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Research, part of a Special Feature on Managing Surprises in Complex Systems

Developmental Disorders as Pathological Resilience Domains

Rodrick Wallace

ABSTRACT. Ecosystem resilience theory permits novel exploration of developmental psychiatric and chronic physical disorders. Structured psychosocial stress, and similar noxious exposures, can write distorted images of themselves onto child growth, and, if sufficiently powerful, adult development as well, initiating a punctuated life course trajectory to characteristic forms of comorbid mind/body dysfunction. For an individual, within the linked network of broadly cognitive psysiological and mental subsystems, this occurs in a manner almost exactly similar to resilience domain shifts affecting a stressed ecosystem, suggesting that reversal or palliation may often be exceedingly difficult. Thus resilience theory may contribute significant new perspectives to the understanding, remediation, and prevention, of these debilitating conditions.

Key Words: *chronic disease, cognition, comorbidity, developmental disorder, ecosystem, resilience*

INTRODUCTION

Ecosystem theorists recognize several different kinds of resilience (e.g., Gunderson 2000). The first, which they call engineering resilience, since it characterizes of machines and man-machine interactions, involves the rate at which a disturbed system returns to a presumed single, stable equilibrium condition, following perturbation. From that limited perspective, a resilient system is one that quickly returns to its single stable state. Not many biological phenomena, including those of human physiology and psychology, are actually resilient in this simplistic sense. Holling's (1973) great contribution was to recognize that sudden, highly punctuated, transitions between different, at best quasi-stable, domains of relation among ecosystem variates were possible, i.e., that more than one “stable” state was possible for real ecosystems (e.g. Gunderson 2000). Thus ecosystem resilience differs greatly from the engineering perspective.

This paper reexamines a large class of broadly cognitive mental and physiological phenomena, focusing on a spectrum of comorbid human developmental disorders that may, in fact, constitute complex, pathological resilience domains. The usually irreversible and punctuated nature of path dependence in ecosystem domain shifts sheds new light on the therapeutic intractability of many such conditions. It is important to note that punctuated biological phenomena are found across a great range of temporal scales (e.g., Eldredge 1985, Gould 2002). For example species appear suddenly on a geologic time scale, persist relatively unchanged for a fairly long time, and then disappear suddenly again on a geologic time scale. Evolutionary process is vastly speeded up in tumorigenesis, which nonetheless seems amenable to similar analysis (e. g., Wallace et al. 2003*a*). We will describe a model that adapts the asymptotic limit theorems of information theory to ecosystem resilience theory much in the way the central limit theorem is used in parametric statistical inference. The strength of such an approach is that it is almost independent of the detailed structure of the interacting information sources inevitably associated with both cognitive and ecosystem processes, important as such structure may be in other contexts. We begin with a brief overview of developmental pathologies and their comorbidities at both community and individual scales.

COMORBID DISORDERS

Certain mental disorders, for example depression and substance abuse, and many physical conditions like lupus, coronary heart disease, hypertension,

breast and prostate cancers, diabetes, obesity, and asthma show marked regularities at the community level of organization according to the social constructs of race, ethnicity, socioeconomic status, and, appropriately, gender. Population-level structure in disease permits profound insight into etiology because, to the extent these are environmental disorders, the principal environment of humans is, in fact, other humans, moderated by a uniquely characteristic embedding cultural context (e.g., Durham 1991, Richerson and Boyd 2004). Thus culturally sculpted social exposures are likely to be important at the individual, and critical at the population, levels of organization in the expression of certain mental disorders and a plethora of chronic diseases. Further, mental disorders are often comorbidly expressed, both among themselves and with certain kinds of chronic physical disorder: picture the obese, diabetic, depressed, anxious patient suffering from high blood pressure, asthma, coronary heart disease, and so on. Such comorbidity is the rule rather than the exception for the seriously ill, and is the central focus of this work. As Cohen (2000) describes for autoimmune disease, however, the appearance of co- and antico-morbid conditions is, given the possibilities, rather surprisingly constrained to a relatively few often recurring patterns.

