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Review

# Rising rates of depression in today's society: Consideration of the roles of effort-based rewards and enhanced resilience in day-to-day functioning

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**Abstract**

Despite the existence of a vastly improved health care system and a multi-billion dollar antidepressant industry, the rates of depression in the US remain alarmingly high. An exploration of lifestyle changes over the past century suggests that the level of physical activity necessary to provide life's basic resources, referred to as *effort-based rewards*, has diminished in our industrialized, technologically advanced, service-oriented society. The evolution of the accumbens–striatal–cortical circuitry and its modulating neurochemicals in our ancestors played a significant role in sustaining the continued effort critical for the acquisition of resources such as food, water and shelter; consequently, vast reductions in the degree of physical activity required to obtain necessary resources in today's society likely lead to reduced activation of brain areas essential for reward/pleasure, motivation, problem-solving, and effective coping strategies (i.e. depressive symptomology). Comparative cultural and gender analyses reinforce the significant role of effort-based rewards in mood regulation, suggesting that minimal engagement in such endeavors leads to compromised resilience upon exposure to life's stressful challenges. If physical activity is indeed important in the maintenance of mental health, increased emphasis on behavioral and behavioral/cognitive preventative life strategies, as opposed to an emphasis on psychopharmacological strategies directed at very specific neurochemicals after the onset of depression, should be adopted as protective measures against the onset of depressive symptomology. Thus, strategies that include more global neurobiological activation in the relevant context of directed efforts provide a fresh perspective for depression research.


*Keywords:* Depression; Effort-based rewards; Behavioral/cognitive therapy; Accumbens–striatal–cortical circuitry; Sociocultural influences; Resilience

**Contents**



## 1. Introduction

*Happiness, then, is something final and self-sufficient, and is the end of action. (Aristotle, Nicomachean Ethics, 350 B.C.)*

Over the course of the last century, developing countries have enjoyed unprecedented gains in prosperity and health. Life expectancies have increased by over 50% in countries such as Egypt and India; additionally, diseases such as

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smallpox, once killing millions annually, have been eradicated (Kleinman and Cohen, 1997; Seligman, 1990). Examples of such strides in physical well-being are abundant; however, this progress has not extended to mental health. Even though a multi-billion dollar antidepressant industry exists, The World Health Organization estimates that depressive and anxiety disorders lead the list of mental illnesses across the globe—and these disorders are responsible for approximately 25% of all visits to health care centers around the world. Currently, it is estimated that (Parker et al., 2001) 121 million people are suffering from depression. In the US, depression is one of the most prevalent forms of mental illness with lifetime rates ranging from approximately 10 to 22% for men and women, respectively (World Health Organization, 2005; Kessler et al., 2003; Un, 2004). The irony that, in the midst of unprecedented affluence and a substantial antidepressant pharmaceutical industry, rates of depression are continuing to rise, presents a conundrum to researchers, requiring further exploration of relevant factors related to the onset of depression.

As we have recently entered the new millennium, perhaps it is beneficial to step back and examine the larger picture of depression that has emerged over the past century. A flurry of research activity has emphasized the role of serotonin in the onset of depression and, no doubt, we have acquired an immense amount of information about this neurochemical system. In spite of the marketing success of antidepressants, however, many researchers have questioned the efficacy of this therapeutic approach. Researchers have yet to identify a biological test of depression; additionally, a clear relationship between serotonergic activity and depressive symptoms has yet to be firmly established. These observations have prompted many scientists and clinicians to question the pervasive use of antidepressants, especially SSRIs, in today's society (Healy, 2004; Healy, 1997; Kirsch and Antonuccio, 2002; Valenstein, 1998). As we contemplate the aforementioned increases in depression over the past century, an important question arises as we consider how the serotonergic system, or any other neurobiological system for that matter, deemed to be a critical factor related to the onset of depression, has changed so drastically in such a short period of time to accompany the changing rates in depression. Aside from mutations, such rapid evolutionary alterations of essential biological systems are unprecedented in mammals. Focusing on the bigger picture of human lifestyle, however, it is evident that in many cultures across the world there have been drastic changes over the past several generations in the way humans live. Accordingly, the mental health field has been criticized by anthropologists and others for focusing too narrowly on the biological causes of depression at the cost of discounting variables such as culture and socioeconomic status. In fact, mental health researchers have been challenged to 'formulate a perspective that better explains the interplay among the socioeconomic, cultural, and biological aspects of mental illness' (Kleinman and Cohen, 1997, p. 89)

The purpose of this theoretical article is to attempt to meet the aforementioned challenge by developing a perspective that incorporates neurobiological evidence and sociocultural variables to provide new insights into causes of depressive symptoms and, more importantly, consider strategies leading to protection against the onset of these symptoms. To accomplish this goal we will consider (1) lifestyle and cultural variables providing clues about rates of depression, emphasizing alterations in the amount of physical effort required to survive in contemporary societies (2) the neurobiology of the reward system of the brain and its interconnectedness with brain areas sustaining directed effort, (3) the evolution of brain areas supporting manual dexterity and tool use and implications for mood alterations, and (4) a reassessment of current therapeutic approaches (in light of the proposed behavioral effectiveness perspective of depressive symptoms) including serious consideration of the value of gaining more neurobiological information about response strategies corresponding with resilience, as opposed to the current focus of response strategies accompanying depression.

## 2. Influence of lifestyle and cultural variables in the onset of depression

Two epidemiological studies of depression conducted in the 1970s provided strong evidence that lifestyle changes over the past century were worth examining as potential causes in increased rates of depression. These studies focused on lifetime prevalence of depression in a cross-sectional design. Because common wisdom suggests that older individuals would have more opportunities and reasons to develop depression; higher rates of depression were hypothesized in older populations. Surprisingly, this hypothesis was not supported. Overall, one study found that individuals born in the middle third of the 20th century were 10 times more likely to suffer major depression than individuals born in the first third of the century (Klerman et al., 1985). Thus, individuals who had endured more adverse conditions—wars, the great depression, typical losses associated with living to an advanced age—reported less depression than their younger cohorts in this study (Seligman, 1990). These findings were corroborated in a second epidemiological study (Robins et al., 1984).

An examination of the nature of lifestyles over the 20th century reveals a plethora of changes related to physical exertion. Focusing on the workforce, with the onset of industrialization, the nature of the labor force shifted from industries comprised of 'production' occupations such as foresters and farmers, to professional, service and technical workers. The percentage of farmers in the work force was 38% at the beginning of the century but only 3% at its end. Service-related jobs comprised the growth sector of the 20th century—rising from 31% in 1900 to 78% of all workers in 1999 (Fisk, 2001). In the production jobs that remained, the entrance of technology greatly reduced the amount of physical exertion required to manufacture products.

