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Gender differences in depression

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Abstract
It is commonly suggested that a female preponderance in depression is universal and substantial. This review considers that proposition and explanatory factors. The view that depression rates are universally higher in women is challenged with exceptions to the proposition helping clarify candidate explanations. 'Real' and artefactual explanations for any such phenomenon are considered, and the contribution of sex role changes, social factors and biological determinants are overviewed. While artefactual factors make some contribution, it is concluded that there is a higher order biological factor (variably determined neuroticism, 'stress responsiveness' or 'limbic system hyperactivity') that principally contributes to the gender differentiation in some expressions of both depression and anxiety, and reflects the impact of gonadal steroid changes at puberty. Rather than conclude that 'anatomy is destiny' we favour a diathesis stress model, so accounting for differential epidemiological findings. Finally, the impact of gender on response to differing antidepressant therapies is considered briefly.

Introduction

> Epidemiological studies across a number of cultures consistently show that, beginning at puberty, major depression, dysthymia and anxiety disorders are two to three times more common in women than in men. (Leibenluft, 1999)

This paper will consider a number of gender differences that bear on the epidemiology of depression, on the manifestations of depression, on help seeking, and on some indicative treatment differences.

Epidemiology

More than thirty years ago, Weissman and Klerman (1977) wrote a definitive epidemiological review demonstrating a distinctly higher prevalence of depression in women in community and clinical samples, and which they judged as reflecting both real and artefactual factors. As women are more likely to seek help for depression, such a factor would artefactually influence the female preponderance in clinical samples, but would largely be circumvented in community samples – and argue (by default) for the difference principally being contributed to by 'real' factors.

Large community studies subsequently conducted over the last three decades in differing countries – and which have used standardised case-finding measures – have consistently established much higher rates of lifetime depression (both major depression and dysthymia) in women (see Weissman et al., 1996; Wilhelm, Parke, Geerlings, & Wedgwood, 2008). A representative US study – the National Co-morbidity Survey Replication or NCS-R (Kessler et al., 2005) – which surveyed over 9000 English-speaking respondents, quantified the lifetime risk of 'any mood disorder' to be 1.5 times higher for women. Thus, the earlier reporting by Weissman and Klerman (1977) of a female preponderance in depression rates has largely been replicated.

There are, however, some intriguing qualifications to the seemingly consistent finding. Oakley Browne, Wells, Scott, and McGee (2006) undertook a regional study of the lifetime prevalence of many psychiatric disorders in New Zealand. Lifetime rates were significantly higher for women than for men for major depression (20.3% versus 11.4%) and for dysthymia (2.6% versus 1.6%), but with the overall gender ratio for 'any mood disorder' (24.3% versus 15.6%) being somewhat attenuated as a consequence of a slightly lower rate of bipolar disorder in women (3.6% versus 4.1%). Several studies have suggested that rates of bipolar I disorder are comparable across the genders (e.g. Kessing, 2004) but that rates of bipolar II disorder are somewhat higher in women (e.g. Benazzi, 1999). When identified, such a gender difference in bipolar disorder is less distinctive than described for major depression.

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While 'melancholia' is variably viewed as a separate depressive sub-type or a 'more severe' expression of clinical depression, and is quite variably defined on the basis of its clinical features, some commentators (e.g. Kessing, 2005) have suggested that there is no clear evidence of gender differences in the prevalence of melancholia. Thus, any female preponderance in clinical depressive conditions is less obvious or non-existent in the quintessential biological disorders (i.e. melancholia and bipolar I disorder).

Further, when socially homogeneous (in terms of education, culture, parity, etc.) population sub-sets are surveyed, gender differences are not always observed – with illustrative samples including British civil servants (Jenkins, 1985), the Amish community (Egeland & Hostettet, 1983), college students (Grant et al., 2002) and a UK Jewish community (Loewenthal et al., 1995).