Here we are interested in how cognitive submodules of human physiology and mental process may become synergistically linked with embedding, culturally structured psychosocial stress to produce comorbid patterns of illness associated with mental disorder and chronic disease. A broad body of research suggests that many such disorders either have their roots in utero, as a stressed mother communicates environmental signals across the placenta, and programs her developing child's physiology, or else are initiated during early childhood (e.g., Bandelow et al. 2002, Barker 2002, Barker et al. 2002, Coplan et al. 2005, Egle et al. 2002, Eriksson et al. 2000, Godfrey and Barker 2001, Lalumiere et al. 2001, Mealey 1995, Osmond and Barker 2000, Repetti et al. 2000, Smith et al. 1998, Smith and Ruiz 2002, Wright et al. 1998). This pattern may affect underlying susceptibility to chronic infections or parasitic infestation as well as more systemic disorders (e.g., Wallace and Wallace 2004). The questions of central interest are the effects of stress on the interaction between mind and body over the life course. Stress is not often random in human societies, but is most frequently itself a socially constructed cultural artifact, very highly organized, having both a grammar and syntax. That is, certain stressors are meaningful in a particular developmental context, and others are not, with little or no long-term physiological effect. Stress is, then, often a kind of language.

The formal analysis begins with a recitation of some cognitive submodules of human biology, in a large sense, which interact both with each other and with structured psychosocial stress. Next follows an exploration of cognition as a kind of language. Ultimately there emerges a generalized model based on Cohen's vision of autoimmune disease that accounts for a punctuated life trajectory of chronic comorbid psychiatric/physical disorder as involving a usually transient excited state of the system that becomes a pathologically permanent, or semi-permanent zero-mode. The particular innovation here is to express this mechanism in terms of ecosystem resilience theory.

SOME COGNITIVE MODULES OF HUMAN BIOLOGY

Immune function

Atlan and Cohen (1998) have proposed an information-theoretic cognitive model of immune function and process, a paradigm incorporating cognitive pattern recognition-and-response behaviors analogous to those of the central nervous system. This work follows in a very long tradition of speculation on the cognitive properties of the immune system (e.g., Tauber 1998, Podolsky and Tauber 1998, Grossman 1989, 1992, 1993, 2000, Grossman et al. 1992). We focus particularly on the Atlan and Cohen (1998) work, not because it conceived the idea of a cognitive immune system, but rather because it reinterprets cognitive process in terms of information in a particular manner. From the Atlan/Cohen (1998) perspective, the meaning of an antigen can be reduced to the type of response the antigen generates. That is, the meaning of an antigen is functionally defined by the response of the immune system. The meaning of an antigen to the system is discernible in the type of immune response produced, not merely whether the antigen is perceived by the receptor repertoire. Because the meaning is defined by the type of response, there is indeed a response repertoire and not only a receptor repertoire.

To account for immune interpretation Cohen (1992, 2000) has reformulated the cognitive paradigm for the immune system. The immune system can respond to a given antigen in various ways, it has options. Thus the particular response we observe is the outcome of internal processes of weighing and integrating information about the antigen. In contrast to Burnet's view of the immune response as a simple reflex, it is seen to exercise cognition by the interpolation of a level of information processing between the antigen stimulus and the immune response. A cognitive immune system organizes the information borne by the antigen stimulus within a given context and creates a format suitable for internal processing; the antigen and its context are transcribed internally into the "chemical language" of the immune system (Cohen 2000).

The cognitive paradigm suggests a language metaphor to describe immune communication by a string of chemical signals. This metaphor is apt because the human and immune languages can be seen to manifest several similarities such as syntax and abstraction. Syntax, for example, enhances both linguistic and immune meaning. Although individual words and even letters can have their own meanings, an unconnected subject or an unconnected predicate will tend to mean less than does the sentence generated by their connection.The immune system creates a "language" by linking two ontogenetically different classes of molecules in a syntactical fashion. One class of molecules is the T and B cell receptors for antigens. These molecules are not inherited, but are somatically generated in each individual. The other class of molecules responsible for internal information processing is encoded in the individual's germline. In other words, the chosen type of immune response is the outcome of the concrete connection between the antigen subject and the germline predicate signals. The transcription of the antigens into processed peptides embedded in a context of germline ancillary signals constitutes the functional `language' of the immune system. Despite the logic of clonal selection, the immune system does not respond to antigens as they are, but to abstractions of antigens-in-context.