As technology entered the homes—refrigerators, dishwashers, vacuum cleaners, clothes washers and dryers, etc.—less physical exertion was required to maintain households, enabling homemakers of the time to shift their efforts and time from energy directed toward home production to paid jobs. Also influencing activity levels was the availability of prepackaged food, frozen dinners, and, eventually an onslaught of cheap, convenient fast food. Anthropological evidence suggests that our hunter and gatherer human ancestors expended excessive physical effort to obtain their food; their skeletal remains indicate the presence of considerably more muscular tissue than observed in contemporary humans. According to S. Boyd Eaton, an expert on Paleolithic diets, "Life during the agricultural period was also strenuous, but industrialization has progressively reduced obligatory physical exertion" (Eaton et al., 1996, p. 1734).

Considering these rapid societal changes, our society is in the early stages of an interesting experiment. When one considers that, following 100,000 generations of hunter–gatherer and 500 generations of agricultural ancestors, only 10 generations of humans have lived since the commencement of the industrial age (with a mere two generations living in the era of processed fast foods), it is obvious that lifestyle changes are occurring at a dramatically faster pace than have ever been experienced in the history of the human race. It is important to emphasize that, in the midst of all these changes, our genes are executing the same biological programs seen in the earliest humans with the majority of our neurochemistry tuned to the lifestyles enjoyed by our ancestors over 10,000 years ago (Eaton et al., 1988). Certainly, the changes in nutritional content of foods have dramatically influenced our neurochemistry since the evolution of the earliest humans; but, more central to this article, the *physical exertion* necessary to produce the food essential to the sustenance of our bodies has decreased dramatically as well.

Thus, although there is no convincing evidence that our genetic or biochemical makeup has changed throughout the past century, there is dramatic evidence of lifestyle changes. If our bodies evolved to maintain significant increases in levels of activity to produce food, shelter, and other important resources, how has the sudden decrease of such required effort influenced the neurobiology of individuals in contemporary society? Although there are many factors that have been firmly established as contributing to the onset of depression—hormones, neurotransmitters, stress, lack of social support, decreased perception of control, etc.—a unique theoretical approach is presented herein. The current theoretical approach considers the interplay between cultural and neurobiological systems and, further, how a brain that evolved to exert physical exertion to obtain tangible resources/consequences is profoundly affected when it suddenly finds itself in a world in which it can order dinner, purchase a home, make travel arrangements, entertain itself for hours—all without having to exert any effort (other than dialing a cell phone or pressing a button on a computer). The aforementioned decline over the past century in required physical exertion in the US, and the corresponding rapid increases in rates of depression during this time, provides preliminary evidence that directed physical effort yielding desired consequences (i.e. effort-based rewards) necessary for survival may be an important variable contributing to the dramatically increased rates of depression in today's society.

Another statistical correlate of depression, namely gender differences, may also provide insights into the causes of this condition. As mentioned previously, women suffer depression at about twice the rate of men (Nolen-Hoeksema, 2001; Nazroo, 2005) Certainly, many biological variables influence this disparity, but it is interesting to consider the role of cultural variables as well. In a review of studies examining rates of depression in numerous cities and countries across the world, regardless of the overall rate of depression, women's rates were consistently twice that of the men (Nolen-Hoeksema, 1990). There were a few exceptions, however, noted in this review. Gender differences in rates of depression were not observed in a few cultures such as Nigeria or in rural areas of Iran. Although the methodologies utilized in these studies lacked consistency in several cases, the causes of the lack of gender differences in these cultures is interesting to consider, albeit cautiously until more controlled studies can be conducted (Nolen-Hoeksema, 1990). Additionally, within the US population, no sex differences were found in pre-pubescent children, in college students, or in the Old Order Amish (Nolen-Hoeksema, 2001). Looking closer at these exceptions, it is interesting that in both Nigeria and rural Iran women play a significant role in society, and are expected to contribute to the economic resources. Women in Nigeria engage in farming, fishing, and craft work along with Nigerian men (The Post Colonial Web, 2005). In rural Iran, women are also active in agriculture and handicrafts and contribute to the economic success of their families (The Embassy of the Islamic Republic of Iran, 2005). Hence, although studies specifically addressing these issues have yet to be conducted, these observations suggest that the disparity between rates of depression in men and women decreases in societies in which the women's physical efforts produce meaningful outcomes for their survival.

Looking more closely at women in the US, working mothers with husbands contributing to household chores, who also report no problems arranging childcare, exhibit lower levels of depression than working women with less consistent childcare and less help at home (Wollersheim, 1993). Working women who report being responsible for things outside of their control report high depression rates. Further, women staying at home who have more control over their efforts yet perceive themselves engaging in repetitive actions lacking meaningful outcomes also report high depression rates (Lennon, 1994). Thus, although gender differences in depression likely represent multifaceted interactions between environmental and biological factors, these studies suggest support for the effort-based reward theory in that women who perceive more control and more meaning associated with the consequences of their efforts experience lower levels of depression than women perceiving less control and meaning associated with their actions.

Regarding the lack of gender differences in college students, there are fewer gender-dependent expectations for individuals during this time prior to entering the work force, and for most, having their own families. Further, in Amish cultures, women are expected to engage in many activities to produce products necessary for their family's well being—similar to US women at the turn of the last century and earlier. In one study, the activity of the Old Order Amish was monitored and reported that they engaged in about six times the amount of physical activity performed by modernized communities, spending 10 h a week in vigorous physical activity and approximately 43 h in moderately intense activity (Basset et al., 2004). It is important to emphasize that these 'active' hours are not spent on a treadmill at a gym—the resources necessary for this traditional lifestyle are dependent on these actions—making them extremely meaningful endeavors. Although the effect is sometimes indirect, these cultural data provide further support for the notion that individuals such as the Old Order Amish, who have the opportunity to engage in directed efforts that lead to meaningful outcomes; have lower rates of depression than their cultural counterparts who either lack control in the consequences of their efforts or have diminished opportunities to engage in physical effort that leads to desired consequences (US Public Health Services, 2005; Egeland and Hosteller, 1983).

These epidemiological and cultural studies provide evidence that, in addition to genetic predispositions, trauma, dietary alterations, lack of control, low socioeconomic status, and decreased social support, the opportunity to engage in physical activities that lead to desired outcomes (i.e. *effort-based rewards*), is an important variable that deserves consideration as a contributing factor in the depression equation. Although other lifestyle changes accompanying the modernization of society (e.g., information overload, fast-paced schedules, and high personal expectations) have been offered as explanations for rising rates of depression (Yapko, 1997), lack of effort-based rewards has yet to be considered in a serious manner in mental health research. The statistics recently released by a German health insurance firm conveying that depression rates in Berlin have increased by 70% since 1997, a rise accompanied by Germany's high unemployment rate (approximately 5 million unemployed) (BBCNews World Edition, 2005) also confirm the importance of one's work environment in the maintenance of mental health. The high unemployment rate, a lifestyle alteration, limits the opportunities for effort-based rewards and could very likely lead to depression. Further, considering the gender differences in depression once again, it has been suggested that the coping strategies observed in men and women may be associated with higher rates of depression in women in most cultures. Specifically, men are more likely to distract themselves with an activity, whereas females are more likely to ruminate—thinking and talking excessively about a problem—perhaps enhancing the perception of the magnitude of the problem (US Public Health Services, 2005).

