The Importance of Neurobiological Research to the Prevention of Psychopathology

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There is both a biological and environmental component to the neural substrates for various forms of psychopathology. Brain dysfunction itself not only constitutes a formidable liability to psychopathology, but also has an impact on environmental and social responses to the individual, compounding the risk for an adverse outcome. Environmental conditions, such as social and physical stimulus deprivation, poverty, traumatic stress, and prenatal drug exposure, can further compromise brain function in the context of existing liabilities. The relationship between genetic and environmental processes is interactive, fluid, and cumulative in their ability to influence an individual's developmental trajectory and alter subsequent behavioral outcomes. Given the codependent relationship between these processes, brain function is now believed to be malleable via manipulations of the environment in ways that may decrease liability for psychopathology. Research that explores these relationships and ways in which interventions can redirect this developmental track may substantially advance both the science and practice of prevention. Studies attempting to isolate the neurobiological effects of socioenvironmental factors are reviewed, implications for intervention strategies are discussed, and a future research agenda is proposed to provide greater insight into specific brain-environment relationships. Armed with this knowledge, prevention scientists may eventually design programs that directly target these effects to reverse or attenuate negative outcomes.

KEY WORDS: neurobiology; neurotransmitters; prevention; antisocial behavior; drug abuse.

Although we know a great deal about the effects of socioenvironmental conditions on the propensity to certain behavioral disorders, only recently have discoveries in the field of neuroscience linked brain function with a predisposition for psychopathology, such as depression, schizophrenia, drug abuse, and antisocial behaviors. Several markers indicative of brain dysfunction have been identified and associated with particular behaviors and temperaments that characterize liability for psychopathology. For example, studies suggest that individuals prone to highly aggressive behavior possess a greater number of particular genetic variations (i.e., polymorphisms) involving serotonin and dopamine systems than those who do not (see Fishbein, 1998). Also, physiologic, neuropsychologic, and imaging studies implicate dysfunction of particular brain regions in several aspects of vulnerability to drug addiction and related behaviors, including impaired judgment, sensation-seeking, attention deficits, and impulsivity (see Raine, 1993). Research has clearly established that the origins of brain and behavioral dysfunction are both genetically determined and environmentally induced (McGuire *et al.,* 1994; O'Connor *et al.,* 1998a; Pike *et al.,* 1996; Reiss *et al.,* 1995); thus, their presence can cumulatively alter an individual's developmental trajectory to influence subsequent development and behavioral

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outcomes. Because brain function is now known to be at least partially alterable by our environment in ways that may increase or decrease liability for psychopathology, it is critical that prevention research begin to explore these relationships and devise ways in which prevention programs can redirect this developmental track.

STRUCTURING THE ENVIRONMENT TO MINIMIZE RISK FACTORS

There is a critical need for research-based prevention programming to optimize individual potentialities in the context of prevailing social and biological conditions. Under optimal socioenvironmental circumstances, a responsive social system supports and encourages constructive choices, lifestyles, and opportunities. And on an individual level, the necessary internal controls are present to select and sustain a productive path. The potential to take advantage of existing external resources, make adaptive choices, and reach potentialities depend upon executive decision making and rational thought capacities—functions modulated within the central nervous system. In the dual absence of favorable external resources and developmentally appropriate brain function, high-risk or maladaptive behavior more likely becomes the default option. In general, therefore, research-based prevention strategies must achieve three goals: (1) to structure the environment to be more responsive to human needs and expand the availability of constructive choices and opportunities, (2) to optimize brain functioning, and (3) to introduce an intervention that will have an impact on one or both of these processes when they are somehow in deficit.

To effectively accomplish these goals, the relationship between environmental and biological liabilities must be better understood. This identification process will generate a better understanding not only of how environmental conditions influence brain function, but also how genes and aspects of brain function moderate the social environment. Such information will more fully explain why some individuals are susceptible to psychopathology, e.g., more likely to choose to alter brain function via abusable drugs or engage in risky and antisocial behaviors, than others under certain conditions. Although there is ample research demonstrating the role of innate strengths and vulnerabilities in propensity for various types of psychopathology, this article focuses on the external environment's contribution to behavioral disorders through its impact on brain function.

The purposes of examining neurobiological research in the context of prevention approaches are many and varied:

1. To aid practitioners in the identification of individual vulnerability factors by virtue of neurobiological vulnerabilities, and prevailing environmental conditions.
2. To eventually be able to consistently identify environmental conditions that act as triggers, enhancing the expression of vulnerabilities, such as depressive, aggressive, impulsive, or drug taking behaviors.
3. To develop more effective methods for early detection and intervention that are targeted and developmentally appropriate with respect to existing environmental conditions and biological liabilities.
4. To provide support for public health and medical approaches in lieu of simple incarceration or institutionalization, which generate many extraordinary personal, social, and financial costs.

The discussion begins with a conceptual perspective for explorations of the brain-environment relationship. Then, a review of the literature is presented specific to the impact of environmental factors on brain function and behavioral outcomes, including exposure to adverse conditions from the prenatal environment through adulthood, with a focus on traumatic stress. In conclusion, implications of the neurobiological research for prevention strategies are discussed, and a prospective research agenda is proposed.

RESPECTIVE ROLES OF GENETIC, BIOLOGICAL, AND ENVIRONMENTAL CONDITIONS

Both biological and behavioral traits are the product of an ongoing interaction between genes and environmental conditions, from the in utero environment to the social mileau. The ''genotype'' is the complement of genes inherited from parents, although genetic mutations or recombinations during embryonic development also contribute to an individual's genetic complement. The ''phenotype'' includes observable biological and behavioral traits that are reflective of the interaction between the genotype and environment; i.e., gene functions are me-

diated and modulated by environmental influences and subsequently expressed in biological processes and behavioral outputs. For example, neurogenetic mechanisms such as brain chemistry and its activity levels are genetically designed with respect to the synthesis and metabolism of brain chemicals, the number of receptor sites present, and the activity of competing or regulating enzymes. Nevertheless, environmental inputs and experiences can modify the expression of affected genes, thereby altering behavioral outcomes for better or for worse. Understanding this interactive process translates into the ability to redirect behavior by providing particular experiences, directive training and opportunities that influence critical neurobiological functions. Thus, although gene functions cannot be ''reprogrammed'' by altering the molecular genetic structure to change behavioral outcomes, they can be manipulated. Genes establish the framework for brain function while the environment customizes and fine-tunes it.