Tumor control

Another cognitive submodule appears to be a tumor control mechanism that may include "immune surveillance," but clearly transcends it. Nunney (1999) has explored cancer occurrence as a function of animal size, suggesting that in larger animals, whose lifespan grows as about the 4/10 power of their cell count, prevention of cancer in rapidly proliferating tissues becomes more difficult in proportion to size. Cancer control requires the development of additional mechanisms and systems to address tumorigenesis as body size increases, i. e., a synergistic effect of cell number and organism longevity. Nunney (1999:497) concludes:

> *This pattern may represent a real barrier to the evolution of large, long-lived animals and predicts that those that do evolve ... have recruited additional controls [over those of smaller animals] to prevent cancer.*

Forlenza and Baum (2000) explore the effects of stress on the full spectrum of tumor control, ranging from DNA damage and control, to apoptosis, immune surveillance, and mutation rate. Elsewhere (Wallace et al. 2003*a*) we argue that this elaborate tumor control strategy, particularly in large animals, must be at least as cognitive as the immune system itself, which is one of its components. That is, some comparison must be made with an internal picture of a healthy cell, and a choice made as to response: none, attempt DNA repair, trigger programmed cell death, engage in full-blown immune attack. This is, from the Atlan/Cohen (1998) perspective, the essence of cognition.

The hypothalamic-pituitary-adrenal (HPA) axis

The hypothalamic-pituitary-adrenal (HPA) axis, a part of the general flight-or-fight system including the sympathoadrenomedullary system (SAM), is clearly cognitive in the Atlan/Cohen (1998) sense. Upon recognition of a new perturbation in the surrounding environment, memory and brain or emotional cognition evaluate and choose from several possible responses: no action needed, flight, fight, helplessness, i.e., flight or fight needed, but not possible. Upon appropriate conditioning, the HPA system, in coordination with the SAM axis, is able to accelerate the decision process, much as the immune system has a more efficient response to second pathogenic challenge once the initial infection has become encoded in immune memory. Certainly hyperreactivity in the context of post-traumatic stress disorder (PTSD) is a well-known example. Chronic HPA axis activation is deeply

implicated in visceral obesity leading to diabetes and heart disease, via the leptin/cortisol diurnal cycle (e.g., Bjorntorp 2001, Wallace and Wallace 2005).

Blood pressure regulation

Rau and Elbert (2001) review much of the literature on blood pressure regulation, particularly the interaction between baroreceptor activation and central nervous function. We paraphrase something of their analysis. The essential point, of course, is that unregulated blood pressure would be quickly fatal in any animal with a circulatory system, a matter as physiologically fundamental as tumor control. Much work over the years has elucidated some of the mechanisms involved. Increase in arterial blood pressure stimulates the arterial baroreceptors that in turn elicit the baroreceptor reflex, causing a reduction in cardiac output and in peripheral resistance, returning pressure to its original level. The reflex, however, is not actually this simple. It may be inhibited through peripheral processes, for example under conditions of high metabolic demand. In addition, higher brain structures modulate this reflex arc, for instance when threat is detected, and fight or flight responses are being prepared. This suggests, then, that blood pressure control cannot be a simple reflex, but is a broad and actively cognitive modular system that compares a set of incoming signals with an internal reference configuration, and then chooses an appropriate physiological level of blood pressure from a large repertoire of possible levels.

Emotion

Thayer and Lane (2000) summarize the case for what can be described as a cognitive emotional process. Emotions, in their view, are an integrative index of individual adjustment to changing environmental demands, an organismal response to an environmental event that allows rapid mobilization of multiple subsystems. Emotions are the moment-to-moment output of a continuous sequence of behavior, organized around biologically important functions. These lawful sequences have been termed behavioral systems by Timberlake (1994).

Emotions are self-regulatory responses that allow the efficient coordination of the organism for goal-directed behavior. Specific emotions imply specific eliciting stimuli, specific action tendencies including selective attention to relevant stimuli, and specific reinforcers. When the system works properly, it allows for flexible adaptation of the organism to changing environmental demands. Thus an emotional response represents a selection of an appropriate response and the inhibition of other less appropriate responses from a more or less broad behavioral repertoire of possible responses. Such choice leads directly to something closely analogous to the Atlan and Cohen (1998) language metaphor.

Consciousness

Although a Cartesian dichotomy between rational thought and emotion may be increasingly suspect, nonetheless humans, like many other animals, do indeed conduct conscious individual rational cognitive decision making as most of us would commonly understand it. Various forms of dementia involve characteristic patterns of degradation in that ability. Dehaene and Naccache (2001) describe the global neuronal workspace model of consciousness, and our own extension of that model is available elsewhere (Wallace 2005*a*, 2006, Wallace and Fullilove 2008), as is its explicit application to a spectrum of mental disorders (Wallace 2005*b*).