The idea that effort-based rewards play a central role in mood disorders, especially in depression, is not new. A closely related line of research, i.e. the classic learned helplessness paradigm, for example, is a mainstay of depression research. In the 1960s a flood of research was conducted on learned helplessness, in which dogs, and later rats, were exposed to shock and not allowed to escape. Later, when given the opportunity to escape, the animals exhibited depressed activity, refusing to attempt to escape the painful shocks. This finding was attributed to the idea that the dogs learned that their actions were not associated with desired consequences, leaving them helpless as they endured the shocks. The explanation for these observations, however, is somewhat controversial due to the intensity of shock necessary to produce the depressed activity and the short duration of the effect found in some studies (Seligman and Weiss, 1980).

The proposed theory that effort-based rewards play an important role in the prevention of depression is in many ways an extension of the classic learned helplessness research. In fact, after decades of thinking about his research on learned helplessness, Seligman has stated his opinion that the cause of depression boils down to one's belief that his/her actions are futile. The focus of the proposed theory, however, is shifted from the inability to produce an escape behavior, to the importance of having repeated opportunities to direct our physical efforts toward meaningful outcomes. Certainly, even with adequate experience with effort-based rewards in our lives, a traumatic experience in which individuals find that their efforts fail to diminish physical or psychological distress will alter one's neurobiology and lead to emotional vulnerability. The establishment of strong relationships between efforts and rewards, however, may speed one's recovery from this emotional vulnerable spot or prevent a clinical episode of major depression. In the absence of trauma or intense stress, significantly reducing effort-based rewards from our lives—as seen in many modernized societies or in low socioeconomic strata of societies—potentially leads to diminished effective coping abilities and subsequent increased anxiety and for many, eventually, depression (Lorant et al., 2003). The importance of effective coping mechanisms in the face of mild challenges was recently observed in rats. Rats categorized as active and exploratory had lower corticosterone levels when exposed to subsequent novel stimuli than their shy counterparts; additionally, the life spans of the active, uninhibited rats were approximately 30% longer than the shy, inhibited rats (Cavigelli and McClintock, 2003). Thus, coping strategies utilized in day-to-day functions may have a significant impact on our physical and mental health.

In sum, the concept of effort-based rewards is proposed to provide consideration of the importance of physical effort (and all of its accompanying neurochemical, neuroanatomical, neurophysiological, cognitive, and affective correlates) in mental health. Although extensive research has been conducted to elucidate the neurobiological correlates of goal-directed behaviors (including components such as response initiation) (Robinson et al., 2005; Carelli, 2004), the concept of effort-based rewards emphasizes the role of *physical effort* and its association with the emergence of rewarding and/or meaningful consequences. Now that the importance of life-long effort based rewards in the maintenance of mental health has been proposed, it is appropriate to turn our attention to the neurobiological mechanisms sustaining the directed effort necessary to obtain the resources essential for our survival—that is, up until the last 10 generations of our species.

## 3. Neurobiological mechanisms of effort-based rewards: relevance for depressive symptomology

A majority of the symptoms the DSM-IV-TR lists as criteria for obtaining a diagnosis of depression has been associated with known functions of the basal forebrain structure, the nucleus accumbens (American Psychiatric Association, 2000). Mogenson described the unique aspects of this structure several decades ago, noting that the nucleus accumbens was anatomically positioned between the brain's motor system (striatum) and emotional circuit (limbic system) (Mogenson et al., 1980). Considering that both of these systems extend to the cortex, this structure may serve as a common denominator for the genesis of several depressive symptoms including diminished interest or pleasure, psychomotor agitation or slowness, decreased motivation or energy, and diminished cognitive abilities.

The nucleus accumbens, described as a 'limbic–motor integrator' by Kelley, (1999), could also be viewed as the brain's monitoring system as is receives inputs from many areas across the brain including the prefrontal cortex, thalamus, hippocampus, amygdala, ventral pallidum, ventral tegmental area, noradrenergic cells in the nucleus of the solitary tract and the serotonergic medial raphe nucleus (Groenewegen et al., 1999). The nucleus accumbens is comprised of at least two compartments, the *core* and the *shell*. The core region extends anatomically to the basal ganglia motor structures whereas the shell projects to limbic regions such as the hypothalamus, ventral tegmental area, ventral pallidum and autonomic centers of the brain stem (Kelley, 1999; Zahm, 1999). Functionally, the core is thought to be involved with voluntary movement and the shell thought to be involved with motivational systems; more specifically, Kelley has argued that the core, with its NMDA receptors, is intimately involved with instrumental learning, and the shell, with its GABA and AMPA receptors, is involved in feeding behavior (Kelley, 1999). Projections between the nucleus accumbens and the ventral pallidum have been further deemed as the 'motive circuit' as it generates adaptive motor responses from motivationally relevant stimuli (Kalivas et al., 1999). Essentially, this circuit processes the meaningfulness of the stimuli through the limbic nuclei, passes the information through the thalamus to the prefrontal cortex for evaluation of relevance, and projects further to the accumbens–motor system that eventually initiates the suitable behavioral response (Kalivas et al., 1999); however, although a full discussion is beyond the scope of the current article, the function of the nucleus accumbens and associated circuitry extends beyond the simple notion of rewards (see review by Kelley and Berridge for a discussion of the putative role of this circuit in aversive conditioning as well as a distinction between its role in 'wanting' and 'liking') (Kelley and Berridge, 2002). Finally, the striatal component of this motive circuit also influences the experience of rewards as it has been found to play a role in the expectation and detection of reward stimuli as well as the preparation and execution of the movements required to obtain the reward (Schultz et al., 2000; Schultz, 2000). See Fig. 1 for a simplistic overview of afferent and efferent projections of the nucleus accumbens that are necessary for effort-based rewards.