Preliminary research has identified numerous putative neurogenetic mechanisms (i.e., features of brain function that are genetically designed and environmentally influenced) in various forms of psychopathology. For example, alterations in brain dopamine functioning have been found in different types of behavioral disturbances, implicating genetic influences on this association (Cabib *et al.,* 1997). Research on Tourette's syndrome, a neuropsychiatric disorder with co-occurring attention deficits and conduct problems, has provided valuable information regarding relationships between genetic vulnerability, likely involving dopaminergic systems and environmental influences (Cohen, 1992). The disorder is genetically transmitted through alterations in neuroanatomical and chemical systems. However, its clinical manifestations are environmentally sensitive. Attention Deficit Hyperactivity Disorder (ADHD) is yet another example of the relationship between neurogenetic mechanisms and environmental factors. Neuroanatomical, physiologic, and chemical differences found in this population are thought to be modulated by cultural and familial factors (Taylor, 1998). Current thinking is that environmental conditions do not forecast a particular type of pathology, but that genetic factors may be somewhat more predictive. In other words, environmental influences act in a nonspecific way on specific genetic processes, manifested as neurobiological risk factors (e.g., low serotonergic tone or executive cognitive deficit), to induce their expression.

Neurogenetic factors increase liability for psychopathology by influencing related, core phenotypes that antedate and are associated with the eventual behavioral outcome, such as temperament, personality traits, patterns, and orientations of behavior and relationships. Phenotypes related to and predictive of psychopathology include impulsivity, cognitive deficits, attention deficits, high activity levels, sensation or novelty seeking, conduct disorder, negative affect, risk imperception, poor conditionability, lack of pain avoidance responses, abnormal levels of arousal, and low verbal ability. Several of these phenotypes have been associated with particular neurogenetic mechanisms, such as irregularities in neurotransmitter function and hormone responses, and genetic variants (see Cloninger *et al.,* 1993; Fishbein, 1998; Raine, 1993). Prevention strategies will be most effective if they focus on these underlying phenotypes, in conjunction with particular forms of environmental stimulants and supports as indicated by the needs of targeted individuals and neighborhoods.

Neurobiological conditions are, therefore, mutable; although genes underlie their expression, they are environmentally influenced and can be altered via environmental manipulations. For example, highly stressful experiences produce measurable differences in brain chemistry; in particular, a decline in serotonin activity levels (Davis *et al.,* 1997; Fichtner *et al.,* 1995; Graeff *et al.,* 1996; Southwick *et al.,* 1997; van der Kolk, 1997). This finding implies that traumatic experiences directly affect biological traits, which can subsequently increase risk for negative behavioral outcomes. One might anticipate, as a result, increases in serotonergic activity levels with an effective intervention. Another example is that of stimulus deprivation, associated with a variety of cognitive and neurologic deficits that favorably respond to environmental enrichment programs (see later section on ''environmental stimulation''). In sum, genetic risks are expressed through vulnerability or heightened sensitivity to adverse environmental factors; thus, biological features can be either suppressed or expressed in response to environmental inputs. No individual is predestined strictly by virtue of their genes or their biology to psychopathology; environmental conditions carry significant weight in this equation.

A Heuristic Biosocial Model of Antisocial Behavior

A model has been proposed (Raine *et al.,* 1997a) to guide investigations into biological and social interactions which has import for the use of neurobio-

logical findings in prevention strategies. In their model, biological and psychosocial risk and protective factors interact in a dynamic, constantly fluctuating, and cumulative process to determine risk for behavioral disorders. Protective factors exert an influence and can alter this pathway at any point in the developmental process to reduce risk status and improve the outcome. The behavioral outcome can also, in a feedback loop, affect risk and protective conditions to further strengthen or weaken risk status. For example, a child with ADHD (one of many childhood behavioral disorders with genetic origins) may be easily frustrated and difficult to manage. Parents without proper coping skills may harshly and inconsistently punish the child, further strengthening the child's risk for antisocial behavior (O'Connor *et al.,* 1998a, 1998b). The child may react to such parenting with hostility and defiance, providing further fuel for a negative developmental outcome. The results may be quite different for a learning disabled child in the presence of a supportive home with appropriate intervention.

This integrated model readily applies to the widely accepted drug abuse prevention principles outlined by Hawkins and Catalano (1995). The authors suggest that the most promising route to effective strategies for the prevention of alcohol and other drug problems is through a focus on risk and protective factors, from the individual to the community level. Their framework can easily accommodate biological and genetic factors as they interrelate with the social and psychological conditions the authors include to formulate a comprehensive and contemporary model for prevention strategies. An understanding of differential vulnerability to social and environmental conditions, i.e., individual differences in resiliency against similar social stressors (Anisman *et al.,* 1998), would be subsequently enhanced. The resulting more encompassing model implies that prevention programs will be infinitely more effective when they account for both neurobiological and environmental aspects of risk and resiliency factors.

ENVIRONMENTALLY INDUCED BIOLOGICAL ASPECTS OF PSYCHOPATHOLOGY

Understanding the dynamics and consequences of stress is key to unraveling etiologic mechanisms in psychopathology. Stress is the physical and psychological response to an excess of stimulation compared with an individual's resources for coping (Meaney *et al.,* 1996). The source of stimulation may be either environmental (e.g., child abuse, family dysfunction, sensory deprivation), biological (e.g., lead poisoning, prenatal drug exposure, head trauma) or a function of the relationship between the two. Resources for coping may also be grounded in conditions that are either biological (e.g., IQ, executive cognitive skills), social (e.g., parenting techniques), psychological (e.g., self-esteem) or, most likely, a combination. Stressful experiences can temporarily or permanently alter brain function and chemistry. An acute stressor occurs in the short term and generally produces only a temporary effect; biological and physiologic adjustments in the brain's response to the stressor take place after the stressor terminates. The presence of a chronic or recurring stressor, in contrast, more often results in a cumulative effect on biological and physiologic responses, constituting a formidable risk factor. Chronic stress primes the brain for maladaptive responses to the environment by altering brain function, disengaging coping mechanisms, and compromising ability to formulate and act on rational choices, thereby increasing the likelihood of psychopathologic behavior (Anisman & Zacharko, 1986). Inherent susceptibilities or vulnerabilities help to determine particular behavioral outcomes of that stress, e.g., from schizophrenia to depression to violence, whereas positive attributes of either the individual or the environment can provide some protection from these outcomes.