Sociocultural network

Humans are particularly noted for a hypersociality that inevitably enmeshes us all within group processes of decision, that is, collective cognitive behavior within a social network, tinged by an embedding shared culture (Wallace and Fullilove 2008). For humans, culture is truly fundamental. Durham (1991) argues that genes and culture are two distinct but interacting systems of inheritance within human populations. Information of both kinds has influence, actual or potential, over behaviors, which creates a real and unambiguous symmetry between genes and phenotypes on the one hand, and culture and phenotypes, on the other. Genes and culture are best represented as two parallel lines or tracks of hereditary influence on phenotypes.

COGNITION AS "LANGUAGE"

Atlan and Cohen (1998) argue that the essence of cognition is comparison of a perceived external signal with an internal, learned picture of the world, and then, upon that comparison, the choice of one response from a much larger repertoire of possible responses. We make a very general model of this process.

A pattern of broadly sensory input is mixed in a systematic algorithmic way with internal ongoing activity to create a path of composite signals according to some algorithm, which we call x. This path is then fed into a highly nonlinear, but otherwise unspecified, "decision oscillator" $h(x)$, which generates an output that is an element of one of two presumably disjoint sets $B0$ and $B1$. Thus, we permit a graded response, supposing that if $h(x)$ is in $B0$ the pattern is not recognized, and if $h(x)$ is in $B1$, the pattern is recognized and some action takes place.

We are interested in composite paths x which trigger pattern recognition-and-response. That is, given a fixed initial state, such that $h(a0)$ is in $B0$, we examine all possible subsequent paths x beginning with $a0$ and leading to the event "$h(x)$ is in $B1$." For each positive integer n let $N(n)$ be the number of paths of length n, which begin with some particular $a0$ having $h(a0)$ in $B0$ and lead to the condition $h(x)$ in $B1$. We shall call such paths meaningful and assume $N(n)$ to be considerably less than the number of all possible paths of length n, i.e., pattern recognition-and-response is comparatively rare, and occurs according to rules. We further assume that the finite limit

$$H = (\text{limit } n \dashrightarrow \text{oo}) \log[N(n)]/n$$

both exists and is independent of the path x. We call such a cognitive process ergodic (Ash 1990).

After some development it is possible to define an ergodic information source as "dual" to the ergodic cognitive process (Wallace and Fullilove 2008). A critical problem then becomes the choice of a "normal" zero-mode language among a very large set of possible languages representing the hyper- or hypo-excited states accessible to the system (Wallace and Fullilove 2008). In sum, meaningful paths, creating an inherent grammar and syntax, have been defined entirely in terms of system response, as Atlan and Cohen (1998) propose.

A MULTIPLICITY OF RESILIENCE TOPOLOGIES

An essential homology between information theory and statistical mechanics lies in the similarity of the expression for information source uncertainty (e.g. Ash, 1990),

$$H = \text{limit}(n \dashrightarrow \text{oo}) \log[N(n)]/n$$

with the infinite volume limit of the free energy density. If $Z(K)$ is the statistical mechanics partition function derived from the system's Hamiltonian, then the free energy density is determined by the relation (e.g., Landau and Lifshitz 2007).

$$F[K] = \text{limit}(V \dashrightarrow \text{oo}) \log[Z(K)]/V.$$

F is the free energy density, V the system volume and $K=1/T$, where T is the system temperature.

It can be shown (e.g., Wallace and Wallace 1998, 1999, Wallace 2000, 2005*a*, Wallace and Fullilove 2008, Rojdestvensky and Cottam 2000, Feynman 1996) that this systematic mathematical homology permits importation of renormalization symmetry and other tools of statistical mechanics into information theory. Imposition of invariance under renormalization on the information splitting criterion H implies the existence of phase transitions analogous to learning plateaus or punctuated evolutionary equilibria in the relations between cognitive mechanism and external perturbation.