The latter finding allows some important caveats – firstly, that while 'clinical depression' (as a domain) appears more common in women, the female preponderance may not be consistent across all depressive sub-types, and that it is more evident in the unipolar non-melancholic depressive disorders (which we conceptualize as reflecting the impact of precipitating life events on predisposing personality or temperament styles). Even within the non-melancholic groups, it might be expected that there would be variable gender ratios – and later we will consider 'atypical depression', where the female preponderance appears particularly distinctive. The second caveat, that gender differences are most evident in heterogeneous community samples and may be absent in samples of socially homogeneous groups, again argues for the relevance of social factors, whether proximal and/or distal. Such epidemiological findings have encouraged us to hypothesize (as detailed later) that a 'diathesis stress' model may operate. In essence, rather than argue that 'anatomy is destiny', and that women are, of necessity, more likely to develop depression, we suggest that women are merely more predisposed (i.e. the 'diathesis') and that social factors (i.e. the 'stress' component) modulate that predisposition. In socially heterogeneous communities we assume that women experience more precipitating social factors and/or are more vulnerable to certain social factors (so accounting for findings in large community studies), whereas in socially homogeneous communities, gender-specific social precipitants are less relevant or have less impact.

There is one other domain that is rarely considered in reviews of the general proposition that women are more likely to be depressed than men. In the last decade there has been increasing scientific interest in the topic of 'happiness' or 'well-being'. In an interesting review (Stevenson & Wolfers, 2009) of community survey studies, not only were women less 'happy' than men, but the data indicated that the difference has been widening over recent decades. In representative studies, individuals were asked 'In general, how satisfied would you say you personally are with your life today?' Study findings indicated that there had been 'a pervasive decline in the relative well-being of women in nearly all European countries'. For the USA the authors quantified that 'a man in 2006 is happier than a similarly situated man was 34 years ago, while women...are less happy by a roughly equal amount'. The review noted that such findings were evident across women who remained at home as well as women who were in employment, and judged that the 'common thread appears to be an increasing ambition of young women beyond the domestic sphere'. They suggested that women were under increasing pressure to be 'successful' at multiple levels, including at work, as a family member, in making a contribution to society, and in being a community leader. Clearly, such findings would weight social stress factors, alone or in activating any predispositional diathesis factors.

Pursuit of causal factors is assisted by examining for age effects. In community studies where gender differences are identified, such differences are not constant across age groups. In pre-adolescents, rates of depression are low and either comparable for boys or girls, or slightly higher rates are reported in boys than in girls (Jorm, 1987a). Any such excess in young boys might reflect a real difference or be an artefact of reporting or observation. As a generalization, when young girls become depressed they tend to go quiet and keep to themselves, while boys are more likely to act out with anger and irritability, with such 'externalizing' behaviours in boys resulting in their 'depression' being more likely to be observed by others and so artificially inflating the rate of 'observed depression' in boys. Jorm (1987a) further quantified males and females as having their highest rates in their twenties (at 17% and 26% respectively) and falling at a steady rate from 40 years onwards.

Most epidemiological studies that have examined the impact of age on gender differences have indicated that the female preponderance commences at around a 10–12 age band but that such a differentiation is far more distinctive for 'major depression' than it is for 'dysthymia' (Parker & Hadzi-Pavlovic, 2004). Following that separation emerging at puberty, the peak differentiation would appear to be from 15 to 30 years of age. From the late thirties onwards, rates for both men and women decrease progressively, although the gender difference persists and never fully reaches parity. Such studies of lifetime rates predictably rate initial and recurrent episodes

or 'prevalence'. When rates of first onset or 'incident' depression are quantified, as undertaken by Parker and Hadzi-Pavlovic (2004) in an analysis from the US National Co-morbidity Study or NCS (Kessler et al., 1994), a similar pattern in the gender difference emerging in adolescence is evident. In addition – but in women only – there was a second distinct increase in rates of initial episodes of major depression in their late forties and early fifties. Such a secondary peak is compatible with the historical description of 'involutional melancholia', in that it was previously suggested that women (in particular) were likely to develop an episode of depression around menopause. As the bimodal incidence peaks in depression rates in women correspond to expected ages of menarche and menopause, sex role hormones and/or psychosocial factors are suggested.

Such rich epidemiological findings allow interpretative attempts a firmer footing, and serve to shape the next section.

How do the epidemiological findings inform us?

Such epidemiological findings are capable of two broad explanations – in essence, that gender differences are (to some extent) artefactual or essentially real. The artefactual possibility essentially supposes that, as women are more likely to seek help, volunteer depressive features when specifically asked, report differentially when seeking help and respond differentially to depression rating measures, they will score as more depressed purely as a consequence of such artefactual influences. As noted, however, community surveys (where a female preponderance is consistent) are unlikely to involve a 'help seeking' component. This artefactual factor can therefore be effectively discounted as having explanatory power in community survey populations. However, the possibility that women might, in clinical contexts where help-seeking components may be operative, be more likely to 'volunteer' depressive symptoms must be conceded. As we will later note that gender differences in depression only relate to first episode and not to repeat episodes, the suggestion of a 'help-seeking' explanation appears less viable as a substantive explanation.

