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GUEST EDITORIAL

Evolution, depression and the interplay between chance and choices

Depression is a common and disabling mental disorder that affects people of all ages, cultures and ethnic backgrounds (Henderson *et al.*, 2000; Mathers *et al.*, 2001; Kessler *et al.*, 2005; Prince *et al.*, 2007). Its presence has been recorded throughout history (Berrios, 1985), which suggests that the signs and symptoms of depression are not simply a product of our time. However, given the overwhelmingly negative consequences of depression (Broadhead *et al.*, 1990; Ellis and Gordon, 2004), it may seem surprising that depression is so ubiquitous and that evolution by means of natural selection has not eliminated it from our midst.

This paper outlines a model of depression that suggests that some behavioral and physiological features associated with the "depressive phenotype" are not necessarily maladaptive and disadvantageous. The paper will also argue that such an approach to understanding depression may offer opportunities to decrease the burden of depression in our society. But first, it is important to describe some of the principles that support the theory of evolution and how these may apply to depression.

What is evolution?

Evolution is the process of change in the inherited traits of a population of organisms from one generation to the next (Darwin, 1985). The driving force behind this change is "natural selection", a process by which the inherited traits that enhance reproduction and survival become, and remain, more common in successive generations of the population (Palmer and Barrett, 2009). The heritable traits that are subject to natural selection are not the genes, but their expression: the phenotypes. Phenotype refers to any observable trait of an organism, such as the color of the eyes, shape of the mouth, and specific physiological response patterns or behaviors – without phenotypic variation there would be no evolution! Importantly, natural selection exerts benefits by maximizing reproductive success of the organism, even when that occurs at the expense of the individual's health or happiness.

Has the depression phenotype been subject to natural selection?

Depression is a clinical syndrome characterized by specific physiological and behavioral manifestations that can be triggered by specific contexts (such as stress) (Krishnan and Nestler, 2008). These characteristics indicate that depression is a valid phenotype and, as such, has been and will continue to be subject to natural selection.

If depression were maladaptive, we would expect people with this phenotype to be less successful at surviving and reproducing, which would ultimately lead to the extinction of this phenotype. However, there is no compelling evidence that this might be the case. For example, we asked over 20,000 Australians aged 60 years or over to report the number of children born alive that they had (Williamson *et al.*, 2007). The 643 people with symptoms consistent with a major depressive disorder reported an average of 3.0 children (standard deviation, SD = 1.5) compared with 2.9 (SD = 1.5) for those without depression. Although such observational data are far from conclusive, it does suggest that people with depression may not be at a disadvantage regarding reproduction.

In fact, social theories of depression indicate that, in some circumstances, the behaviors associated with depression may be adaptive and facilitate survival. For example, people with depression may minimize the risk of exclusion from a particular social group by highlighting the presence of risk or stress to members of that group, by displaying behaviors that reduce the perception of threat and elicit social support, or by reducing the individual's propensity to engage in risk behaviors that may hinder survival and their subsequent chance of reproduction (Gilbert, 2006).

Another factor to consider is that phenotypic traits are often inherited together rather than in isolation. For example, people with blue eyes are more likely to have fair skin and straight fair hair than dark skin and black curly hair. This does not mean that blue eyes never occur in people with dark skin and black curly hair, but such a grouping of phenotypic traits is uncommon. Moreover, the combination of certain traits may offer some advantages. For example, people with

blue eyes, fair skin and blond hair are better adapted to the living conditions of regions where there is limited exposure to sunlight. They also have the advantage of being more competent at synthesizing vitamin D, thereby decreasing their risk of osteoporosis and fractures. In contrast, people with dark skin and associated traits cope better with greater exposure to sunlight (and associated ultra-violet rays) in regions closer to the Equator and have a lower risk of developing skin cancer than fair-skinned people (Neer, 1975). Likewise, there is some evidence that the signs and symptoms of depression are not inherited in isolation, but together with other traits that may be adaptive in some, but not all, circumstances.

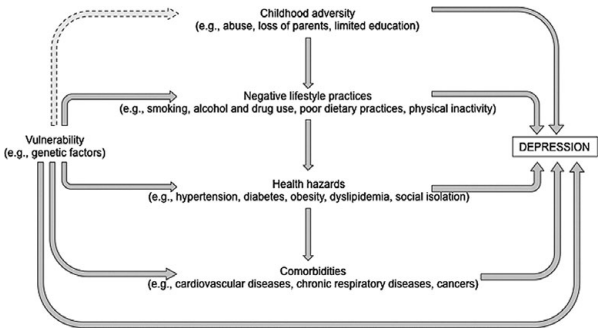

Figure 1. The figure shows possible pathways linking vulnerability, life experiences, lifestyle, and health hazards and morbidities to depression. The dashed arrow indicates the presence of a link that is not well established.