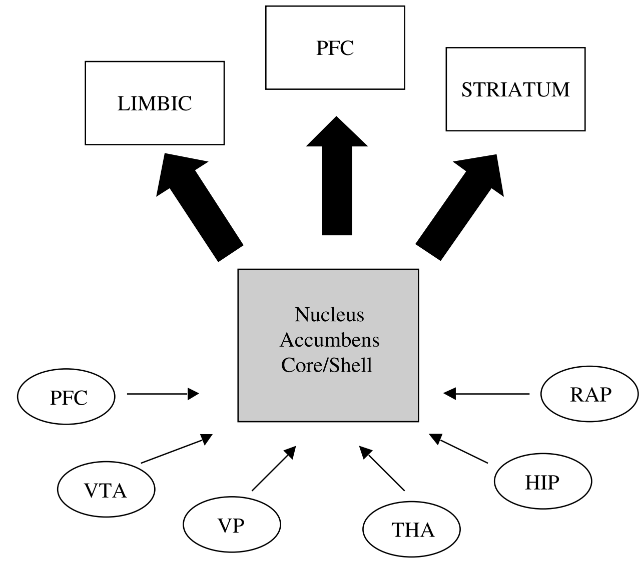


Fig. 1. Accumbens–striatal–cortical neuroanatomical circuit. The Nucleus Accumbens receives input from multiple and diverse areas of the brain including the Prefrontal Cortex (PFC), the Ventral Tegmental Area (VTA), the ventral pallidum (vP), the thalamus (THA), the hippocampus (HIP) and the Raphe Nuclei (RAP). More central to the thesis of the current paper, however, are the accumbens' projections to the limbic system, the PFC, and the striatum. Hence, the Nucleus Accumbens shell and core receives information from multiple areas throughout the brain and projects to areas of the brain involved in emotion and learning (Limbic system), attention/arousal/problem solving (PFC), and movement (Striatum)—all involved in common symptoms of depression (e.g. learning difficulties, fatigue and slowness of movement, and altered emotions).

Research with rodent models suggests that the nucleus accumbens and related areas play an integral role in decisions made about costs and benefits of engaging in various courses of action (Salamone et al., 1997; Cardinal et al., 2001). For example, animals shift to response strategies in which they engage in behaviors requiring less effort—leading to smaller rewards—following depletion of dopamine in the nucleus accumbens (Neill and Justice, 1981; Cousins and Salamone, 1994; Salamone et al., 1994; Cousins et al., 1996); additionally, rats with nucleus accumbens lesions exhibited a preference for smaller rewards requiring shorter wait periods over larger rewards following longer wait periods (Cardinal et al., 2001). Given the role of the rat's medial prefrontal cortex in functions associated with attention, visceromotor activity, decision-making, goal-directed behavior, and working memory, and the well established connections between the nucleus accumbens circuit and the medial frontal cortex (specifically, projections originating in the prelimbic component of the medial prefrontal cortex extend primarily to the nucleus accumbens core and on to the ventral pallidum, whereas the projections originating from the infralimbic cortex of the medial prefrontal cortex extend primarily to the shell of the nucleus accumbens before projecting to the ventral pallidum (Berendse et al., 1992; Brog et al., 1993; Vertes, 2004; Maurice et al., 1997)), one study examined the role of the medial frontal cortex (MFC) in effort-based decision making

(Walton et al., 2002). Prior to surgery, animals chose to traverse a large barrier in a T-Maze to obtain a large reward rather than choosing the path with the small barrier and small reward. Following excitotoxic lesions to the MFC, however, the rats preferred the less challenging barrier path and the smaller reward. After ruling out spatial memory impairment and reduced sensitivity to rewards, the researchers concluded that the MFC was essential in the animals' choice to exert more physical effort to obtain larger rewards. These findings corroborated another study reporting increased DA signals in the MFC of rats when their training protocol was shifted from a continuous fixed ratio-1 schedule to fixed ratio schedules requiring more effort to get the same reward (Richardson and Gratton, 1998).

Looking more specifically at the infralimbic and prelimbic regions of the ventral medial prefrontal cortex, researchers recently found that this structure plays a role in the determination of the controllability of the stressor (Amat et al., 2005). Using a rat model requiring animals to escape tail shock with wheel-turns, it was determined that the dorsal raphe nucleus (involved in serotonergic activity) is inhibited by this area of the cortex upon shock presentation, squelching the HPA axis activation typically evoked in stressful situations. This study incorporates the role of serotonin and the dorsal raphe nucleus into the accumbens motive circuit, potentially explaining the effects of SSRIs on depressive symptomology. In response to this study, Robbins recently suggested that chronic stress could lead to dysregulation of the ascending serotonergic system, leading to compromised processing in the various striatal and limbic projection sites and ultimately, to compromised cortical information processing—all increasing one's vulnerability for the onset of depression or other affective disorders (Robbins, 2005). Thus, the 5-HT system may be considered an indirect, rather than a central component, of the underlying neuroanatomy involved in depression (i.e. the accumbens–striatal–cortical anatomical system); this perspective may explain the typical lag in time (typically 3–8 weeks) from the administration of antidepressants to clinical effectiveness. Further, reinforcing the importance of effective coping strategies (as previously described), it was proposed that lower brain limbic responses to aversive stimuli initially evolved but, as higher executive centers of the cortex evolved, these centers could be inhibited if the organism perceived a sense of control over the stressors.

A recent morphological study provided further evidence of the intimate relationship between chronic stress and the medial prefrontal cortex. After three weeks of daily restraint stress, the number and length of the apical dendrites of pyramidal neurons in the medial prefrontal cortex were significantly reduced (Cook and Wellman, 2004). Together with prior research establishing a detrimental effect of chronic stress on hippocampal neurons (Watanabe et al., 1992; Woolley et al., 1990), it is likely that this stress-induced reorganization of the hippocampal and frontal cortical areas contributes to alterations in cognition, not unlike the cognitive impairment characteristic of depression. More specifically, hippocampal impairment may lead to an inability to properly evaluate the meaningfulness (e.g. danger) of a situation (McEwen, 1998) and PFC impairment may lead to an inability to modify the fear response triggered by stressors and select the most appropriate coping strategy and cognitive processing to overcome a particular stressful situation (Lupien et al., 1994; Lupien and McEwen, 1997). It is important to note, however, as mentioned parenthetically above, that the nucleus accumbens is also likely involved in the processing of aversive stimuli and accompanying responses, and may play a role in altered responses following repeated presentation of aversive stimuli in various contexts (McCullough et al., 1993; Salamone et al., 2005).

The relationship between the extended nucleus accumbens motive circuit and depressive symptomology has also been investigated in humans. fMRI scans revealed that when subjects had the opportunity to 'work' for a monetary reward, more activation in the brain's striatum, including the caudate and nucleus accumbens, was observed compared to subjects who received the same monetary reward in the absence of required work (Zink et al., 2004). Further, saliency of the money, assessed by skin conductance response and self-report, was greater when the money was earned rather than simply given to subjects. Thus, directed effort toward a reward seemed to enhance the saliency of the reward. This observation that the striatum plays a central role in the modulation of effort-based rewards is corroborated by a MRI study indicating that patients diagnosed with major depression, and experiencing diminished pleasure, possessed abnormal lateralization and degeneration in basal ganglia structures (Lacerda et al., 2003). Finally, another study identified altered brain reward systems in patients diagnosed with major depressive disorder based on observations that the depressed patients reported more reward following a single 30 mg dose of the brain reward neurochemical probe, dextroamphetamine (Tremblay et al., 2002).

