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Review Article

'*Plus ca change*': Back to the future

Malcolm P Weller

Where several different objects produce the same effect, it must be by means of some quality, which we discover to be common amongst them. For as like effects imply like causes, we must always ascribe the causation to the circumstance, wherein we discover the resemblance.
David Hume, A Treatise of Human Nature

The present findings suggest that even if everyone was treated in the best possible fashion, about 60% of the burden of mental disorders appears to be unavertable in the light of current knowledge…even with perfect coverage and treatment, half the burden of anxiety disorders would remain unavertable.
Andrews G, Issakidis C, Sanderson K, Corry J, Lapsley H: Utilising survey data to inform public policy: comparison of the cost-effectiveness of treatment of ten mental disorders. Br J Psychiatry 2004; 184:526–533

Psychiatric conditions tend to cluster together so that if a person suffers from one neurotic psychiatric disorder that person is significantly more likely to simultaneously suffer from another, so called comorbidity, and sufferers from psychiatric disorders are more likely to suffer psychiatrically again in the future in comparison to a random population.

The situation in respect of post traumatic stress disorder (PTSD) might be expected to be somewhat different because, atypically, in this disorder we presume that we know the aetiology and it is a necessary diagnostic criterion that a person has been exposed to an unusually threatening event. Nevertheless, there is recent evidence that the likelihood of recurrence of PTSD is high, despite the low frequency of catastrophic precipitating events.

The various symptomatic manifestations, upon which specific psychiatric diagnoses are based, may be surface phenomena of a unifying underlying predisposition with common biological substrates. This would accord with the fact that antidepressants are effective not only in psychotic depression, melancholic type depression and non-melancholic depression but confer a wide spectrum of additional therapeutic benefits, including benefit in panic disorder, phobic disorders, obsessive compulsive disorder and PTSD.

Alternative or aggravating factors are that people who suffer from a neurotic disorder or disorders tend both to complain more and to attract adversities.

These issues will be discussed in relation to the psychological concepts of neuroticism and recent biological factors.

Recurrence of disorders

Depression

Once initiated depression tends to recur (DSM - IV), in his review, Judd[1] found that about 80% of persons experiencing a major depressive episode will have at least 1 more such episode during their lifetime, with the rate of recurrence being even higher if minor episodes are included. The review by Judd[1] is close to the more recent estimate of Andrews[2] that over the 10 years following a depressive episode, 75% of patients experience a recurrence[2].

Depression resulting as a reaction to stress (in which environmental demands are perceived as exceeding resources) is particularly likely to pursue a chronic and relapsing course[3;4].

Anxiety Disorders

Anxiety is often an appropriate emotion which should lead to behaviour which reduces the anxiety rather than a disordered state of frozen inactivity or maladaptive actions which exacerbate the anxiety.

Anxiety disorders are known to be familial and heritable[5] and tend to be persistent. They can be associated with depression or be the prelude to depression[6].

The severity of symptoms may vary with time and be less problematic in calm, uneventful circumstances but panic disorder with or without agoraphobia often remains a chronic condition[7;8].

PTSD

The definition of PTSD stands in contrast to adjustment disorder. In DSM IV an adjustment disorder is characterised by a disproportionate reaction to the stressor and therefore probably indicative of prior psychiatric vulnerability. This interpretation is reinforced in ICD 10; "Individual predisposition or vulnerability plays a greater role in the risk of occurrence and the shaping of the manifestations of adjustment disorders than it does in the other conditions in F43 (Acute Stress Reaction)". However, the notion that certain experiences can trigger a disproportionate reaction in some people by virtue of some perhaps occult vulnerability exhibiting a much greater susceptibility, a disproportionate effect, was commented on in the second World War for conditions which we would now diagnose as PTSD (e.g.[9]). An early Israeli study of soldiers exposed to combat traumas[10] suggested that prior combat stress reactions was a marker for subsequent similar problems rather than part of a process of aggregation of stress.

The majority of people will experience one or more traumatic events in their lifetimes, with estimates ranging from 51% to 90%11;12. Despite the shared nature of the experience, after natural disasters such as earthquakes, volcanic eruptions, tsunamis and of combat, only a minority of the population exposed to similar stressful experiences suffer from PTSD. Those who succumb are likely to have experienced prior psychiatric problems[13;14;15].

Prior psychiatric problems, less education, high neuroticism, extroversion, and certain ethnic grouping are associated with the development of PTSD [16;14;15;17;18;19;20;21;22]. In the Blanchard et al[17] study, prior depression was associated with Post Traumatic Stress Disorder following a motor vehicle accident to a highly significant extent, (P<0.004).

Risk factors

Pervasive factors which reconciles the various studies is the finding that temperamental characteristics, detected very soon after birth, proved to endure and to predict later behaviour and adjustment[23]. The personality dimension of adult neuroticism renders an individual vulnerable to neurotic disorders but there are elements of double counting. However, it is stable trait when corrected for age[24].

