Is neuroticism a modifiable risk factor for depression?

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The importance of personality in the aetiology of mood disorders has long been recognised. Neuroticism, which reflects an individual's emotional lability, is the personality trait most closely linked to the onset and course of depressive illness.

Eysenck and Eysenck[1] have described the high neuroticism individual as follows: "He is overly emotional, reacting too strongly to all sorts of stimuli, and finds it difficult to get back on an even keel after each emotionally arousing experience".

By contrast, the stable individual "tends to respond emotionally only slowly and generally weakly, and to return to baseline quickly after emotional arousal". Neuroticism has a significant impact on a wide range of health related behaviours, including the reporting of medical problems, perceived health status, self report of pain, and frequency of general practitioner visits.[2,3]

High neuroticism has been shown to be a risk factor for depression. Wilhelm *et al*,[4] in a prospective study of 164 teachers, found that high neuroticism at initial assessment predicted the subsequent development of major depression. In Kendler *et al's* longitudinal study of female twins,[5] stressful life events, genetic factors, previous episodes of major depression, and neuroticism all predicted the development of a depressive episode.

Neuroticism has also been linked to poor short-term and long-term outcomes in depression. In Newcastle[6] and Dublin[7] inpatient samples, premorbid neuroticism and pretreatment illness duration were the strongest predictors of time to remission following the onset of treatment. Duggan *et al*,[8] in an 18 year follow-up of 89 depressed inpatients, found that high neuroticism scores on admission and on recovery predicted poor overall outcome and chronicity.

Neuroticism has also been shown to play an important role in the aetiology of late life depression. Henderson *et al*[9] in a longitudinal study found that high neuroticism (as well as health deterioration and poor social support) predicted the development of depressive symptoms in 1,045 elderly subjects. This group, in a subsequent study of 2,725 adults aged 18-79 years, suggested that a decrease in depressive and anxiety symptoms with age may, in part, be attributed to a decline in neuroticism scores.[10] High neuroticism has been shown to act both as an independent risk factor for late life depression, as well as moderating the effect of medical illness on depression.[11] In contrast, low neuroticism appears to protect against the development of depressive illness in men who develop memory problems.[12]

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Mechanisms of action

How might higher neuroticism predispose to the onset or persistence of depression? Preliminary evidence suggests that higher neuroticism is associated with a predisposition to experience negative life events, reduced levels of social support, and delayed presentation following illness onset.[13-15] The impact of neuroticism on other psychological factors has been more extensively evaluated. Roberts *et al*[16] have suggested that the persistent dysphoria associated with high neuroticism is mediated through a ruminative response style. This style is characterised by an individual's propensity to repetitively focus on the symptoms of depression, and on the causes, meanings and consequences of depressive symptoms.

Bothwell and Scott[17] studied the predictors of recovery from depression in an inpatient sample: severity of index episode, higher levels of dysfunctional attitudes related to the need for approval and low self-esteem were independent predictors of outcome. Both cognitive variables were correlated with neuroticism score.

Neuroticism has also been linked to central serotonin function. Lesch *et al*,[18] in a study of 505 individuals in the general population, found a significant association between serotonin transporter genotype and neuroticism scores. CSF concentrations of the serotonin metabolite 5-hydroxyindolacetic acid have been found to correlate with neuroticism in depressed patients,[19] although this association may reflect colinear relationships between both variables and depression.

Interestingly, selective serotonin reuptake inhibitors (SSRIs) may have an impact on trait neuroticism. Andrews *et al*,[20] in a retrospective study of patients who had responded to SSRIs, reported that irritability and neuroticism scores improved following treatment. Anecdotally, individuals prescribed SSRIs following recovery from a depressive episode occasionally describe feeling more 'carefree' than usual. While this may simply reflect remission of a longstanding mild depression, an alternative explanation is that SSRIs modify personality vulnerability factors. Andrews *et al's* findings suggest that the beneficial effects of SSRIs in depression, obsessive compulsive disorder and panic disorder may be due, in part, to an ability to reduce irritability and neuroticism.

Research priorities

Research is required to address two important issues. First, what are the optimal strategies for the management of depression in high neuroticism individuals? As high neuroticism is associated with dysfunction in the cognitive processing of emotional information, cognitive therapy might play an important role in high neuroticism individuals by directly modifying personality factors such as a ruminative response style, dysfunctional attitudes or low self-esteem.

Secondly, can the risk of relapse be reduced through the modification of trait neuroticism? Personality traits tend to remain stable over time, leading to the view that they are determined predominantly by genetic factors.[1] However, it appears that only 20%-50% of the variance in neuroticism is genetically determined, which challenges the view that this trait is biologically set and unchangeable.[21,22] Preliminary evidence suggests that psychotherapy can modestly reduce neuroticism,[23] although the clinical significance and durability of these effects have yet to be evaluated.

There is encouraging evidence that combined maintenance treatment with antidepressant medication and psychotherapy is associated with lower recurrence rates compared to monotherapy.[24] Targeting limited psychotherapeutic resources at depressed patients with high neuroticism may prove to be a cost effective means of improving outcome in this vulnerable group.

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