The homology between information source uncertainty and free energy density allows us to analyze the dynamical properties of interacting cognitive systems using an analog to the Onsager relations of nonequilibrium thermodynamics, a matter explored at great length in Wallace and Fullilove (2008). The essential idea is that it is possible to define an entropy-analog using information source uncertainty as a "free energy," and then define, in first order, a kind of Onsager relation driving the dynamics of the system. After some development, this formalism permits identification of three levels of, possibly interacting, topologies (Wallace and Fullilove 2008). The first involves the dual information sources defined by equivalence classes of states connected by the high-probability meaningful paths connecting to some base state in the construction above. States linked by such a path to the same base point form an equivalence class (Wallace and Fullilove 2008). Next, "languages" that are similar in a precise sense

form a dynamical equivalence class whose time dynamics are defined by the generalized Onsager relations above. These constitute formal dynamical manifolds and are associated with yet another groupoid. Finally, paths within individual dynamical manifolds, individual dynamical paths can form directed homotopy equivalence classes.

This latter behavior mirrors the change in resilience mode when, for example, the normal forest state of low levels of spruce budworms shifts to a large-scale outbreak (Fleming and Shoemaker 1992). The effects of a crown forest fire on a spruce forest would be equivalent to a wholesale shifting of dynamics between different manifolds, in this formulation. Thus the set of possible dynamic manifolds, as a set of equivalence classes of behaviors, becomes itself a groupoid subject to linkages by crosstalk (Wallace and Fullilove 2008, Glazebrook and Wallace, *unpublished manuscript*).Thus, shifts in underlying topological equivalence classes, in this model, generalize the idea of resilience, and may involve both punctuated events within dynamical manifolds, which are similar to conventional views of ecosystem resilience, and may involve in addition wholesale shifts between dynamical manifolds akin to clear-cutting or other catastrophe. Our association of dual information sources with a spectrum of cognitive physiological phenomena thus implies that resilience analysis could be a new and very fundamental tool for understanding a broad range of physical and mental dysfunction in humans and their comorbid interactions.

DISCUSSION AND CONCLUSIONS

The developments of this paper, which are essentially ecosystem models, are best viewed as sources of new speculation (Pielou 1977:106), subject to empirical examination, of the possibly great utility of resilience approaches in understanding a broad spectrum of chronic developmental mental and physical disorders. The inference that a pattern of co- and antico- morbid mental and chronic physical disorder can represent the pathological permanent or semi-permanent establishment of an ordinarily atypical, or transient, state as a quasi-stable resilience mode is consistent, not only with recent ecosystem resilience theory, but with theorizing in both autoimmune disease and mental disorder.

Gilbert (2001), for example, uses an evolutionary approach to conclude that the relatively small number of evolved adaptive defense mechanisms, for example the flight-or-fight hypothalamic-pituitary-adrenal (HPA) axis, may become pathologically activated to produce mental disorder. Jones and Blackshaw (2000) likewise argue that behavioral similarities between humans and animals show that many psychiatric states are distortions of evolved behavior, a perspective providing, in their view, a new etiological approach to psychiatry transcending current mainstream empirical and phenomenological approaches which are principally forms of symptom classification. Although individual pathologies of both mind and body may predominate in particular cases, the analysis here encompasses a broad swath of chronic diseases, emotional disorders, and classic cognitive dysfunction, in the context of the local sociocultural network so important to human biology (Richerson and Boyd 2004).

Comorbidity may well be to medicine what the dirty open secret of punctuation in the fossil record has been to evolutionary theory (e.g., Gould 2002), providing an opportunity for significant extension of our understanding and our ability to intervene against individual and population-level patterns of pathology. For certain classes of mind/body symptomatology, early experiences of exposure to structured psychosocial stress, particularly childhood poverty, appear particularly able to trigger identification of a highly atypical mode as the normal zero-reference state, in a punctuated manner. This will often initiate a life course of co- or antico- morbid psychiatric and physical disorders. The characteristic pattern would involve individual and population-level comorbidity among obesity, asthma, diabetes, hypertension, depression, anxiety, substance abuse, ruthless or violent behaviors, coronary heart disease, certain cancers, and asthma or lupus, i.e., what might well be characterized as oppression disorder at the individual level.

In conclusion, this work suggests that, at the individual scale, chronic, comorbid, mind/body dysfunctions are very much parallel to, and can be viewed as examples of, the more general ecosystem processes studied by resilience theory. Further development according to that theory, in particular use of its methods to study linkages across scale, should offer much to the understanding, treatment, and prevention of developmental disorders and their comorbidities.

Responses to this article can be read online at:
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LITERATURE CITED

Ash, R. B. 1990. **Information theory.** Dover, New York, New York, USA.