Those who are psychiatrically vulnerable are likely to succumb to the impact of significant life events, particularly if they have demonstrated that they have already done so in the past, which situation could be interpreted to indicate that they have less resilience to stress.

Provocation tests are used in medicine, such as the glucose tolerance test for unmasking diabetes and the dexamethasone suppression test for testing for possible pituitary autonomous or semiautonomous malfunction in Cushing's syndrome. In an analogous fashion, it could be assumed that a latent psychiatric vulnerability would be revealed by psychosocial stress.

The propensity to experience traumatic events has cultural, educational and personality roots. Among young American adults, those with less education, blacks, and those with high extroversion scores (with a propensity for sensation seeking) are more likely than others to be exposed to traumatic events and are thus at greater risk for PTSD[16].

Age, gender, race, and socioeconomic status are relevant parameters, with youth, female sex and low socioeconomic status being markers for an increased likelihood of developing PTSD[25;26;27;28]. The level of social support and individual self-esteem, have also been implicated in the onset and course of PTSD across cultures[29;30;31].

This literature is suggestive of prior psychiatric, social and socio-economic pressures being conducive to PTSD and would inferentially support prior PTSD as being a marker, amongst other psychiatric markers, of psychiatric vulnerability arising from a variety of factors.

A very recently published study from Naomi Breslau and her team, who have conducted a series of influential studies, brings additional and more direct evidence that prior PTSD is in fact a vulnerability marker, rather than the consequence of cumulative stress for the eruption of subsequent PTSD[32].

In this study, a sample of 1200 persons was randomly selected in 1989 from all 21-to 30-year-old members of a large health maintenance organization and were repeatedly assessed over a 10 year follow-up.

The conditional risk of PTSD during the follow-up periods was found to be significantly higher among trauma-exposed persons who had experienced previous PTSD, relative to those with no prior trauma (odds ratio, 3.01; 95% confidence interval, 1.52-5.97). The estimates were only marginally revised after adjustment for sex, race, education, and pre-existing major depression and anxiety disorders.

In contrast, the conditional risk of PTSD during follow-up among trauma-exposed persons who had experienced prior traumatic events but not PTSD was not significantly increased, relative to trauma-exposed persons with no prior trauma. The difference between the 2 estimates was significant (P = 0.005). The authors concluded that *"prior trauma increases the risk of PTSD after a subsequent trauma only among persons who developed PTSD in response to the prior trauma. The findings suggest that pre-existing susceptibility to a pathological response to stressors may account for the PTSD response to the prior trauma and the subsequent trauma."*

One can only speculate as to why the individual developed PTSD in the first place. It has been argued on the basis of the Israeli combat data[10] and natural disasters[16;13;14;15] that the first

episode of PTSD is likely to be a manifestation of psychiatric vulnerability rather than a manifestation of exposure to universally intolerable stress. These studies, particularly the most recent of Breslau and her team, have medico-legal implications which accord with the U.K. legal concepts of "nervous shock" and "eggshell personality" (Malcolm v Broadhurst [1970] 3 All ER 508).

In a similar fashion, Hammen et al[33] found that non depressed persons were relatively resistant to the onset of depression, even when exposed to high- impact stressful events, whereas those who were symptomatic continued to have both more depression and more high-impact events over time. This may be partially a recording bias, because depressed people may better remember adversities and problems but there may be a further reason. In our competitive society, there seems to be some magnet-like effect of depressed people inducing others to assert their dominance and, metaphorically, to kick them while they are down, probably because of inadvertent signals of loss of self esteem and being an incapacitated adversary[34].

The converse is also true, with well-being decreasing life events vulnerability[35].

Brown Harris and Eales[36] have illustrated the various implications of this interaction, particularly as to anxiety in the early and residual phases of depression.

Recent biological evidence has shown a strong interconnection between the personality trait of neuroticism and depression. Neuroticism is associated with characteristics of serotonin receptors[37;38] and the weight of evidence is that the short variant of the serotonin transporter gene is associated with depression[39;40;41], although there is a contradictory study[42].

Comorbidity

Between 48.6% and 51% of patients with a DSM-IIIR/DSM-IV diagnosis of major depression had at least one concomitant ('comorbid') anxiety disorder and only 26% to 34.8% had no comorbid mental disorder[43;44].

Comorbid depression occurred in 44.5% of PTSD patients at 1 month and in 43.2% at 4 months in 211 trauma survivors and was associated with greater symptom severity and lower levels of functioning[13].

In an Australian study, 21% of people fulfilling DSM-IV criteria for any mental disorder met the criteria for three or more comorbid disorders[45]. In a recent large-scale epidemiological study of 9,282 English-speaking respondents 18 years and older the researchers found that almost a quarter (23%) had 3 or more diagnoses, a situation which correlates with severity[46]. Using data from community surveys, many researchers have noted that if the range of psychiatric symptoms properly dictates 2 or more diagnoses, this is associated with greater symptom severity[47;48;49;50;51], poorer outcome[47;50] and poorer treatment response[52], more functional impairment[47,48;53] and increased use of medical service[54;55;56;57] (see Wittchen[58] for theoretical discussion of comobidity).