We have previously described one intriguing gender difference in reporting. In pursuing the relevance of artefactual influences (Wilhelm & Parker, 1994) in our longstanding cohort study, we used a case-finding measure to quantify lifetime episodes of depression at 5-year intervals and with lifetime depression rates of cohort members being assessed and re-assessed at each review. Such a strategy allowed us to check on their consistency of reporting episodes over time. In essence, we found that over time men were more likely to 'forget' episodes (absolutely, or 'remember' fewer symptoms so that episodes no longer met 'case' criteria), while women were more likely to 'remember' episodes that had generally not been nominated or had not previously reached 'case' criteria. Such a difference may reflect differential rates of denial or other reporting biases that have been described in men, as well as women being particularly more likely to show 'mood amplification', with Briscoe (1982) reporting that women were more likely to report higher levels of both negative and positive affects.

Measurement influences may also contribute. For example, depression measures that have items such as crying (which is much more likely to be experienced and reported by women), or appetite and weight changes (when women are more likely to engage in comfort eating), will inflate depression rates. Similarly, and as reviewed previously by us (Wilhelm & Parker, 1989), women are more likely to rate as 'cases' if the criterion is the actual number of symptoms, with Angst and Dobler-Mikola (1984) therefore arguing for the need to convert the current weighting given to symptom numbers in diagnostic measures. In our cohort study (Wilhelm, Parker, & Asghari, 1998), we quantified that women reported more symptoms than men and were more likely to report certain symptoms (e.g. feeling self-critical, irritability, tearfulness, experiencing appetite gain and weight changes).

Angst and Dobler-Mikola (1984) demonstrated that the distinct preponderance of depression in women was attenuated when social impairment criteria were deleted, again suggesting that much of the contribution to the female preponderance relates to a gender difference in experiencing and/or reporting affect and mood symptoms, and weighting symptom severity as against social and work impairment.

In conclusion, there are a number of artefactual factors (help-seeking, mood amplification, differential experiential and symptom influences on presentation, and measurement nuances) that are likely to contribute to the quantified higher rates of 'depression' in women.

Beyond artefactual factors, what might be 'real' determinants of gender differences?

The emergence of a female preponderance in clinical depression in late childhood or early adolescence could reflect (1) sex role changes, (2) social factors, and/or (3) biological factors.

The 'sex role' hypothesis is that certain gender-based role experiences shape the development of 'self' and, as a consequence, any diathesis to anxiety and depression. For example, pink baby clothes for girls and blue clothes for boys, providing dolls for

girls and war figures for boys with which to play might lead to girls having a greater propensity to 'internalize' or be more passive and less 'mentally tough' than boys, and therefore create a stronger predisposition to anxiety or depression.

The 'social factor' hypothesis argues that women are either differentially exposed to a greater number of life event stresses and/or are more vulnerable to them. One exemplar is the generalization that women preferentially invest their self-esteem in an intimate dyadic relationship whereas men have more diffuse self-esteem investments – being spread across intimate and social relationships as well as invested in their work. The hypothesis therefore supposes that, by women putting all their eggs (here self-esteem) in one basket, they are more vulnerable to depression if their investment is put in jeopardy (e.g. their husband neglects, abuses or leaves them). This hypothesis is indirectly supported by gender differences in depression being influenced by marital status (Tennant, Bebbington, & Hurry, 1982), with married men having lower rates of depression then single and divorced men while married women are more likely to have the highest rates of those three groups, and has led to the aphorism that 'marriage is toxic to women and protective to men'.

While such sex role and social factor hypotheses have some intuitive appeal and with the latter (in particular) likely to make some contribution (as earlier overviewed), there are also strong arguments against them being distinctive contributors. If the sex role hypothesis was valid we should anticipate a gender difference to emerge at a young age (i.e. in childhood) and not, as occurs, at adolescence. Secondly, in relation to social factors, Kessler (2000) showed that after controlling for rape and other sexual traumas in the NCS survey, the gender difference was halved, while the gender differential was restored by broadening social stressor variables to include traumatic experiences more likely to be experienced by men. Thus, certain social factors may have quite differing salience to men and to women and, depending on the prevalence of such gender-specific factors (e.g. bullying, sexual abuse, rape, loss of employment, work harassment) in any community, might contribute to the gender difference in prevalence.