Depression and the interplay between chance and choices

Numerous risk factors have been associated with the development of depressive symptoms throughout the lifespan. Most seem to represent some form of exposure to stress, either psychological or physiological (Tennant, 2002). Real or perceived losses increase the risk of depression, even when they do not have a close temporal relationship with the onset of depressive symptoms (Brown *et al.*, 1977). For example, physical and sexual abuse during childhood, early loss of parents and limited education increase the risk of depression throughout the lifespan, including later in life (Almeida *et al.*, 2011). These early negative experiences seem associated with the adoption of potentially harmful lifestyle practices, such as smoking, hazardous or harmful alcohol or drug use, poor diet and limited physical activity. Further stresses accrue, with the development of financial and social concerns (including broken relationships), hypertension, diabetes and obesity. These, in turn, may increase the risk of cardiovascular diseases and events (such as myocardial infarction and strokes) as well as of various chronic morbidities, such as respiratory diseases and cancers (Almeida *et al.*, 2011). Figure 1 illustrates this putative pathway of cumulative stresses and their possible contribution to the onset of depressive symptoms.

Clearly, some of the stressors that contribute to the onset of depressive symptoms are not amenable to change (such as genetic makeup and loss of parents), but most seem potentially modifiable by means of public health interventions (such as greater access to education) or personal choices (Almeida *et al.*, 2011). The question remains, however: why do some people seem to cope better with stressors (and not develop depression) than others (who do develop depression)?

Nearly ten years ago, Caspi and colleagues reported a surprising finding. They observed that a common polymorphism in the promoter region of the serotonin transporter gene was associated with increased risk of depression and suicide behavior only when stressful life events increased in number (Caspi *et al.*, 2003). In other words, this particular polymorphism seemed to decrease the individual's ability to cope with insults, and led to the expression of a depressive phenotype as stressors accumulated. Dozens of independent studies have since confirmed these associations (Karg *et al.*, 2011).

More recently, Almeida and colleagues showed that a polymorphism of the C-reactive protein (CRP) gene that undermines the physiological response to acute stress increases the risk of depression in older men (Almeida *et al.*, 2009). They argued that the rise in the serum concentration of CRP that has been associated with depression (Almeida *et al.*, 2007) might be adaptive and potentially protective. In this case, the association between CRP and depression would be analogous to indication bias, where treatment for a disease is associated with that disease. That means that it would be the inability of the individual to mount an effective response to stress that would increase the risk of depression, not the response itself.

McEwen suggested that organisms react to real or perceived challenges in two ways (McEwen, 1998): (i) they mount an acute allostatic response that initiates a complex adaptive pathway (for example, to combat an infection), and (ii) they turn off the allostatic response when the threat or harm is no longer present. Whilst the acute allostatic response is commonly adaptive (for example, coagulation cascade triggered by bleeding associated with a cut or other injury), chronic allostatic load may result in damage to the organism because of repeated hits, lack of adaptation (i.e. decreased ability to turn off the allostatic response),

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prolonged (i.e. no recovery) or inadequate responses. McEwen suggested that a flattened or inadequate acute allostatic response to an insult leads to compensatory hyperactivity of other stress-related mediators (such as cytokines), and that this could contribute to the development of sickness behavior (i.e. behaviors and experiences associated with poor health) and depression (McEwen, 2006). Such a model would be consistent with the idea that depression results from the interaction between repeated stresses (partly determined by one's choices) and inefficient response to stress (partly determined by the genetic makeup of the individual).

Is there any advantage in having a suboptimal response to stress?

Korte and colleagues described the way in which two broad phenotypes manage stress (Korte *et al.*, 2005). The first, which they labeled the "Hawk", shows a behavioral pattern that is dominant and aggressive, ready to confront risks, proactive, efficient in managing acute stress, and successful in times of abundance. Physiologically, Hawks display a high concentration of testosterone and low concentration of cortisol. The second phenotype, the "Dove", flees danger; is cautious and collaborative, adaptable to the circumstances, and copes relatively well with scarcity. Doves display low concentration of testosterone and high concentration of cortisol (Korte *et al.*, 2005).

Consistent with this model, Almeida and colleagues showed that depression is more prevalent amongst older men with low free testosterone (Almeida *et al.*, 2008), and there is some evidence that people with depression display an augmented secretion of cortisol in response to stress (Strickland *et al.*, 2002). In addition, the behavioral pattern of "harm-avoidance" suggests that a robust acute allostatic response may be unnecessary and potentially wasteful amongst Doves, even though this may render them more vulnerable to repeated stressful events. However, one could argue that evading harm and maintaining a collaborative and non-threatening attitude might increase the chance of reproduction and survival in a hostile environment where resources are sparse.