Earlier, Kessler[59] and Angst[60] had noted that people who had more than one diagnosis at some time used services more often. Later work in a study of 10,641 adults showed a strong relationship between the number of disorders and disability and distress, with the combination of affective and anxiety disorders associated with four-fifths of the disability and service utilization[45].

Ubiquity of stress

Certain stresses are inevitable, such as bereavement and one expects a period of readjustment. Despite the fact that stresses rain down upon us[61;11;12;62] it is still the majority of the population who are not given a formal psychiatric diagnosis. A genetically determined constitution or an adverse childhood could well determine resilience and susceptibility to their impact. Complicating a model of exclusive social inculcation, childhood adversity is generally the product of parental behaviour by persons of shared genetic constitution.

Social Factors

The interaction between adversity and vulnerability, and the moderating effects of social integration and support are well known. Writing in the late 70's, a major research programme by Brown and Harris concluded: *"attention to a person's environment may turn out to be at least as effective as physical treatment."* Clinically significant anxiety is much commoner amongst single people[63]. The situation is interactive in both directions. Psychiatric symptoms are likely to cause adverse social consequences and to be aggravated by these consequences, and multiple symptoms are more likely to have even greater adverse social resonances[64;65;66;67;68;69;70;71].

A unifying model

"The child is father of the man" and half of all lifetime psychiatric cases start by age 14, and three fourths by age 24 [46a], later-onset disorders occur in large part as temporally secondary comorbid conditions[46b] and the effect of aging on brain function may explain some of the late onset depressions[72;73;74;75;76].

Linkage between the various neurotic disorders (i.e., anxiety, depressive, phobic, and obsessional neurosis) and the centrality of the neurotic disposition pervading all used to be commonly assumed. The subdivision in the DSM classificatory systems beginning with the third edition created a more rigid subdivision, which has been criticised adversely (e.g.[77]).

The personality factor of neuroticism is a pervasive risk factor for a variety of psychiatric illnesses (e.g.[24;16;45]). The temperamental characteristics may be no more than a *forme*

fruste of illness which is highlighted by stress. People have varying coping capacities which are a product of their temperament and childhood experiences but the interaction, with adaptive and maladaptive responses, has even greater explanatory power. Parenting style and adequacy has been emphasised by the psychoanalytical movement and includes parental adjustment as interwoven with child rearing practices as well as with shared genetic propensities. On the other hand, enduring temperamental characteristics have been exhibited extremely early in life[23;78;79] and are likely to be biologically determined and to introduce interactional biases in the developmental trajectory.

There are 3 models of the impact on mental health of adult trauma:

1. Repeated traumas, sometimes beginning in childhood produce a cumulative destructive effect and increasing sensitisation to further traumas (e.g.[80]).

2. Repeated small traumas produce a "stress inoculation" increasing resilience, in a manner analogous to the term “battle hardened”.

3. Prior psychiatric problems, perhaps surprisingly including PTSD, are markers of psychiatric vulnerability and predictors of subsequent psychiatric problems, including a further episode or episodes of PTSD.

The models do not conflict with one another but the recent study of Breslau et al[32] provides empirical data emphasising the third possibility.

Treatment

Neurotic psychiatric disorders have a common underlying predisposing cause which can be modified by SSRIs and CBT.

Claims are made for the effectiveness of exploring and reconciling childhood experiences and relationships and short-term psychodynamic psychotherapy has also proved to be an effective treatment (e.g.[81]).

Depression is often mixed with anxiety or develops from anxiety. Anxiety disorders are by far the most common mental disorders but the proportion of serious cases is lower than for other classes of disorder. Mood disorders are the next most common with a higher proportion of serious cases[46].

Cognitive factors, especially the way people interpret or think about stressful events, are considered to play a pivotal role in the aetiology of anxiety[82] and negative thoughts are frequently found in individuals with anxiety[83].

Anxiety is associated with a tendency to overestimate the association between a feared cue and personal harm[84;85;86]. Prominent negative thoughts in anxiety are underpinned by a sense of uncontrollability, feelings of helplessness and a perception that the sufferer is unable to predict, control, or obtain desired results[82].

An amplifying factor in demands upon treatment is that high neuroticism contributes to patients' over-reporting of mood symptoms and help seeking, e.g.[87]. Appropriate treatment of neurotic disorders includes educating sufferers to identify and examine their negative thoughts, and to see if they can re-construe them in a more realistic and constructive way.

Such cognitive behavioural therapy both promotes recovery and also guards against recurrence. In accord with biological findings regarding variance of the serotonin receptor, these twin advantages can also be obtained from continuing pharmacological treatments (e.g.[88;67;89;90;91;92;93]). The effect is amplified if the two approaches are applied in combination[94;95;96;97].

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COMPETING INTERESTS
I have prepared expert witness evidence where I have been instructed by claimants and defendants both jointly and severally

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