Atlan, H., and I. Cohen. 1998. Immune information, self-organization and meaning. *International Immunology* **10**:711-717.

Bandelow, B., C. Spath, G. Tichauer, A. Broocks, G. Hajak, and E. Ruther. 2002. Early traumatic life events, parental attitudes, family history, and birth risk factors in patients with panic disorder. *Comprehensive Psychiatry* **43**:269-278.

Barker, D. 2002. Fetal programming of coronary heart disease. *Trends in Endocrinology and Metabolism* **13**:364-372.

Barker, D., T. Forsen, A Uutela, C. Osmond, and J. Erikson. 2002. Size at birth and resilience to effects of poor living conditions in adult life: longitudinal study. *British Medical Journal* **323**:1261-1262.

Barkow, J., L. Cosmides, and J. Tooby, editors. 1992. *The adapted mind: biological approaches to mind and culture.* University of Toronto Press, Toronto, Canada.

Bjorntorp, P. 2001. Do stress reactions cause abdominal obesity and comorbidities? *Obesity Reviews* **2**:73-86.

Bonner, J. 1980.*The evolution of culture in animals.* Princeton University Press, Princeton, New Jersey, USA.

Cohen, I. 1992. The cognitive principle challenges clonal selection. *Immunology Today* **13**:441-444.

Cohen, I. 2000. Tending Adam's garden: evolving the cognitive immune self. Academic Press, New York, New York, USA.

Cooke, D. 1996. Psychopath personality in different cultures: what do we know? *Journal of Personality Disorders* **10**:23-40.

Coplan, J., M. Altemus, S. Matthew, E. Smith, B. Scharf, P. Coplan, J. Kral, J. Gorman, M. Owens, C. Nemeroff, and L. Rosenblum. 2005. Synchronized maternal-infant elevations of primate CSF CRF concentrations in response to variable foraging demand. *CNS Spectrums* **10**:530-536.

Cover, T. and J. Thomas. 1991. *Elements of information theory.* John Wiley and Sons, New York, New York, USA.

Dalgleish, A., and K. O'Byrne. 2002. Chronic immune activation and inflammation in the pathogenesis of AIDS and cancer. *Advances in Cancer Research* **84**:231-276.

Dehaene, S., and L. Naccache. 2001. Towards a cognitive neuroscience of consciousness: basic evidence and a workspace framework. Cognition **79**:1-37.

Durham, W. 1991. *Coevolution: genes, culture, and human diversity.* Stanford University Press, Palo Alto, California, USA.

Egle, U., J. Hardt, R. Nickel, B. Kappis, and S. Hoffmann. 2002. Long-term effects of adverse childhood experiences: actual evidence and needs for research. *Zeitschrift fur Psychosomatische Medizin und Psychotherapie* **48**:411-434.

Eldredge, N. 1985. *Time frames: the rethinking of Darwinian evolution and the theory of punctuated equilibria.* Simon and Schuster, New York, New York, USA.

Eriksson, J., T. Forsen, J. Tuomilehto, C. Osmond, and D. Barker. 2000. Fetal and childhood growth and hypertension in adult life. *Hypertension* **36**:790-794.

Feynman, R. 1996. *Feynman lectures on computation.* Addison-Wesley, Reading, Massachusetts, USA.

Fleming, R., and C. Shoemaker. 1992. Evaluating models for spruce budworm-forest management: comparing output with regional field data. *Ecological Applications* **2**:460-477.

Forlenza, M., and A. Baum. 2000. Psychosocial influences on cancer progression: alternative cellular and molecular mechanisms. *Current Opinion in Psychiatry* **13**:639-645.

Gilbert, P. 2001. Evolutionary approaches to psychopathology: the role of natural defenses. *Australian and New Zealand Journal of Psychiatry* **35**:17-27.

Godfrey, K., and D. Barker. 2001. Fetal programming and adult health. *Public Health and Nutrition* **4**:611-624.

Gould, S. 2002. T*he structure of evolutionary theory.* Harvard University Press, Cambridge, Massachusetts, USA.

Grossman, Z. 1989. The concept of idiotypic network: deficient or premature? Page 3852 *in* H. Atlan and I. R. Cohen, editors. *Theories of Immune Networks.* Springer Verlag, Berlin, Germany.

Grossman, Z. 1993. Cellular tolerance as a dynamic state of the adaptable lymphocyte. *Immunology Reviews* **133**:45-73.