The Physical Environment and its Stressors

Prenatal Influences

Integrity of the internal environment of the developing fetus is predictive of future outcomes in terms of organ function, anatomic features, cognitive ability, intelligence level, psychiatric status, and behavioral patterns (Glover, 1997). The mother's experiences and mental state influence this internal environment and, consequently, play an active role in determining the range of abilities the child will have in interaction with his or her genetic make-up. Her nutritional intake, use of substances, and even stress levels directly affect fetal development. Hundreds of studies document the relationship between suboptimal prenatal conditions and later behavioral and psychological disorders. One particular study (Lou *et al.,* 1994) followed 3021 women through their pregnancy and compared the 70 most stressed with 50 controls

from the sample. Both antenatal stress and smoking contributed independently and significantly to lower gestational age, lower birth weight, and small head circumference when corrected for birth weight. Prenatal stress was also significantly associated with poorer scores on the neonatal neurologic examination. Further investigations have begun to examine the specific effects of the prenatal environment on various dimensions and risk factors for psychopathology.

One of the most profound and also preventable precipitants of behavioral and psychological disorders during pregnancy is prenatal drug exposure. Animal and human studies indicate that repeated prenatal exposures to abusable drugs leads to disruptions in normal neurotransmitter function and may enhance development of tolerance and/or sensitization to later drug use in the offspring (Allan *et al.,* 1998; Battaglia *et al.,* 1995; Henry *et al.,* 1995; Howard & Takeda, 1990; Legido, 1997; Slotkin, 1998).

Alcohol. One very profound and direct cause of mental retardation which is entirely preventable is fetal alcohol exposure. Fetal alcohol syndrome (FAS) is easily diagnosable owing to the obvious facial deformities and mental retardation that occur in the offspring when alcohol was consumed in large quantities throughout pregnancy. However, subtler forms of FAS can also result from lower or less frequent intake of alcohol, which contribute to less obvious physical deformities, making diagnosis more difficult. Rather than profound mental retardation, these cases may present themselves with cognitive deficits, learning disabilities, hyperactivity, and behavioral problems. Individuals so affected are more vulnerable to psychopathology and, in particular, conduct disordered behavior by virtue of the many risk factors they possess (Backon, 1989; Famy *et al.,* 1998; Stressguth *et al.,* 1991).

Damage to the brain from fetal alcohol exposure may increase vulnerability to psychopathology specifically by affecting executive cognitive functioning and verbal skills. Also, neurobiological research suggests that the activity levels of serotonin in the offspring are lower (Gorio *et al.,* 1992; Guerra, 1998; Tajuddin & Druse, 1988), possibly contributing to the development of impulsivity and aggressiveness. Impairments are exhibited in the following forms:

- An inability to calculate the consequences of one's actions
- Difficulty linking cause with effect
- Impaired logic
- Relative lack of remorse
- Memory and learning impairments
- Inappropriate behaviors and impulsivity
- Defects in abstract thought
- Difficulty in following directions

The social consequences of these neuropsychological deficits include a tendency to suggestibility, poor judgment, gullibility, increased vulnerability to abuse, rejection by peers, frustration, hostility, association with like-peers, and alienation in school. The impairments suffered by victims of FAS last a lifetime and frequently remain undiagnosed.

Tobacco. Maternal smoking during pregnancy also increases the risk for behavioral problems and cognitive deficits in the offspring. Prenatal exposure to nicotine is associated with adverse reproductive outcomes, including alterations in neural structure and functioning, cognitive deficits, and behavior problems in the child. Wakschlag *et al.* (1997) reported that mothers who smoked more than half a pack of cigarettes daily during pregnancy were significantly more likely to have a child with conduct disorder. A significant effect of maternal smoking on externalizing behavior problems, e.g., oppositional, aggressive and/or overactive behaviors, was also reported by Orlebeke *et al.* (1997). Rantakallio *et al.* (1992) found an association between maternal smoking in pregnancy and delinquency in the offspring during adolescence and early adulthood, although the nature of causal mechanisms was unclear. Milberger *et al.* (1996) reported an association between maternal smoking during pregnancy and ADHD in the children they sampled.

The assumption underlying these and other studies is that maternal smoking causes brain damage by reducing oxygen to the fetal brain and by interfering with the development of neurotransmitter and modulator systems. For example, there is evidence that acetylcholine receptor activity is disrupted in fetuses exposed to nicotine (Navarro *et al.,* 1989; Slotkin, 1998; Tizabi *et al.,* 1997), contributing to lower cognitive, psychomotor, language, and academic performance, in addition to hyperactivity and attention deficits (Dunn *et al.,* 1997; Milberger *et al.,* 1996, 1997). Although particular forms of psychopathology have been associated with maternal smoking, it is not yet possible to predict the development of a specific disorder. Also, many who are exposed to tobacco in utero are seemingly unaffected. Nevertheless, in combination with a disadvantageous or suboptimal environment (e.g., poor parenting or family dysfunc-

tion), the effects of maternal smoking during pregnancy on behavioral problems are expected to be stronger.

Cocaine. In some large urban areas, between 10 and 15% of all women in their child-bearing years are users of cocaine (Giacoia, 1990). Cocaine readily crosses the placental barrier and rapidly becomes concentrated in fetal brain tissue. Chronic prenatal exposure results in depletion of brain chemicals (e.g., dopamine) and damage to receptors. For example, prenatal cocaine exposure increases release of the adrenergic amines, such as norepinephrine, to initiate the "stress response" (fight/flight mechanism). These chemicals are also involved in basic neuropsychological functions (e.g., attention, activity levels, and regulation of anxiety and other emotional states). Cocaine further affects blood flow, possibly resulting in fetal hypoxemia and decreased nutrient transfer. Mothers who use cocaine are also less likely to obtain prenatal care, follow a proper diet, or experience appropriate weight gain. Similarly, most cocaine users also consume alcohol, complicating the isolation of specific effects.