Thus, research suggests that the nucleus accumbens, with its motor and emotional components and extensive communications with numerous components of the brain, is poised to influence many behaviors observed in individuals diagnosed with depression. The notion that the accumbens is involved in the modulation of both the behavioral relevance of stimuli and the accompanying effort expended to obtain the stimuli is not new to this article. Several researchers have conducted supporting research and, additionally, presented convincing theoretical evidence of this critical role of the accumbens circuitry (Mingote et al., 2005; Willner, 1983a; Willner, 1983b; Willner, 1983c; Greenfield, 1991). Further, the close relationship between the accumbens–striatal–cortical system and the brain's stress response system provides insight into the toxicity of prolonged, unpredictable, uncontrollable stress on behavioral, emotional, and cognitive functions, leading to increased susceptibility to affective disorders such as depression.

## 4. The role of manual dexterity in the evolution of effort-based rewards: has a clue to increased rates of depression been in our hands all along?

Perhaps it was when our primate ancestors descended from the trees about 2.5 million years ago that our brains, wrists, and hands began morphing into their contemporary structure and form that provided the fine-tuned motor skills necessary for sophisticated tool use. Without the need for arboreal locomotion, primates' long curved fingers and short thumbs were no longer needed and the more flexible wrist, short straight fingers and long thumbs began to evolve to maximize stability while gripping tools. Examination of cranial endocasts of *Homo habilis,* considered the first tool maker, indicate an impression of Broca's area in the left hemisphere (involved in the fine motor control of language). This early Broca's area is adjacent to the motor cortex and is thought to be derived from the motor cortex that controls precise hand movement (Greenfield, 1991). As tool use became more sophisticated, it required advanced problem solving and planning—likely influencing the evolution of the frontal lobe (Ambrose, 2001). Hence, higher-order areas of the human brain likely evolved to accommodate the increasingly sophisticated hand movements necessary for effective tool use; because such tool use required planning and complex problem solving, integral neuroanatomical bonds emerged between our hands and our higher executive functioning areas of the brain.

As areas of our brains evolved to accommodate the effective use of our hands, a considerable amount of brain *real estate* was devoted to their efforts. Tactile discrimination, bilateral coordination of hands, and manual dexterity are involved in the humans' use of hands to manipulate and explore their physical environments. In addition to the involvement of the primary motor cortex, research suggests that areas such as the sensorimotor cortex play significant roles in the brain's control of hands (Disbrow et al., 2001). Thus, although there are many ways that a body can exert effort to acquire resources, humans are unique in their ability to acquire resources through manipulations with their hands, and it is likely that activities requiring fine motor skills, and the accompanying brain activity associated with these manual efforts, activate the 'motive' circuit and related areas to produce strong associations between one's efforts and acquired rewards.

An unlikely mammal, i.e. the raccoon *Procyon lotor*, may provide additional insights into the relationships between directed manual efforts and mental health. Known as ecological opportunists, raccoons have remarkably sensitive paws and, perhaps more than any other nonhuman mammal, are highly adept at manipulating objects in their physical environments (Zeveloff, 2002). Accordingly, the somatosensory area of the raccoon's brain receiving tactile information from the forepaws is significantly larger than observed in other mammals. This observation is interesting considering that research on human tool use suggests that the somatosensory cortex plays a more significant role in neural networking developed to support tool use than in hand movement not utilizing tools (Schaefer et al., 2004). Although the area of the motor cortex devoted to hand/forepaw movement in the raccoon is larger than observed in dogs or cats, it is not as enlarged as the sensory areas related to the paws. Thus, the use of paws to obtain resources is very important to the survival of raccoons as they search for food in streams, as it is necessary for their tactile stimulation to be quite sophisticated to discern a meal (e.g. crayfish) from other nonappetizing components of the environment (a rock) (Zeveloff, 2002; Fox, 2001).

With so much evolutionary energy devoted to the use of the raccoon forelimbs and paws in food acquisition, it would be interesting to conduct an experiment evaluating the effects of depriving the animals of the necessity to forage for food on their mental health. To the author's knowledge such a formal experiment has not been conducted, but informal observations of such an experiment have been reported anecdotally for years. When raccoons are held in captivity and merely presented with their food, regardless of effort, they have been reported to repeatedly douse their food in water as if they are excessively washing the food. Although the latin name 'lotor' actually means *washer*, it is not evident that raccoons ever submerge items/food in the water for the purpose of cleaning them (Fox, 2001). Another explanation is that, because the raccoons run their forepaws along the banks of streams and rivers to catch prey such as frogs and crayfish in their natural habitat, this behavior has become a 'fixed motor program' in these animals, and, when disrupted or no longer required for food acquisition, the neurobiological systems underlying these behaviors are disrupted. In this case, the disruption likely leads to anxiety and the repeated, almost compulsive dousing, may be an attempt to mitigate this anxiety generated from the artificial environment of captivity and re-establish neurobiological homeostasis. In fact, one report of a raccoon in the London Zoo in the 1960s indicated that a maternal raccoon doused her newborns so often that she drowned them (Lydall-Watson, 1963). Although this captivity-induced behavior may be a better model for obsessive–compulsive disorder (Lambert and Kinsley, 2005) than depression, both disorders involve disruptions in movement patterns and are influenced by stress and anxiety.

Considering the amount of brain area devoted to the sensitivity and movement of the hands, it is likely that behavior maximizing the use of the hands (requiring movement of arms/forelimbs, wrists, and fingers) may be the most engaging for the accumbens–striatal–cortical circuit. Although many individuals work in excess of 40 h per week, this work (e.g. pushing buttons, typing, sitting, talking) may not activate our brains to the extent observed in the more intricate and demanding manual tasks performed by various artisans across the world. A wood worker, Harrison Higgins, in Richmond VA recently wrote, "the types of jobs where people actually make something are disappearing, but it is a fundamental part of who we are as human beings, physically, mentally, aesthetically, and it gives a tremendous amount of satisfaction to the maker and the recipient." (Kollatz, 2005; P. H16)

It is important to point out that the thesis of the current article, i.e. the disruption of effort-based rewards, or directed energy leading to desirable outcomes, has compromised our mental health, has been around for centuries. In Gottried Wilhelm Leibniz's *Society and Economy* (1671), as he was describing his scientific conception of the ideal Christian economy, he wrote:

"One might think that artisans today work out of necessity; if all their needs were satisfied, then they would do no work at all. I, however, maintain the contrary, that they would be glad to do more than they now do out of necessity. For, first of all, if a man is unsure of his sustenance, he has neither the heart nor the spirit for anything: will only produce as much as he expects to sell (which is not very much given his few customers); concerns himself with trivialities; and does not have the heart to undertake anything new and important. He thus earns little, must often drink to excess merely in order to dull his own sense of desperation and drown his sorrows, and is tormented by the malice of his journeymen. But, it will be different there: Each will be glad to work, because he knows what he has to do. Never will he be involuntarily idle, as he is now, since no one will work for himself, but rather jointly; and if one has too much and the other not enough, then one will give to the other. (Chambless, 1992)".