On the other hand, when resources are plentiful, being competitive and taking risks might maximize the chances of success, although people with the "Hawk" phenotype may also be more impulsive, rigid and violent, seek immediate reward, and struggle to adapt when resources are limited (Korte *et al.*, 2005). So, is it better to be a Hawk or a Dove? It really depends on the circumstances. But one thing is certain: such phenotypic variability has contributed to our survival thus far.

Why does the prevalence of depression decline with increasing age?

Psychological and physiological stresses accumulate throughout the life course. Thus, one would expect the prevalence of depression to increase as people age. However, most epidemiological data that is currently available indicate that this is not the case (Kessler *et al.*, 2003; Australian Bureau of Statistics, 2008). How can we reconcile these seemingly contradictory findings?

Older adults are, by definition, survivors. And those who survive have either been exposed less frequently to substantial adverse events throughout their lives or have been more successful at managing stresses (behaviorally or physiologically) than those who perished before reaching old age. Hence, the prevalence of depression would be expected to be lower in this particular group of survivors living in the community. However, when stresses become overwhelming in later life, depressive symptoms may arise and the prevalence of depression increase, as is the case in special groups, such as hospital patients, nursing home residents, and older adults with chronic medical conditions such as cardiovascular diseases and neurodegenerative conditions (Djernes, 2006). In fact, this model suggests that cases of late onset depression may indicate a decline in the ability of the individual to cope with mounting stresses (social, psychological or physiological), or the development of frailty (Katz, 2004; Andrew and Rockwood, 2007).

Conclusion

Depression is a phenotype characterized by specific behavioral and physiological manifestations that may be adaptive in some but not all circumstances. Currently available evidence suggests that depression arises when perceived or real stressors overwhelm the capacity of the individual to cope with them. Such a "capacity to cope with stress" is partly determined by the genetic make-up of the individual and by early life experiences, so chance plays a part in modulating the risk of depression. But the capacity to cope with stress can also be enhanced by the acquisition of relevant skills (e.g. those acquired during some psychotherapies) (Alexopoulos *et al.*, 2003), medical interventions (e.g. pain control, antibiotics, surgical corrections, etc.), and circumstances (e.g., availability of social support). Hence, living in an environment that

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mitigates the deleterious effects of stress may decrease the risk of depression.

In addition, if stress causes depression, then reducing the number of stressors should also decrease its risk. And here, choices may play a prominent part. People cannot choose the genes they are born with, their family, or even some of their early life experiences (e.g. early loss of parents, physical or sexual abuse, early access to education), but they can choose whether or not to engage in risk behaviors, such as harmful/hazardous alcohol or drug use, smoking, physical inactivity, poor diet, and inappropriate management of chronic health hazards (such as hypertension, diabetes and obesity) or diseases.

Chance and choices interact during the entire lifespan to modulate the expression of certain phenotypes. Like many other health disorders (Beer *et al.*, 2011), depression is a probabilistic rather than a deterministic product of such an interaction (Almeida *et al.*, 2011). Depression is not caused by a specific gene, or by smoking, obesity, cerebrovascular disease, low serotonin in the brain, physical abuse or early loss of a parent; at least not by any of them alone. Instead, these and various other factors contribute to increase or decrease the probability that a certain individual will express the depression phenotype at some point during his/her life.

We may need to let go of our comforting but unhelpful deterministic theories and embrace the uncertainties of probabilistic models if we wish to increase our ability to modify the risk of depression in our communities. But then, deterministic models of depression may still be more successful at reproducing and surviving in our current environment . . .

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References

Australian Bureau of Statistics (2008). *National Survey of Mental Health and Wellbeing: Summary of Results, Australia – 2007*. Cat. No. 4326.0. Canberra: Australian Bureau of Statistics.

Alexopoulos, G. S., Raue, P. and Arean, P. (2003). Problem-solving therapy versus supportive therapy in geriatric major depression with executive dysfunction. *American Journal of Geriatric Psychiatry*, 11, 46–52.

Almeida, O. P., Norman, P., Hankey, G. J., Jamrozik, K. and Flicker, L. (2007). The association between C-reactive protein concentration and depression in later life is due to poor physical health: results from the Health in Men Study (HIMS). *Psychological Medicine*, 37, 1775–1786.

Almeida, O. P., Yeap, B. B., Hankey, G. J., Jamrozik, K. and Flicker, L. (2008). Low free testosterone concentration as a potentially treatable cause of depressive symptoms in older men. *Archives of General Psychiatry*, 65, 283–289.

Almeida, O. P. *et al.* (2009). Polymorphisms of the CRP gene inhibit inflammatory response and increase susceptibility to depression: the Health in Men Study. *International Journal of Epidemiology*, 38, 1049–1059.