Consequences to the fetus are believed to be many and varied, from cerebral infarction and seizures to disrupted sleep patterns and irritability (see Mott *et al.,* 1993). Problems with attention regulation, activity levels, and capacity to modulate behavior have been reported, which are all risk factors for later psychopathology. Neurobiological research shows that receptor activity of serotonin, dopamine, and norepinephrine is disrupted in exposed newborns, resulting in developmental delays that may pose a liability to negative outcomes (Battaglia *et al.,* 1995; Legido, 1997; Seidler & Slotkin, 1992; Slotkin, 1998). Also, EEG abnormalities in the newborn exposed to cocaine prenatally suggest cerebral irritation, in addition to tremors, irritability, and hypertonicity. Fetal weight tends to be lower, length of the body shorter, and head circumference smaller, but lags in the development of these features become more trivial as the infant matures. There are also indications of:

- impairments in interactive capabilities, state regulation, and habituation
- hyperexcitability or depression
- lowered mental and psychomotor developmental scores
- deficits in context of free play
- less representational play
- a high rate of scattering, batting, and picking up and putting down toys rather than sustained play or curious exploration
- minimal brain dysfunction and learning disabilities
- difficulty in concentrating, interacting with other kids, and playing alone
- impairment in basic attentional regulation processes

Nevertheless, there are controversies regarding the effects of prenatal cocaine exposure on offspring behavior, which have not been documented consistently across studies. Also, it is difficult to isolate the effects of cocaine on the fetus when cocaine-abusing mothers so often are polysubstance abusers.

Cognitive effects are strongly dependent upon the quality of home environment. The prevailing lifestyle can complicate the outcome for the developing child (Azuma & Chasnoff, 1993; Brooks-Gunn *et al.,* 1994). Conditions that often prevail in the homes of children exposed prenatally to cocaine include a chaotic environment, lack of appropriate stimulation, lack of parenting skills, mother with impaired mental functioning by virtue of her addiction, inappropriate developmental modeling, as well as abuse and neglect. The presence of these conditions increases the likelihood of further impairments to intellectual capability and social-ethical behavior.

Maternal Social Conditions

The social environment of a mother during pregnancy may also alter the prenatal biological environment, subsequently affecting outcomes for the offspring. Exposure to high levels of stress during pregnancy can influence the integrity of physiologic, hormonal, and neurotransmitter systems developing in the fetus, subsequently increasing the risk for psychopathology in the child (Benes, 1997; McIntosh *et al.,* 1995; Roughton *et al.,* 1998; van Os & Selten, 1998; Ward, 1991). Recent studies suggest that environmental stress during this period can activate genes linked to psychological disorders (Benes, 1997; Kaufer *et al.,* 1998; Smith *et al.,* 1997; Stabenau, 1977; Van Os & Selten, 1998). In particular, the gene called "*C-fos*" may be turned on in the fetus by exposure to both maternal stress and drug abuse (Kaufer *et al.,* 1998; Senba & Ueyama, 1997). Increased *C-fos* activity is believed to contribute to the development of abnormal neural connections, causing neurons to fire in the absence of a trigger, which may elicit feel-

ings or behaviors that are out of context, given environmental conditions. Children who experience high levels of stress, hypothetically either in utero or in early life, may become sensitized to future stressful experiences and exhibit inappropriate emotions associated with mental disorders (Post, 1992).

Perinatal Complications

Perinatal conditions occur between the seventh month of pregnancy to 28 days after birth (Brennan & Mednick, 1997). They include prematurity and delivery complications such as hypoxia, infectious disease, prolapsed cord during delivery, irregular heart beat in the child during delivery, late-stage drug use, and other difficulties immediately before, during, or after birth. These conditions are believed to increase the risk for negative outcomes, particularly aggressive behavior, presumably as a function of the fetal brain damage they can cause. Piquero and Tibbetts (1999) provide a thorough overview of research summarizing the relationship between perinatal factors and antisocial behavior, showing support for the relationship (although there are some discrepancies). Importantly, the most recent studies cited suggest a strong interactive relationship between the effects of perinatal complications and the social environment on antisocial outcomes. They conclude from their review that ''poor or deficient familial and socioeconomic environments may magnify the effects of pre/perinatal complications.'' Piquero and Tibbetts surmise that perinatal complications may contribute to neuropsychological deficits that impede the socialization process. In the dual presence of neuropsychological impairment and a poor familial environment, characterized by family dysfunction, neglect or abuse, inconsistent parenting, or lack of supervision, the socialization process is further compromised, exponentially increasing risk for an antisocial outcome.

Overall, exposure to adverse physical stimuli, particularly during gestation and the birth process, can compromise later brain function. Postnatally, numerous other physical insults can also alter neurobiological processes, such as head injury and neurotoxic factors. Although individuals are differentially affected by similar exposures, it is impossible at this juncture to predict who will be affected and to what extent. Ongoing research in the fields of genomics and epigenetics (the study of inherited alterations in gene expression) may eventually help to flesh out differential response tendencies.

The Social Environment and its Stressors

The physical and social environment of the mother and her offspring contributes in substantial and necessary ways to brain development and function. Not only does the growing brain of a child require a certain amount of physical stimulation, there are also strong biological needs for positive social interactions, bonding, and protection against traumatic experiences. For example, children who were not provided with the most basic academic skills (e.g., learning colors or how to spell their names) during the first few years may have difficulty once they enter school and become academically disadvantaged, even though they may be innately quite bright. More intense stimulation to sensory and cognitive functions may be necessary for these children to advance appropriately.

Caregiver-Child Social Interactions

The bond between caregiver and child, and the regular sensory contact that stems from this bond, are basic biological needs; even the most basic biological systems depend on the quality of social stimulation early in life. The brain continues to develop neural connections during the first year of life, by which time approximately 50% of all human learned responses have formed. Between year one and year three, adaptational responses to the environment are formed, including the essential stage called ''basic trust.'' Through attachments to caregivers, infants and children develop a sense of security, self-efficacy, reassurance about the safety of their environment, and successful experiences with others. Children who do not develop basic trust often have attachment disorders, aggressiveness, attention deficits, anxiety, emotional disturbances, and withdrawal. In the absence of adequate levels of early social stimulation, children lack the foundation to deal with the rigors of daily life and its stressors. Thus, even in the presence of prenatal trauma or perinatal complications, manipulations of the environment can minimize biological risks or disadvantages to alter outcomes.

An example highlighting the importance of adequate caregiver-child interactions in offspring behav-

ior is found in reports on maternal depression. Both animal and human studies have shown that primate development is influenced by infants' attachment relationship primarily with the mother (see Goodman & Gotlib, 1999). Mothers who interact infrequently, with less intensity, inconsistently, or with relative unresponsiveness compromise a stable attachment relationship. Studies suggest that, as a result, offspring manifest various disturbances in affect and mood, cognitive ability, sociability and coping responses (Allen *et al.,* 1998; Cicchetti *et al.,* 1997; Goodman & Gotlib, 1999). The specific risks for psychopathology in the offspring may be a function of inheritance, innate dysfunction of neuroregulatory processes, exposure to negative maternal orientations, and/or the stressful environment (Goodman & Gotlib, 1999). Rosenblum and Andrews (1994), in particular, discuss evidence that the long-term effects of disturbed mother-child interactions on infant development may be partially a product of alterations in the function of serotonergic and noradrenergic systems.