In this treatise, Leibniz suggests that an artisan's work is important for the maintenance of mental health, above and beyond the acquisition of necessary resources. When disrupted, he describes symptoms currently associated generally with anxiety, including depression—e.g. a lack of control, lack of energy for life's pursuits, increased anxiety with unimportant stimuli, and enhanced vulnerability to addiction.

In another unlikely mental health source, a nineteenth century author presented a similar argument for the manual art of knitting, writing that the needle arts:

"…occupy a distinguished place, and are capable of being made, not only sources of personal gratification, but of high moral benefit, and the means of developing in surpassing loveliness and grace, some of the highest and noblest feelings of the soul (Macdonald and Macdonald, 1988, p. 55)"

These thoughts do not specifically mention accumbens–striatal–cortical circuitry in the implementation of manual artistry; nonetheless, women were making associations between the manual efforts necessary for knitting and mental health at the turn of the last century. A knitting magazine, *Stitches*, claimed that physicians recommended working on a simple piece of knitting, nothing too elaborate in this case, to counteract 'restlessness and discontent.' It was thought that the quick manual movements and the subtle clicks of the needles had a soothing effect on the 'overwrought' women. (Macdonald and Macdonald, 1988). Indeed, research conducted by Barry Jacobs and his colleagues suggests that repetitive movement leads to increased serotonergic activity, which may play a role in relieving anxiety/stress (Jacobs, 1994). Additionally, research indicates that dopamine release in the nucleus accumbens, especially the shell, is more closely associated with the response rates of rats in operant conditioning tasks than the magnitude of the reward (i.e. number of food pellets received) (Sokolowski et al., 1998). Although multiple neurochemical and neuroanatomical systems are likely involved in the maintenance of repetitive movement of the arms and hands, the aforementioned neurochemicals, serotonin and dopamine, significantly influence an organism's affective state.

Thus, our brains have deep roots in the efficient implementation of the manual efforts necessary to acquire the resources of our ancestors. Consequently, it is possible that our technologically advanced lifestyles, requiring minimal physical effort and less complex manual movements in some cases than conducted by our ancestors, has led to compromises in pleasure, motivation, and cognitive abilities in contemporary humans—symptoms that have been collectively referred to as depression. Interestingly, considering the increased rates of depression in women, it may be important to consider that female chimpanzees exhibit enhanced persistence and skill in tool use, suggesting that they may be more sensitive to the disruption of manual complexity accompanying the day to day functions than males (Boesch and Boesch, 1984). Looking in our recent evolutionary past, however, suggests that manual artistry, requiring maximal engagement of this neural circuitry, has been an integral component of past cultures across the world. The recent prevalence of these activities in the lives of our ancestors may explain why, today, with clothing being made quite easily with technologically advanced equipment, knitting is becoming a popular pastime for women—and men—and children—across the US, with most knitters claiming that they engage in this 'work' because it is relaxing (Macdonald and Macdonald, 1988). About a decade ago researchers followed over 2000 individuals over the age of 65 years in France and found that participation in leisure activities such as knitting and gardening protected against the onset of dementia (Fabrigoule et al., 1995).

If effort-based rewards are necessary for the maintenance of mental health, especially protection against depression, there is likely a multitude of individual differences in the threshold of the intensity of motor effort—and the degree to which fine-tuned complex movements of the hands and arms are required. Although the emphasis has been placed on manual movements in this section, certainly other movements are also necessary for survival and are likely integrated with and supported by the accumbens–striatal–cortical pathways. For example, unlike our primate relatives, humans are well-adapted for endurance running (Summers, 2005). Research suggests that the serotonergic system that has been extensively implicated in depression symptomology is activated during certain aspects of the quadrupedal stepping cycle—with the spike discharge rate increasing with faster running speeds or greater respiration responses (Jacobs et al., 2001). As discussed earlier, the serotonergic system, receiving input from the MFC, is involved with perception of control over stressors and plays a definite role in the expression of anxiety/depression symptoms. Running has also been associated with increased neurogenesis, another factor that has been associated with diminished depressive symptomology (Jacobs et al., 2001).

Focusing on types of physical activity exhibited by children, increased involvement in sports and hobbies is related to adaptive functions whereas more involvement with other activities conducted during free time such as 'hanging out with friends' and playing outdoors has been associated with maladaptive functions. Hence, activities involving more intense and organized physical activity, including manual dexterity, seem to be more adaptive than other types of activities (McHale et al., 2001). If certain forms of physical activity are important for adaptive adjustment/responses, then increasing rates of television viewing in children (i.e. children spend 20 or more hours viewing television per week: (University of Michigan Health System)) could be problematic for the mental health of developing children.

## 5. Reassessment of current therapeutic approaches for depression

Currently, consumers who approach two US authorities on mental illness, i.e. the National Institutes of Mental Health (NIMH), (2005) and the National Alliance on Mental Illness (NAMI), (2005) quickly learn that the most information provided about treatment for depression on their respective websites concerns medications (e.g. SSRIs, MAOIs) while considerably less information is provided about other forms of therapy such as psychotherapy and electroconvulsive therapy. When one considers the efficacy rates of various treatment strategies for depression, it is interesting that two forms of psychotherapy (i.e. cognitive/behavioral and interpersonal therapies) have comparable effectiveness with pharmacotherapy (Hollon et al., 2002). Although psychotherapy, more broadly defined, was deemed ineffective a half century ago by Eysenck, (1952), more current uses of cognitive/behavioral and interpersonal therapies show more promise—as much as medication in fact, without the aggravating side-effects. Further, Kirsch and Antonuccio recently stated the controversial view that, although the response to antidepressants is statistically significant from inert placebo treatment, the effect may not be 'clinically' significant (Kirsch and Antonuccio, 2002). Thus, the controversial and confusing results within the depression treatment literature seem to be converging to suggest that a variety of treatment approaches yield improvement—corroborating the theory of directed efforts described within this manuscript.

If some forms of psychotherapy are just as effective as pharmacotherapy, these avenues of treatment deserve considerable research attention and endorsement. Absent of high costs and side-effects, such treatment strategies have clear benefits over medications. Cognitive/behavioral therapeutic strategies encouraging individuals to engage in behaviors leading to desirable outcomes in the presence of a realistic cognitive context utilize the accumbens–striatal–cortical circuit. Compared to specific, streamlined pharmacological approaches altering certain receptors of a single neurotransmitter system (e.g. SSRIs) in the absence of relevant behavioral and cognitive contexts, the broad neurobiological activation accompanying cognitive/behavioral therapeutic approaches is more likely to have a meaningful and long-lasting effect on the accumbens–striatal–cortical circuitry. Further, as previously mentioned, because repetitive motor activity is associated with increased serotonergic activity, many behavioral therapies (e.g. exercise) modulate the serotonergic and related neurochemical systems (Jacobs, 1994).