Almeida, O. P. *et al.* (2011). A practical approach to assess depression risk and to guide risk reduction strategies in later life. *International Psychogeriatrics*, 23, 280–291.

Andrew, M. K. and Rockwood, K. (2007). Psychiatric illness in relation to frailty in community-dwelling elderly people without dementia: a report from the Canadian Study of Health and Aging. *Canadian Journal on Aging*, 26, 33–38.

Beer, C., Alfonso, H., Flicker, L., Norman, P. E., Hankey, G. J. and Almeida, O. P. (2011). Traditional risk factors for incident cardiovascular events have limited importance in later life compared with the Health in Men Study cardiovascular risk score. *Stroke*, 42, 952–959.

Berrios, G. E. (1985). The psychopathology of affectivity: conceptual and historical aspects. *Psychological Medicine*, 15, 745–758.

Broadhead, W. E., Blazer, D. G., George, L. K. and Tse, C. K. (1990). Depression, disability days, and days lost from work in a prospective epidemiologic survey. *Journal of the American Medical Association*, 264, 2524–2528.

Brown, G. W., Harris, T.and Copeland, J. R. (1977). Depression and loss. *British Journal of Psychiatry*, 130, 1–18.

Caspi, A. *et al.* (2003). Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. *Science*, 301, 386–389.

Darwin, C. (1985). *The Origin of Species* (first published 1859). London: Penguin Classics.

Djernes, J. K. (2006). Prevalence and predictors of depression in populations of elderly: a review. *Acta Psychiatrica Scandinavica*, 113, 372–387.

Ellis, P. M. and Gordon, S. R. (2004). Beyond description. In P. M. Joyce and P. B. Mitchell (eds.), *Mood Disorders: Recognition and Treatment* (pp. 3–14). Sydney: The University of New South Wales Press Ltd.

Gilbert, P. (2006). Evolution and depression: issues and implications. *Psychological Medicine*, 36, 287–297.

Henderson, S., Andrews, G. and Hall, W. (2000). Australia's mental health: an overview of the general population survey. *Australian and New Zealand Journal of Psychiatry*, 34, 197–205.

Karg, K., Burmeister, M., Shedden, K. and Sen, S. (2011). The serotonin transporter promoter variant (5-HTTLPR), stress, and depression meta-analysis revisited: evidence of genetic moderation. *Archives of General Psychiatry*, 68, 444–454.

Katz, I. R. (2004). Depression and frailty: the need for multidisciplinary research. *American Journal of Geriatric Psychiatry*, 12, 1–6.

Kessler, R. C. *et al.* (2003). The epidemiology of major depressive disorder: results from the National Comorbidity Survey Replication (NCS-R). *JAMA*, 289, 3095–3105.

Kessler, R. C., Berglund, P., Demler, O., Jin, R., Merikangas, K. R. and Walters, E. E. (2005). Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Archives of General Psychiatry*, 62, 593–602.

Korte, S. M., Koolhaas, J. M., Wingfield, J. C. and McEwen, B. S. (2005). The Darwinian concept of stress: benefits of allostasis and costs of allostatic load and the trade-offs in health and disease. *Neuroscience and Biobehavioral Reviews*, 29, 3–38.

Krishnan, V. and Nestler, E. J. (2008). The molecular neurobiology of depression. *Nature*, 455, 894–902.

Mathers, C. D., Vos, E. T., Stevenson, C. E. and Begg, S. J. (2001). The burden of disease and injury in Australia. *Bulletin of the World Health Organization*, 79, 1076–1084.

McEwen, B. S. (1998). Protective and damaging effects of stress mediators. *New England Journal of Medicine*, 338, 171–179.

McEwen, B. S. (2006). Protective and damaging effects of stress mediators: central role of the brain. *Dialogues in Clinical Neuroscience*, 8, 367–381.

Neer, R. M. (1975). The evolutionary significance of vitamin D, skin pigment, and ultraviolet light. *American Journal of Physical Anthropology*, 43, 409–416.

Palmer, D. and Barrett, P. (2009). *Evolution: The Story of Life*. Toppan, China: Octopus Publishing Group Ltd.

Prince, M. *et al.* (2007). No health without mental health. *Lancet*, 370, 859–877.

Strickland, P. L., Deakin, J. F., Percival, C., Dixon, J., Gater, R. A. and Goldberg, D. P. (2002). Bio-social origins of depression in the community: interactions between social adversity, cortisol and serotonin neurotransmission. *British Journal of Psychiatry*, 180, 168–173.

Tennant, C. (2002). Life events, stress and depression: a review of recent findings. *Australian and New Zealand Journal of Psychiatry*, 36, 173–182.

Williamson, M. K. *et al.* (2007). Recruiting and retaining GPs and patients in intervention studies: the DEPS-GP project as a case study. *BMC Medical Research Methodology*, 7, 42.

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