Environmental Stimulation Needs

Physical and sensory stimulation, from tactile contact to visual explorations of the environment, are essential to develop and maintain proper brain function (Kuhn & Schanberg, 1998). The brain experiences crucial periods when cells must be stimulated adequately to develop vision, language, smell, muscle control, and reasoning ability. Neural connections not supported by the external environment shrink and may die. Animal and human babies who are stimulus deprived are less responsive to their environments and if the condition is chronic, learning impairments, a thinner cortex (especially in the occipital portion), inadequate neurotransmitter activity, less dense connections between neurons, and increased incidence of premature aging can occur (Holsboer, 1989; Kempermann *et al.,* 1998; Kuhn & Schanberg, 1998; McEwen, 1997; Stokes, 1995). As a result, coping skills under stressful conditions may be impaired throughout life in affected individuals. One of the most extreme examples of such deprivation is in substandard orphanages where infants lack routine caregiver interactions, both social and sensory; mental retardation and even physical deformities may result in the absence of genetic abnormalities.

Thus, touch has biological value to maintain normal growth and development. Premature animals (Meaney *et al.,* 1991; Meaney & Aitken, 1985) and human babies (Kuhn and Schanberg, 1998) who are touched frequently gain more weight, are more active and alert, and show more brain growth. A deficit in tactile contact is associated with enzyme deficiencies in the brain and body. For example, ''psychosocial dwarfism'' is a syndrome associated with a lack of environmental stimulation in an infant leading to insufficient stimulation of the hypothalamus which regulates the release of growth hormone (Albanese *et al.,* 1994; Voss *et al.,* 1998). As a result, growth is stunted and can be permanent if not reversed at an early age. Because the hypothalamus also regulates many aspects of both survival and emotional responses, underactivity in the hypothalamus due to stimulus deprivation can affect behavior and emotionality.

Under conditions of sensory deprivation, animals and humans tend to seek stimulation the brain requires for proper functioning. The reticular activating system (RAS), which radiates from the brainstem up through the thalamus with fibers that connect to higher cortical centers, activates neural systems in response to environmental input, enabling an awareness of and reaction to that input. When stimulation from the environment is inadequate, due either to sensory deprived conditions or physiologic deficiencies within the RAS, the tendency to seek stimulation elsewhere increases. As a child, stimulation needs are primarily physical, often resulting in distractibility, constant motion, inability to sit still, and excessive physical contact with others, as seen in hyperactivity.[3] As the child matures, however, high stimulation needs may be met in more sophisticated ways by risk taking, novelty seeking, drug use, and other excessive behaviors. Hypothetically, therefore, even in the absence of a genetic or biological deficit in CNS arousal levels, environmental stimulus deprivation may simulate a condition such as hyperactivity or sensation seeking by creating a deficiency state, resulting in increased needs for external stimulation.

Fortunately, there is a high degree of plasticity in the brain, particularly in the early years of life (Joseph, 1999; Young *et al.,* 1999). Thus, while deprived rearing conditions may induce disturbances of

[3]Hypoarousal within the RAS has been associated with hyperactivity, which may help to explain why the administration of a stimulant, Ritalin, helps to calm and focus a hyperactive child. Their unusual need for external stimulation is counterbalanced when the RAS is receiving proper amounts of internal stimulation.

social and emotional functioning, enriched rearing conditions may help to restore function (Nakamura *et al.,* 1999). Starting as young as 6 weeks old, an enriched environment can produce improvements in brain function in individuals exposed to sensory deprived environments. There is evidence from animal (Kuhn & Schanberg, 1998; Passig *et al.,* 1996; Pham *et al.,* 1997; Schwartz & Goldman-Rakic, 1990), human biological (Meaney *et al.,* 1991; Pham *et al.,* 1997; Weisglas-Kuperus *et al.,* 1993), and neuroimaging (Risch, 1997) studies that changes incurred through environmental enrichment, where complex and intensive inanimate and social stimulation is provided, may endure through adulthood.

In sum, environmental stimulus deprivation has been associated with the development of psychopathology in humans and animals, from aggressive behaviors to depression (Agid *et al.,* 1999; Kuhn & Schanberg, 1998; Post & Weiss, 1997; Siegel *et al.,* 1993). Underlying mechanisms for this relationship are presently not well understood, although it is likely that the development of psychopathology in general is a function of neuropsychological deficits, hormonal and neurotransmitter irregularities, and other biological effects of deprivation. The particular behavioral disorder that emerges in response to stimulus deprivation, however, is more likely a result of phenotypic predisposition.

Child Abuse and Other Traumatic Experiences

Child abuse plays a distinct and significant role in the risk for behavioral disorders owing to the social and psychological trauma (Maxfield & Widom, 1996). What is less well known, however, is the impact of child abuse on the developing brain, which may actually mediate the behavioral response. Child abuse has been associated with alterations in neurotransmitter activity (e.g., serotonin) and stress hormone levels, including cortisol and epinephrine (Kaufman *et al.,* 1997; Lemieux & Coe, 1995; Lewis, 1992). In general, poor parenting has been related to low serotonin levels in the child (Pine *et al.,* 1996, 1997). Furthermore, fewer neural connections, CNS instability (as reflected in EEG abnormalities), and aberrant cortical development have been reported in individuals with a history of child abuse (Ito *et al.,* 1993; 1998; Shin *et al.,* 1997; Stein *et al.,* 1997; Teicher *et al.,* 1997). These findings may help to explain the higher incidence of developmental delays and behavioral disorders in this population.

Sexual abuse during childhood has been linked to negative physiologic changes that can affect childhood development. In particular, abnormal hormonal, and pubertal and neuroendocrine changes have been found (De Bellis *et al.,* 1994; Stein *et al.,* 1997). Subgroups of sexually abused girls tend to mature earlier, have different hormonal reactions, and possibly develop impaired immune functioning compared to control girls, as seen in elevated antinuclear antibodies (ANA), a measure of immune system overactivity (De Bellis *et al.,* 1996). Higher levels of urinary catecholamines (a class of neurotransmitter released by the brain's locus coeruleus and the adrenal glands) were noted in abused girls relative to controls. Excessive catecholamine levels induce stress and hyperarousal in the central and peripheral nervous systems, thus inducing sleep disorders, nervousness, and anxiety. In a related study, responses of the stress hormones cortisol and adrenocorticotrophic hormone (ACTH) to the injection of corticotropin releasing hormone (CRH) were abnormal in sexually abused girls compared with controls. This finding suggested that the hypothalamic-pituitary-adrenal axis, responsible for the ''fight or flight response,'' was disregulated in these girls and other parts of this system were compensating for the abnormality by downregulating cortisol levels. Such disregulation has been linked to depression in other studies of adults (Dinan, 1996).