It is necessary, however, to point out once again that the emphasis of effort-based rewards in the prevention and/or treatment of depression is by no means a novel concept. The aforementioned learned helplessness research prompted Seligman to propose a cognitive-based treatment strategy emphasizing the importance of optimism and healthy 'explanatory' styles of life's events, suggesting that a pessimistic explanatory style when actions fail to produce intended consequences leads to depression (Seligman, 1990). Further, effort expenditure is a central component of Bandura's theory of self-efficacy, defined as one's perception that he/she possesses the ability to produce an appropriate action to obtain a reward. Interestingly, low self-efficacy has been associated with depression (Bandura, 1997). Currently, intervention programs in middle school children focus on the value of successful completion of various tasks (e.g. athletic, artistic, musical) in a contextualized manner on the development of self-esteem and self-efficacy (Winfield, 1994). Although self-efficacy and explanatory style have strong behavioral roots reminiscent of effort-based rewards, they have evolved into more cognitive theories and therapeutic approaches.

While certain forms of psychotherapy are proving quite efficacious for depression, recent questions have been raised about the importance of psychotherapy following a traumatic experience, an event often leading to depression. Bonnano presents a well-justified argument that some current 'standard practices' such as blanket psychological debriefing following trauma may not only fail to improve the functioning of the affected individual but may pathologize normal reactions leading to natural *resilience* (defined as one's ability to maintain equilibrium, or continue to function normally, during adversity) (Bonnano, 2004; Rose et al., 1999; Bisson et al., 1997). Instead of emphasizing the lack of control and ineffective efforts often re-visited in such psychological counseling following trauma, the re-establishment of effort-based rewards via means mentioned above (efforts leading to recognizable desirable outcomes) may be a more effective approach to preventing the onset of depression or post-traumatic stress disorder (PTSD). Although more research needs to be conducted in this area, a recent study found that the ventromedial prefrontal cortex, a component of the accumbens–striatal–cortical anatomical circuit discussed above, was larger in individuals demonstrating successful fear extinction. It was noted that repeated activation of this circuit may lead to enhanced thickness of the mPFC and, consequently, enhance cognition necessary to reduce anxiety in subsequent events—by establishing or diminishing relevant associations. Thus, it was concluded that 'variability in the thickness of the ventromedial PFC across the human population may account for risk (or resilience) factors for anxiety disorders.' (p. 10710) (Milad et al., 2005). Interestingly, the vmPFC has been shown to be functionally deficient in PTSD patients; that is, PTSD patients show little activation of this area upon presentation of trauma-related cues (Bremner, 2003). Finally, PFC volumes are decreased in other anxiety disorders such as panic disorder and compulsive disorder (Szeszko et al., 1999; Vythilingam et al., 2000).

Hence, the PFC and new learning plays a role in diminishing anxiety; however, also important to the current proposal is the determination of the role of the accumbens and striatal circuitry in resilience. Can resilience—increasingly being touted as important in the prevention of depression from both behavioral and neural perspectives Bonnano, 2004; Curtis and Cicchetti, 2003; Maddi, 2005; Tafet and Smolovich, 2004; Fuchs et al., 2004; Fuchs et al., 2002)—be influenced by persistent involvement with effort-based rewards? This is a question my students and I recently asked and designed a rat model to investigate. We assigned two groups of rats, matching in stress responsiveness (as measured by activity in an open field), into either a working group that was trained to dig up food rewards (pieces of Froot loops cereal) daily from mounds of bedding in a large open field that were moved for each test, and a group of rats that were placed in the same arena with mounds of bedding but were simply presented the froot loops, regardless of exerted effort. Following five weeks of training, a challenge test was presented to the rats—a novel stimulus (plastic lattice cat toy with bell) with a froot loop embedded in a way that it could be seen and smelled but could not be removed from the stimulus. Interestingly, the worker group spent 50% more time directing efforts toward the challenge task in an attempt to gain access to the reward than the control group. These results can be interpreted in many ways, but it appears that the increased experience with effort-based rewards led to increased efforts in a subsequent stressful, challenging task (Tu et al., 2005). Although some researchers may be reluctant to claim that such paradigms are assessing resilience, it is highly likely that animal models can be used to discern the neurobiological underpinnings of effort-based conditioning and its corresponding protection against excessive emotionality and expression of depressive symptomology. Certainly the objective behavior characteristic of animal models is easier to simulate than more subjective psychoanalytic approaches. According to Curtis and Cicchetti, (2003), there has been no systematic investigation of the biological underpinnings of resilience. Further, it has been stated that Bonanno's unique perspective concerning depression and resilience 'opened the way for such comparative analytic research through which researchers can further their current knowledge concerning how resilience under stress comes about.' (Bonnano, 2004, p. 261)

## 6. Conclusions

Perhaps the well-known analogy of a 'drunk' and the lamppost sheds some light on the current challenge of discerning the most meaningful causes and courses of action for depression. In this analogy, a police officer sees a drunk stumbling around a lamppost and asks what the problem is. When the drunk replies that he has lost his car keys, the police officer asks exactly where they were lost. The officer is confused when the drunk replies that they were lost several hundred yards away from the lamppost. When the officer asks why he is wasting his time looking around the lamppost, the drunk replies that there's no sense searching where there isn't any light (Healy, 1997).

It certainly appears that a majority of researchers have been searching for clues about depression under the light provided by the 'serotonergic' lamppost. Whether or not this area is close in proximity to the actual cause/s of depression is arguable, but there is considerable evidence pointing to other areas that should be investigated as well—we now know that other neurochemicals such as dopamine, noradrenaline, and glucocorticoids also seem to play either direct or indirect roles in the onset of depression. Additionally, neurotrophic factors, such as brain-derived neurotrophic factor (BDNF) may be most closely related to the onset or delay of depressive symptomology (Lydall-Watson, 1963; Lang et al., 2004). Antidepressant drugs have been shown to modify BDNF and the BDNF receptor, tyrosine kinase receptor B (TrkB), in the nucleus accumbens, and has an anti-anxiety effect in the forced swim test (Nibuya et al., 1995; Eisch et al., 2003). Other research suggests that any compromise in neuroplasticity can lead to the onset of depression symptoms (Fuchs et al., 2002). Even ECT, effective in resistant depression patients, has been found to significantly increase neurogenesis in rodents in a dose-dependent manner (Madsden et al., 2000).

