may be in their microenvironment pathologically significant through a shift to Th1 cytokines and increasing susceptibility to chronic inflammation, which can on the long term trigger various forms of cancer in Doves. Most of tumors contain inflammatory and immune cells macrophages and lymphocytes, which produce cytokines and other factors that promote tumor growth and survival. Tumor-promoting role of immune cells is manifested in inflammation-associated cancers, where tumors arise and grow at sites of chronic inflammation in Doves [25]. Lymphocytes, IL-6, NF B may be part of the translational entry points into the neural circuit regulating immune changes induced by environmental stress in Doves, leading to development of cancer. The stressor significantly increased circulating levels of IL-6 and MCP-1, significantly correlated with stressor-induced changes to three bacterial genera: Cprococcus, Pseudobutyrivibrio, and Dorea [13,26,27].

Social conflicts caused by the interpersonal aggression mediated by authoritarian type A personality of males is involving complicated immune network of the psychosocial threat of cancer in Doves as the end stage of inflammation [28,29]. It has been shown in a population of mice, that males with high testosterone outnumbered those with lower levels, but the presence of too many aggressive individuals resulted in a crisis of the population. This extends into humans a large corpus of animal research, suggesting that an organism's physiology is intimately regulated by the interpersonal context in which s/he resides.

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References

1. Adorno TW, Frankel-Brunswick E, Levinson DJ, Sanford RN (1950) The Authoritarian Personality. Harper and Row, New York.
2. Bollrath J, Greten FR (2009) IKK/ NF- kB and STAT3 pathways: central signaling hubs in inflammation-mediated tumor promotion and metastasis. EMBO Rep 10: 1314-1319.
3. Barnes PJ, Karin M (1997) Nuclear factor- kB: a pivotal transcription factor in chronic inflammatory diseases. N Engl J Med 336: 1066-1071.
4. Slavich GM, Way BM, Eisenberger NI, and Taylor SE (2010) Neural sensitivity to social rejection is associated with inflammatory responses to social stress.
5. Tulogdi A, Toth M, Halasz J, Mikics E, Fuzesi T, et al. (2010) Brain mechanisms involved in predatory aggression are activated in a laboratory model of violent intra-specific aggression. The European Journal of Neuroscience 32: 1744-1753.
6. Stanton SJ, Schultheiss OC (2009) The hormonal correlates of implicit power motivation. J Res Pers 43: 942.
7. Al Zaid SK, Turkson J (2008) STAT3 as a target for inducing apoptosis in solid and hematological tumors. Cell Res 18: 254-267.
8. Raichle ME, MacLeod AM, Snyder AZ et al., (2001) A default mode of brain function. Proc Natl Acad Sci USA 98: 676-682.
9. Sharot T, Korn WK & Dolan RJ (2011) How unrealistic optimism is maintained in the face of reality. Nature Neuroscience.
10. Carhart-Harris RL and Friston KJ (2010) The default-mode, ego-functions and free-energy: a neurobiological account of Freudian ideas. Brain 133: 1265-1283.
11. Tracey KJ (2002) The inflammatory reflex. Nature 420: 19-26.
12. Greten FR, Eckmann L, Greten TF, Park JM, Li ZW, et al. (2004) IK B links inflammation and tumorigenesis in a mouse model of colitis-associated cancer. Cell 118: 285-296.
13. Bailey MT, Engler H, Sheridan JF, Powell ND, Padgett DA (2007) Repeated social defeat increases the bactericidal activity of splenic macrophages through a Toll-like receptor-dependent pathway. Am J Physiol Regul Integr Comp Physiol 293: R1180-R1190.
14. Pikarsky E, Porat AM, Stein I, Abramovitch R, Amit S, et al. (2004) NF- B functions as a tumor promoter in inflammation-associated cancer. Nature 431: 461-466.
15. Bierhaus A, Wolf J, Andrassy M, Rohleder N, Humpert PM,

et al. (2003) A mechanism converting psychosocial stress into mononuclear cell activation. Proc Natl Acad Sci USA 100: 1920-1925.
16. Stark JL, Avitsur R, Sheridan JF, Hunzeker J, Padgett DA (2002) Interleukin-6 and the development of social disruption-induced glucocorticoid resistance. J Neuroimmunol 124: 9-15.
17. Korte SM, Koolhaus JM, Wingfield JC, McEwen BS (2005) The Darwinian concept of stress: benefits of allostasis and costs of allostatic load and the trade-offs in health and disease. Neuroscience and Biobehavioral Reviews 29: 3-38.
18. Meira LB, Bugni JM, Green SL, Lee CW, Pang B, et al. (2008) DNA damage induced by chronic inflammation contributes to colon carcinogenesis in mice. J Clin Invest 118: 2516-2525.
19. He G, Karin M (2011) NF- k B and STAT3 – key players in liver inflammation and cancer. Cell Research 21: 159-168.
20. Zhong Z, Wen Z, Darnell JE (1994) Stat3: a STAT family member activated by tyrosine phosphorylation in response to epidermal growth factor and interleukin-6. Science 264: 95-98.
21. Hirano T, Ishihara K, Hibi M (2000) Roles of STAT3 in mediating the cell growth, differentiation and survival signals relayed through the IL-6 family of cytokine receptors. Oncogene 19: 2548-2556.
22. Takeda K, Akira S (2000) STAT family of transcription factors in cytokine-mediated biological responses. Citokine Growth Factor Rev 11: 199-207.
23. Lee H, Herrmann A, Deng JH, Kujawski M, Niu G, et al. (2009) Persistently activated Stat3 maintains constitutive NF- k B activity in tumors. Cancel Cell 15: 283-293.
24. Mays JW, Bailey MT, Sheridan JF, Hunzeker JT, Powell ND, et 29. al. (2010) Influenza Virus-Specific Immunological Memory Is Enhanced by Repeated Social Defeat. J Immunol 184 : 2014-2025
25. Grivennikov S, Karin E, Terzic J, Mucida D, Yu GY, et al. (2009) IL-6 and Stat3 Are Required for Survival of Intestinal Epithelial Cells and Development of Colitis-Associated Cancer. Cancer Cell 15: 103.
26. Bailey MT, Dowd SE, Galley JD, Hufnagle AR, Allen RG, et al. (2011) Exposure to a social stressor alters the structure of the intestinal microbiota: Implications for stressor-induced immunomodulation. Brain, Behavior and Immunity 25: 397-407.
27. Grivennikov SI, Karin M (2010) Dangerous liaisons: STAT3 and NF- B collaboration and crosstalk in cancer. Cytokine Growth Factor Rev 21: 11-19.
28. Naugler WE, Sakurai T, Kim S, Maeda S, Kim K, et al. (2007) Gender disparity in liver cancer due to sex diffrences in MyD88-dependent IL-6 production. Science 317: 121-124.
29. Stanton SJ, Mulette-Gilman OA, McLaurin RE, Kuhn CM, LaBar KS, et al. (2011) Low-and High-Testosterone Individuals Exhibit Decreased Aversion to Economic Risk. Hormones and Behavior 59: 252-256.