An unusual level of brain cell death can occur due to heightened hormone release (e.g., glucorticoids) in response to child abuse and other traumatic childhood events (McEwen, 1997; McEwen *et al.,* 1995; Sapolsky, 1996; Smith, 1996; Uno *et al.,* 1994). As a result, chronic stress can lead to deficits in learning and memory by the damage stress hormones cause in the hippocampus, a brain structure responsible for memory among other functions. Later in life, the stress associated with traumatic events has been associated with social rank, self esteem and competency in animals and humans (De Goeij *et al.,* 1992; Gust *et al.,* 1991; Higley *et al.,* 1991; Kraemer *et al.,* 1989; Oates *et al.,* 1985; Sapolsky, 1989; Sapolsky & Mott, 1987; Virgin & Sapolsky, 1997). Levels of stress and sex hormones, cholesterol, and immune system function have all been linked to previous stress and present social rank. There is speculation, however, that high quality parenting can minimize problems associated with abnormal levels of neurotransmitter and hormonal activity, regardless of whether the deficit was a function of genetics, environment, or a combination thereof (Field *et al.,* 1998).

Relationships Between Prenatal Conditions and Parenting

Babies exposed to prenatal or perinatal disturbances, or predisposed to a difficult temperament, are often more troublesome to care for. Although some prenatally or genetically disadvantaged babies sleep excessively, others are more volatile and temperamental, cry more frequently, do not develop normal sleep or eating patterns, have colic, and are difficult to soothe. Furthermore, delays in brain development and greater physical needs are often coupled with a lack of appropriate stimulation from their caretakers, particularly in cases when the mother is a drug abuser, a teenager, or unusually stressed or anxious (McIntosh *et al.,* 1995; Ward, 1991); all conditions associated with improper prenatal care, drug exposure, and pre/perinatal complications. As a result, these more ''difficult'' children commonly elicit harsher responses from their primary caretaker who may not have the psychological or physical resources to cope with their baby's special problems and needs. Once the relationship between the caretaker and child is strained, the risk for abuse and/or neglect is much greater. For example, O'Connor *et al.* (1998b) found that adopted children who were at genetic risk by virtue their biological mother's antisocial behavior were more likely to receive negative parenting. Thus, in a developmental sense, these children enter the world disadvantaged and, subsequently, experience harsh, inconsistent, or inadequate parenting (O'Connor *et al.,* 1998a, 1998b). Upon entering school, their difficulties are compounded and risk for behavioral disorders heightened when they exhibit learning disabilities, failure in school, social isolation, and further parental rejection (Moffitt, 1993; Moffitt *et al.,* 1993).

Trauma During Adolescence and Adulthood

Severe and/or chronic traumatic experiences throughout the lifespan can alter brain function. Studies report disruptions in neurotransmitter activity and metabolism as a consequence of trauma. Separation from the mother and social isolation have been shown to increase vulnerability to drug abuse in the affected individual (or animal), with abnormalities in DNA synthesis, hormone responses and neurotransmitter systems as the mediator of this effect (Kuhn & Schanberg, 1998; 1998; Phillips *et al.,* 1997; Piazza & Le Moal, 1996). Post-traumatic stress disorder (PTSD) is also associated with low levels of serotonin activity and other neurotransmitters (Beckham *et al.,* 1997; Fitchner *et al.,* 1995; Kaufer *et al.,* 1998). There is further evidence that severe stress during adolescence can damage coping responses by disrupting neurotransmitter responses (Gerra, *et al.,* 1998; Ryan, 1998). Parental divorce, for example, has been associated with neuroendocrine changes in adolescents (Gerra *et al.,* 1993). Parental divorce can have serious psychological and behavioral consequences during childhood, including problems in peer relationships and a high incidence of aggressive behavior and alcohol consumption. These studies suggest that resulting disorders may be due to changes in the secretion patterns of neurohormones induced by the stress of the parental divorce, thereby reducing adaptation to stress in the adolescent. Fortunately, several factors offer some protection from these deleterious conditions, including quality of the home life, relationships with others, and intimate bonds.

Evidently, exposure to highly stressful and/or novel situations can alter sensitivity of the mesolimbic dopamine reward system, the same system that mediates the rewarding effects of drugs of abuse (Bardo *et al.,* 1996; Cools & Gingras, 1998; Horger & Roth, 1996). Recent studies shed light on individual differences in drug seeking behavior by demonstrating that heightened sensitivity of this system, due to environmental stress or novelty, may increase susceptibility to abuse and addiction (Phillips *et al.,* 1997; Piazza & Le Moal, 1996, 1998). Stress can switch genes on or off at the ''wrong'' times, leading to the development of abnormal networks of brain cell connections, which can result in, for example, excessive secretion of stress hormones (e.g., glucocorticoids). When levels of stress hormones are excessive, their presence increases sensitivity of mesolimbic dopamine neurons to drugs, further exacerbating the risk for drug abuse. Damage to key brain structures has also been associated with stress, producing irregularities in brain function that are similar to those associated with propensity to both drug abuse and impulsive-aggressive behavior. Accordingly, consequences may include learning deficits, mood disturbances, drug abuse, tension, depression, and an inability to cope with external stressors, which all increase risk for psychopathology.

It is evident from this research that social experiences affect psychological processes and can alter neurobiological traits and states. Both acute social stressors that are severe and chronic social stressors, from mild to severe, may produce measurable and long-standing changes in several biological systems

that influence behavior. On the other hand, the extent to which a stressor has an impact on any given individual is also contingent on the unique characteristics and perceptions the individual brings to the situation. Fortunately, the ability of the social environment to alter biological systems is reflective of the malleability of these systems and their outcomes.