If neuroplasticity and related factors in the brain are indeed important factors in the onset of depression, how are these factors influenced by increased activity in general, and more specifically, by effort-based rewards? There is strong evidence that exercise increases neuroplasticity (Gomez-Penelli et al., 2002; Hill et al., 1993); in fact, research generally suggests that neuromuscular activity is necessary in the maintenance of healthy levels of BDNF, and enhance the potential for neuroplasticity to occur in the appropriate context. Further, simple exercise has been associated with the expression of gene profiles predictive of neurobiological plasticity and the prevention against depression (Russo-Neustedt et al., 2000). BDNF and other neurotrophic factors have been described as being under activity-dependent control and thought to be essential for the formation of neural networks and enhanced learning and memory—likely enhancing problem solving in stressful, challenging situations (Cotman and Berchtold, 2002). Similar to the accumbens–striatal–cortical circuit proposed to mediate effort-based rewards and subsequent enhancement in problem solving during challenging situations, neural plasticity has been deemed a basic process by which brains obtain information necessary to facilitate adaptive responses in challenging situations (Duman, 2002; Thomas and Davies, 2005). Thus, neuroplasticity seems to be closely tied to adaptive responding and putative protection against the onset of depression.

Concerning the involvement of the serotonergic system, Jacob's aforementioned research focusing on motor activity and serotonin suggests that the firing rates of serotonergic neurons are closely related to behavioral arousal—firing more often during rhythmic physical activity (for example, running) and the least during times of minimal movement such as drowsiness or sleep. Interestingly, serotonergic neurons increase their firing rate in anticipation of a movement, increasing linearly as the rate of strength required of a movement increases or as the movement requires an increased depth of respiration. Consequently, the serotonergic system is more closely linked to gross motor activity involving the torso and limbs than activity only involving the fingers (Jacobs, 1994). Applied to contemporary lifestyle, days filled with minimal aerobic activity and few movements beyond pressing buttons or typing is likely not tapping maximally or even sufficiently into the serotonergic system to maintain mental health.

Perhaps a modified lamppost analogy—one in which a few keys might be found around the lamppost while others are spread throughout the parking lot thus requiring one to search in areas that are not so well–lit—is a more apt description of the current search for causal factors associated with increasing rates of depression in contemporary society. True progress requires researchers to search beyond the serotonergic lamppost to identify a range of therapeutic approaches that lead to true protection, or resilience, against the onset of depression. Focusing on preventative measures, as opposed to the treatment following the appearance of depressive symptoms, is also important in reducing the incidence and relapse rate of depression. Physical activity—especially directed toward the creation of some product or solving a problem with an unknown answer—provides more activation of the brain (e.g. the accumbens–striatal–cortical circuit) than a single pharmacological agent presented in a decontextualized setting. Further, real-time directed efforts provide meaningful context leading to the enhancement of neuroplasticity, increasing the likelihood of adaptive responding in challenging situations, as opposed to nonadaptive responding characteristic of depression. Although suppression of activity is sometimes quite adaptive, excessive withdrawal and failure to direct one's effort toward life's challenges (again, characteristic of depression) may result in the condition known as depression.

If Aristotle's claim that *happiness is the end of action* is correct, then unhappiness (a symptom of depression) might be construed as the end of suppressed action, a claim that is corroborated by the convergence of evidence described in this manuscript (Ross, 2005). This convergence of evidence, i.e. (1) the association of accumbens–striatal–cortical neurocircuitry with the execution of adaptive motor responses and problem solving; (2) the role of neuroplasticity, produced by sustained directed efforts to solve problems, in the protection against mental illness; (3) the involvement of several neurochemicals either directly or indirectly related to one's sense of control over stressful situations; and (4) the evolutionary importance of physical activity—especially rhythmic activity involving limbs and hands, clearly suggests that preventative behavioral therapeutic strategies deserve serious consideration in the battle against depression.

In closing, the goal of this article was to incorporate both sociocultural and neurobiological views in the formation of a more inclusive, theoretical approach to depression. Consideration of the rates of depression among the Chinese, the world's largest ethnic group, provides a sufficient case from which to re-emphasize the importance of these diverse views in reaching a more comprehensive understanding of depression. An epidemiological study, in which teams of psychiatrists and psychologists assessed nearly 20,000 people in different areas of China who were 15 years or older in 1993, reported that only 16 individuals met the criteria for lifetime affective disorders—resulting in a prevalence rate less than .08%—a rate *hundreds* of times lower than reported in the US (as reviewed in Parker, Gladstone, and Chee, 2001). Although some researchers have attributed the low rates of depression in China to cultural differences (e.g. tendency to deny depression or express it somatically) (Parker et al., 2001), it is difficult to imagine that the skilled clinicians in this study completely missed evidence associated with depression in their diagnostic interviews. In keeping with the perspectives emphasized in this manuscript, an evaluation of the prevalence of effort-based rewards across the diverse Chinese cultures may provide valuable insight into the apparent differences in the prevalence of mood disorders existing between the Chinese and US cultures.

According to a recent examination of Chinese culture in the *Harvard Business Review*, whereas, most US residents live in urban settings, two-thirds of Chinese residents live in rural areas (Graham and Lam, 2003). Hence, *agrarianism*, a lifestyle emphasizing the importance of farming-related efforts and characterized by independence and self-sufficiency, remains a fundamental cultural thread woven among the various populations comprising the Chinese culture (this philosophy also remains important in individuals currently residing in urban settings). Thus, the importance of physical activity and the emphasis of effort-based rewards leading to the famed 'work-ethic' of the Chinese and the putative accompanying activation of the accumbens–striatal–cortical neuroanatomical circuits and related neurochemicals (e.g. serotonin, neurotrophic factors) likely converge to produce a day-to-day behavioral strategy that provides protection against the onset of depression.

Does this mean that US residents have to leave their offices and return to a farming lifestyle in order to protect themselves against the debilitating symptoms of depression? A synopsis of themes introduced in Thomas Inge's book, *Agrarianism in American Literature* (Inge, 1969), seems to answer this question:

"Agrarianism is not identical with the back to the earth movement, but it can be helpful to think of it in those terms. The agrarian philosophy is not to get people to reject progress, but rather to concentrate on the fundamental goods of the earth, communities of limited economic and political scale, and simple living—even when this involves questioning the 'progressive' character of some recent social and economic developments (Agrarianism, 2005)".

Hence, periodic assessments of our lifestyles, confirming that we continue to realize effort-based rewards—in our professional and/or personal lives—is perhaps as important to our mental health as periodic cholesterol and blood pressure checks are to our cardiovascular health. As vast differences in dieting practices have significantly impacted our cardiovascular health, extreme modifications of the neural circuitry and associated neurochemicals that evolved to sustain efforts necessary for survival have the potential of significantly impacting our mental health. Requisite doses of 'simple living, ' viewed as clearly established relationships between our efforts and rewards in this manuscript, injected into our contemporary technologically based lifestyles may be the sufficient 'medicine' necessary for the maintenance of healthy mood-regulatory systems and the avoidance of depression.

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