Grossman, Z. 2000. Round 3. *Seminars in Immunology* **12**:313-318.

Grossman, Z. 1992. Contextual discrimination of antigens by the immune system: towards a unifying hypothesis. Page 7189 *in* A. Perelson and G. Weisbch, editors. *Theoretical and Experimental Insights into Immunology.* Springer Verlag, Berlin, Germany.

Grossman Z., R. Herberman, and S. Livnat. 1992. Neural modulation of immunity: conditioning phenomena and adaptability of lymphoid cells. *International Journal of Neuroscience* **64**:275-290.

Gunderson, L. 2000. Ecological resilience-in theory and application. *Annual Reviews of Ecological Systematics* **31**:425-439.

Herpertz, S., and H. Sass. 2000. Emotional deficiency and psychopathy. *Behavioral Sciences and the Law* **18**:567-580.

Hirsch, J. 2003. Obesity: matter over mind? *Cerebrum* **5**:7-18.

Holling, C. 1973. Resilience and stability of ecological systems. *Annual Reviews of Ecological Systematics* **4**:1-23.

Jones, I., and J. Blackshaw. 2000. An evolutionary approach to psychiatry. *Australian and New Zealand Journal of Psychiatry* **34**:8-13.

Kiecolt-Glaser, J., L. McGuier, T. Robles, and R. Glaser. 2002. Emotions, morbidity, and mortality: new perspectives from psychoneuroimmunology. *Annual Review of Psychology* **53**:83-107.

Landau, L., and E. Lifshitz. 2007. *Statistical physics.* Third edition, Elsevier, New York, New York, USA.

Libbey, P., P. Ridker, and A. Maseri. 2002. Inflammation and atherosclerosis. *Circulation* **105**:1135-1143.

Lalumiere, M., G. Harris, and M. Rice. 2001. Psychopathy and developmental instability. *Evolution and Human Behavior* **22**:75-92.

Massey, D., and N. Denton. 1992. *American apartheid.* Harvard University Press, Cambridge, Massachusetts, USA.

Mealey, L. 1995. The sociobiology of sociopathy: an integrated evolutionary model. *Behavioral and Brain Sciences* **18**:523-599.

National Center for Children in Poverty (NCCP). 2003. Low income children in the United States. Available online at: http://www.nccp.org/publications/pub_681.html.

Nunney, L. 1999. Lineage selection and the evolution of multistage carcinogenesis. *Proceedings of the Royal Society, B* **266**:493-498.

Osmond, C., and D. Barker. 2000. *Environmental health perspectives supplements.* **108**:S3:545-553.

Paris, J. 1993. Personality disorders: a biopsychosocial model. *Journal of Personality Disorders* **7**:53-99.

Pielou, E. C. 1977. *Mathematical ecology.* John Wiley and Sons, New York, New York, USA.

Podolsky, S. and A. Tauber. 1998. The generation of diversity: clonal selection theory and the rise of molecular biology. Harvard University Press, Cambridge, Massachusetts, USA.

Rau H., and T. Elbert. 2001. Psychophysiology of arterial baroreceptors and the etiology of hypertension. *Biological Psychology* **57**:179-201.

Repetti, R., S. Taylor, and T. Seeman. 2002. Risky families: family social environments and the mental and physical health of offspring. *Psychological Bulletin* **128**:330-366.

Richerson, P., and R. Boyd. 1995. The evolution of human hypersociality. Paper for Rindberg Castle Symposium on Ideology, Warfare, and Indoctrination (January, 1995), and Human Behavior and Evolution Society (HBES) meeting, 1995.

Richerson, P., and R. Boyd. 2004. *Not by genes alone: how culture transformed human evolution.* Chicago University Press, Chicago, Illinois, USA.

Rojdestvensky, I., and M. Cottam. 2000. Mapping of statistical physics to information theory with applications to biological systems. *Journal of Theoretical Biology* **202**:43-54.

Smith, G., C. Hart, D. Blane, and D. Hole. 1998. Adverse socioeconomic conditions in childhood and cause-specific adult mortality: prospective observational study, *British Medical Journal* **317**:1631-1635.

Smith, T., and J. Ruiz. 2002. Psychosocial influences on the development and course of coronary heart disease: current status and implications for research and practice. *Journal of Consulting and Clinical Psychology* **70**:548-568.