IMPLICATIONS FOR PREVENTION STRATEGIES

Findings from research in neurobiology provide food for thought for prevention scientists. Neurobiological findings have demonstrated that individuals vary considerably with respect to their biological strengths (protective factors) and weaknesses (risks). Biological weaknesses or vulnerabilities are influential in an individual's risk for psychopathology. Rather than acting alone, however, this body of research suggests that these biological features operate by setting the stage for how adaptively an individual will respond to personal stressors. A stressful environment is more likely to contribute to some form of psychopathology when it is received by a biological system that is somehow compromised. Thus, although the probability of a pathologic response is a function of the number of these individual risk factors present, the probability is even greater in the presence of an adverse environment with severe stressors. As a result, prevention programs that incorporate findings linking environmental stressors to neurobiological impacts and vice versa are likely to produce improvements in integrity of both psychosocial and biological mechanisms. Once communication and exchange between these disciplines occur, investigators will eventually be able to (a) identify the myriad of interacting risk and protective factors, (b) disaggregate populations with behavioral disorders into relatively distinct subgroups based on prevailing risk factors, (c) determine which interventions work best in particular subgroups, and (d) design interventions to correspond with developmental stage.

So far, neurobiological research shows that stress, both internally and externally induced, affects neurologic processes and behavioral outcomes during particular phases of development. The environment can contribute to changes in behavior by altering

- neurotransmitter responses
- CNS and behavioral activity levels
- blood flow and glucose metabolic rates in the brain
- development of neuronal connections over time
- psychoneuroimmunologic responses
- density of autoreceptors affecting regulatory capabilities
- hormonal responses
- physiologic responses and tone

All of these biological processes underlie many forms of psychopathology. Measurable differences and changes in biological processes that are associated with behavioral and mood state have both genetic and environmental origins. Thus, an individual's developmental trajectory is determined by both genotype and environmental experiences.

Prevention Strategies to Increase Resiliency and Minimize the Impact of Risk Factors

Evaluations of several interventions provide evidence for their effectiveness in reducing the incidence of behavioral disorders (see especially Botvin *et al.,* 1995; Eggert *et al.,* 1994; Olds *et al.,* 1998; Spoth *et al.,* 1998; Thompson *et al.,* 1997; Webster-Stratton & Hammond, 1997). However, benefits accrue only to a subset of participants. Questions that remain to be answered, therefore, are which subgroups of participants are most likely to benefit from which programs and, importantly, what differentiates them from those who do not respond favorably. The research cited herein explicitly suggests that tailored, targeted interventions will be most effective when social and environmental manipulations are ''matched'' to an individual's genotype, thereby reinforcing more adaptive and normative phenotypes. On the other hand, even global, community- or school-wide programs would benefit by addressing environmental conditions that are universally ''contraindicated.''

Specific programs that affect critical brain systems to improve behavioral self-regulation may, in effect, reduce the number of individual risk factors and minimize the impact of environmental stressors. Two characteristics of preventive interventions have potential to yield the highest gains: (1) a stress management and reduction component, and (2) early interventions, from prenatal to preschool stages, to exert an influence before problems become magnified across the lifespan. Examples of approaches that aim to improve an underlying dysfunction include neuropsychological enhancements; cognitive remediation; problem solving training program; ''low-tech,'' small

group interventions within an intensive behavioral rehabilitation program; psychoeducational programs; speech and language therapy; environmental enrichment; computer games for sensory and motor rehabilitation; alternative activities; functional and integrative training; and interdisciplinary consultation.

Rehabilitation programs for head injured patients have potential implications for the targeted treatment and prevention of psychopathology. Several lines of evidence implicate dysfunction of the prefrontal cortex, in particular, in aspects of psychopathology: impulsivity, executive cognitive dysfunction, aggressive behavior, inability to assess consequences, disinhibition, poor coping strategies, and so forth (see Bechara *et al.,* 1996; Frith & Dolan, 1997; Kandel & Freed, 1989; Post & Weiss, 1997; Volavka, 1995). Patients with prefrontal lobe head injuries often exhibit impairments in ability to make rational decisions in personal and social matters, in addition to difficulties in the processing of emotion (Damasio *et al.,* 1994). In brain injured individuals, a functional disconnect between frontal cortical regions, and between the prefrontal cortex and the limbic system, may result in impaired impulse control, reasoning, and decision-making. Thus, the cognitive, behavioral, and psychological challenges that often present themselves after injury are, in some cases, also associated with the executive system impairment seen in forms of psychopathology.

Cognitive and behavioral ''neurorehabilitation'' strategies used for traumatic brain injuries may have protective or therapeutic effects in psychopathologic individuals with prefrontal dysfunction. An approach that combines learning theory, cognitive psychology and neuropsychology to focus on the emotional, motivational, and cognitive functions involved in psychopathology may be used to identify and remediate cognitive and behavioral difficulties (Wilson, 1997). There is evidence that the same tools used to assess executive cognitive skills (i.e., neuropsychological tests) can also be employed to strengthen these abilities (see Giancola, 1999 for a review). Computerized versions of these assessment instruments and cognitive ''games'' can be programmed with a hierarchy of difficulty levels so that as executive cognitive capacity increases, the individual could play more demanding versions.

Another example of a universal prevention strategy that incorporates neurobiological research was designed by Bardo *et al.* (1996). Studies have implicated the trait of sensation seeking in propensity to use drugs and engage in antisocial behavior. Because high sensation seekers are ''biologically prepared to attend to novel information more than low sensation seekers'' (p. 36), prevention strategies should incorporate messages that attract individuals with this biological predisposition. Donohew *et al.,* 1994; Lorch *et al.,* 1994; and Palmgreen et al., 1994 have implemented interventions that convey anti-drug messages using highly sensational program content with high-risk teens. Significant changes in attitudes toward drugs were incurred. Lessons learned from this research are that programs simply attempting to extinguish drug abuse may not be sufficient in high-risk populations; instead, treatment and prevention strategies should replace drug seeking behaviors with new behaviors which are inconsistent with drug use (Bardo *et al.,* 1996).

Other externally focused interventions aim to change the environment to minimize effects of existing dysfunctions and may also have primary preventative effects. Some examples are given, which extend from the findings reported herein.

1. Reinforced interaction with a complex cognitive and sensory environment can both stimulate anatomical and biochemical plasticity and ameliorate some of the behavioral consequences of a stressful, inadequate or deprived environment.
2. Mandatory parenting classes within the school curriculum, early detection and intervention strategies, and a better equipped child welfare system can prevent child abuse. Therapeutic strategies that focus on the neurobiological effects of child abuse may improve integrity of affected neuroendocrine systems, hypersensitivity to stressors, and coping strategies.
3. Stress reduction and prevention programs, in some cases with adjunctive serotonergic agonists, may optimize serotonin activity levels in individuals exposed to chronic or high levels of environmental stress.
4. Parent training, postnatal home visitation, and family therapy are warranted in high-risk populations to mitigate the effects of fetal drug exposure and maternal stress.
5. Very early identification of children at risk, and the provision of a stimulating and nurturing environment with strong social bonds, are critical given that a significant amount of brain development occurs within the first year of life.

6. Adequate prenatal care, particularly for low income populations, may reduce our reliance on the mental health and criminal justice systems given the association between pre- and perinatal complications and later conduct problems in offspring.

Although several biological markers for psychopathology and their relationship with environmental influences have been investigated, their clinical usefulness has yet to be fully explored. It is possible that manipulations of the social environment may alter an individual's biological stamina, improving impulse control and coping strategies. At the present time, however, behavioral scientists are discussing the need for an integrated approach to prevention (see for example Lewis, 1992; Mayes, 1999; West *et al.,* 1990), but the actual research has not yet been done. The few studies that have focused on biological effects of environmental manipulations do provide support for further, more intensive efforts to flesh out related research inquiries. For example, Klintsova *et al.* (1997) demonstrated that complex motor training not only improved motor performance in rats impaired by alcohol exposure, but that the number of synapses per purkinje neuron in the cerebellar cortex (which is normally reduced due to alcohol exposure) increased. In another study, Popova *et al.* (1998) examined the ability of a biological feedback test to alter the integrative activity of the brain in humans, which is involved in psychopathology with phobic syndromes. Behavioral change and alterations in EEG traces were provoked during training on this task. Weisglas-Kuperas *et al.* (1993) reported that children at high biological risk for delayed cognitive development showed favorable responses in mental development, neurological scores, and intelligence to a highly stimulating home environment. And Kuhn and Schanberg (1998) administered massage therapy to rats separated from their mothers and showed marked gains in weight, behavioral development, and sympatho-adrenal maturation.

Capitalizing on the malleability of risk and vulnerability factors, prevention approaches can potentially suppress genetic expression of risk factors by, for example, favorable family environment, if neurobiological research can identify which risk factors are inherited and by what mechanisms they become psychopathology. Similarly, prevention strategies can focus on genetic expressions in specific, high-risk communities if this research can identify the endophenotypes that respond to favorable or adverse community factors.

Future Research Agenda

Although research suggests that certain socioenvironmental conditions alter brain function, the mechanisms for that change are not well understood. Scientific examinations are needed to isolate the neurologic effects of these factors, providing greater insight into specific brain-environment relationships. There is a need for additional human studies, because several of the most intriguing bits of evidence are generated from animal research that cannot be easily extrapolated. Furthermore, longitudinal designs are necessary to identify critical periods of neural sensitivity to environmental influences, and to assess relative contributions of psychosocial stress and phenotypic predisposition. Referring to animal models and recent human studies, prevention scientists can eventually design programs that directly target these effects to reverse or attenuate negative outcomes. For example, effects of prenatal drug exposure on cognitive function and related behaviors have yet to be fully delineated and remain controversial. Some reports provide evidence for both gross and subtle deficits as a result of prenatal cocaine exposure while others do not. Identification of drug effects on the growing fetus and child will lead to a better understanding of prenatal exposures and their possible influence on liability to drug abuse. The prevention implications for such studies are substantial.

Future research questions pertaining to potential linkages between neurobiology and prevention sciences are many and varied, and include the following:

1. What are the neural substrates and their behavioral and temperamental manifestations in various forms of psychopathology?
2. What is the impact of the environment on these neurogenetic mechanisms?
3. What are the critical stages of development during which psychosocial stress differentially exerts its effects?
4. How can the assessment of environmental-neurobiological relationships contribute to the design of interventions that impact at critical points in the developmental trajectory to alter risk status?
5. If the genetic make-up sets the stage for responses to environmental input, can environmental interventions alter (a) genetic expression of risk traits and, (b) the behavioral phenotype, and will the outcome of this impact be sufficiently measurable?

6. Can an integrated data set including both socioenvironmental and neurobiological variables account for more of the variability in intervention response than the use of one set of variables alone?
7. What designs and methodologies can be employed to identify neural substrates amenable to prevention interventions and to assess change over time?

One example of an integrated research design is the examination of changes in brain function in relation to behavioral change during treatment. Theoretically, the use of a combination of neuropsychological, imaging (e.g., PET or fMRI) and behavioral measures before, during, and after an effective intervention will demonstrate a trend toward normalization over time. The same design can examine subgroups that do not respond favorably to identify underlying differences. Thus, the biological impact of prevention approaches can be determined by combining assessment techniques to discern change in both brain function and related behaviors.

The development of this proposed research agenda is predicated on findings generated from a multistage process of research. The purpose of the first phase of studies would be to identify underlying, causal mechanisms in psychopathology, including mental illness, drug abuse, and antisocial behavior. The second phase involves the identification of protective factors that suppress vulnerability, including both internal (certain aspects of temperament, verbal intelligence, cognitive function) and external (caregiver bonds, family stability, targeted community services) resources. A third general area of research is to introduce a preventive intervention and assess the ability of a treatment to alter vulnerability factors, both biological and behavioral. It is expected that treatment effectiveness will be directly related to (a) changes incurred in vulnerability markers, (b) the type and number of existing protective factors, and (c) the lack of immutability and/or severity of vulnerability conditions. And fourth, research must address the ways in which protective factors moderate outcomes in the presence of inherent liabilities to psychopathology. In such a rare but informative protocol, neurobiological measures are treated as independent variables in the initial stages of research, while in the later stages, neurobiological factors are manipulated as dependent variables to assess response to an intervention stimulus.

Research in neurobiology suggests that a sole focus on the social contributions to behavioral disturbances is insufficient. Nor is it adequate to simply examine neurobiological influences. Individual vulnerability and protective factors differentially relate to and are altered by environmental conditions to either heighten or minimize risk for psychopathology. In accordance, a more comprehensive and effective approach to the science, treatment and prevention of psychopathology involves exploration of the relationship between neurobiological and psychosocial forces. As a result of the ineffective, unidimensional approaches of the past, we are now defaulting to the mental health and criminal justice systems with troubled individuals. Rather than ignoring the warning signs in childhood and waiting until adulthood to put these systems into motion, spending billions of dollars for legal remedies that do not produce favorable outcomes, the provision of sorely needed services and interventions to high risk individuals can yield far greater benefits.

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