Tauber, A. 1998. Conceptual shifts in immunology: comments on the "two-way paradigm." *Theoretical Medicine* **19**(5):457-473.

Thayer, J., and R. Lane. 2000. A model of neurovisceral integration in emotion regulation and dysregulation. *Journal of Affective Disorders* **61**:201-216.

Thayer, J., and B. Friedman. 2002. Stop that! Inhibition, sensitization, and their neurovisceral concomitants. *Scandinavian Journal of Psychology* **43**:123-130.

Timberlake, W. 1994, Behavior systems, associationism, and Pavolvian conditioning. *Psychonomic Bulletin Review* **1**:405-420.

Wallace, R. 2000. Language and coherent neural amplification in hierarchical systems: renormalization and the dual information source of a generalized stochastic resonance. *International Journal of Bifurcation and Chaos* **10**:493-502.

Wallace, R. 2002*a.* Immune cognition and vaccine strategy: pathogenic challenge and ecological resilience. *Open Systems and Information Dynamics* **9**:51-83.

Wallace, R. 2002*b.* Adaptation, punctuation and rate distortion: non-cognitive `learning plateaus' in evolutionary process. *Acta Biotheoretica* **50**:101-116.

Wallace, R. 2003. Systemic lupus erythematosus in African-American women: cognitive physiological modules, autoimmune disease, and pathogenic social hierarchy. *Advances in Complex Systems* **6**:599-629.

Wallace, R. 2005*a.* Consciousness: a mathematical treatment of the global neuronal workspace model. Springer-Verlag, New York, New York, USA.

Wallace, R. 2005*b.* A global workspace perspective on mental disorders. *Theoretical Biology and Medical Modelling* 2/1/49.

Wallace, R. 2006. Machine hyperconsciousness. Available online at: http://cogprints.org/5005/.

Wallace R., and R. Fullilove. 1999. Why simple regression models work so well describing risk behaviors in the USA. *Environment and Planning A* **31**:719-734.

Wallace, R., and M. Fullilove. 2008. Collective consciousness and its discontents: institutional distributed cognition, racial policy, and public health in the United States. Springer, New York, New York, USA.

Wallace, R., M. Fullilove, and A. Flisher. 1996. AIDS, violence and behavioral coding: information theory, risk behavior, and dynamic process on core-group sociogeographic networks. *Social Science and Medicine* **43**:339-352.

Wallace, D., and R. Wallace. 1998. A plague on

your houses. Verso, New York, New York, USA.

Wallace, D., and R. Wallace. 2000, Life and death in Upper Manhattan and the Bronx: toward an evolutionary perspective on catastrophic social change. *Environment and Planning A* **32**:1245-1266.

Wallace, R., and D. Wallace. 1997. Community marginalization and the diffusion of disease and disorder in the United States. *British Medical Journal* **314**:1341-1345.

Wallace, R., and D. Wallace. 2005. Structured psychosocial stress and the US obesity epidemic. J*ournal of Biological Systems* **13**:363-384.

Wallace, R., D. Wallace, and R. G. Wallace. 2003*a*. Toward cultural oncology: the evolutionary information dynamics of cancer. *Open Systems and Information Dynamics* **10**:159-181.

Wallace, R., and R. G. Wallace. 1998. Information theory, scaling laws and the thermodynamics of evolution. *Journal of Theoretical Biology* **192**:545-559.

Wallace, R., and R. G. Wallace. 1999. Organisms, organizations, and interactions: an information theory approach to biocultural evolution. *BioSystems* **51**:101-119.

Wallace, R., and R. G. Wallace. 2002. Immune cognition and vaccine strategy: beyond genomics. *Microbes and Infection* **4**:521-527.

Wallace, R., and R. G. Wallace. 2004. Adaptive chronic infection, structured psychosocial stress, and medical magic bullets. *BioSystems* **77**:93-108.

Wallace, R., R. G. Wallace, and D. Wallace. 2003*b.* Coronary heart disease, chronic inflammation, and pathogenic social hierarchy: a biological limit to possible reductions in morbidity and mortality. *Journal of the National Medical Association* **96**:609-619.

Wilkinson, R. 1996. Unhealthy societies: the afflictions of inequality. Routledge, London, UK.

Wright, R., M. Rodriguez, and S. Cohen. 1998. Review of psychosocial stress and asthma: an integrated biopsychosocial approach. *Thorax* **53**:1066-1074.