However, there is a key argument for rejecting the possibility that sex role or social factor hypotheses make a distinctive contribution. Kessler (2000) examined survey data from the NCS and other community studies and showed that the male preponderance in lifetime depression rate was only for the first depressive episode and not for second and recurrent episodes. If gender differences were underpinned by sex role or social factors we would expect gender to impact on both onset recurrence, and not merely onset. However, the gender difference is restricted to incidence or initial onset. This might allow support for a diathesis stress model – with an emphasis on the predisposing diathesis factor, rather than on any precipitating social factor components. Our previously referenced cohort study is therefore worthy of detailing and consideration.

In 1978, we recruited a sample of university students (all having completed a primary degree and engaged in their final year of teacher training), and we have now followed them for some thirty years. In an earlier paper (Wilhelm et al., 1997) we reported on their 15-year review, when the sample had a mean age of 39 years. While there was a trend for a female preponderance in lifetime rates of 'major depression' and 'all depression', neither trend was significantly different. As they had all trained as teachers (with most continuing in that profession) and were socially homogeneous in terms of social class, we again interpreted the failure of a gender difference to emerge over time as reflecting their social homogeneity in terms of less exposure to gender-specific stressors that may be more likely to be experienced by women in a general community.

We therefore argued for a diathesis stress model for the gender difference. In essence, that women have a greater predispositional vulnerability to depression and to certain salient social factors that precipitate or activate a depressed state, but that in socially homogeneous groups that diathesis might not be effected. A candidate predispositional personality factor is 'neuroticism', as women tend to score relatively higher on this personality/temperament domain and it is recognized as contributing to depression and anxiety (Wilhelm & Parker, 1989). Unfortunately, the term 'neuroticism' has negative and ad hominem connotations, and in considering its contribution later, we will use alternative terms such as 'limbic system hyperactivity'.

Turning to biological explanations, we should first consider whether it is likely that there is (1) some factor that specifically disposes to a gender difference in depression or (2) a higher order factor that disposes to depression and also to some other (circumscribed) conditions. If the latter model is valid, then not only is the question widened but the search for explanations is narrowed.

Many years ago we contemplated whether there were other conditions that showed a similar epidemiological pattern. Some physical conditions (e.g. migraine) showed some pattern similarities, while most psychiatric conditions either showed a quite contrasting male preponderance (e.g. sociopathy, drug and alcohol dependency) or no gender difference. However, certain anxiety disorders showed a distinctly parallel epidemiological pattern, compatible with the model postulating that the

gender difference in depression might more reflect a gender difference in a 'higher order' diathesis variable which then sequentially impacted 'downstream' on depression and some anxiety conditions. Some overview of that model testing hypothesis is now provided.

As Breslau, Schultz, and Peterson (1995) judged pre-existing anxiety disorder as a 'potential factor' in the emergence of gender differences in major depression, we (Parker & Hadzi-Pavlovic, 2001) accessed the US community survey NCS database (involving nearly 6,000 subjects) and examined the extent to which gender and 'any prior anxiety disorder' influenced the risk of subsequent depression. Survival analyses indicated that 'prior anxiety' made a stronger contribution than 'gender', both in relation to major depression (risk of 1.4 and 1.2 respectively) and to dysthymia (risk of 1.5 and 1.2). Such analyses both implicated the impact of anxiety on subsequent depression and, in indicating that the influence of prior anxiety on depression was similar for both males and for females, suggested a very parsimonious diathesis factor. In a second analysis of the same NCS database, we (Parker & Hadzi-Pavlovic, 2004) examined the age of onset (by gender) for those who received a range of differing anxiety and depressive disorder diagnoses. While some anxiety conditions (i.e. agoraphobia, social phobia, simple phobia and panic attacks) showed a trend for a female preponderance emerging before puberty, two anxiety disorders (i.e. generalized anxiety and panic disorder) showed a distinct increase (and with the increase even more distinctive in girls than boys) in early adolescence and which corresponded temporally with the emergence of a female preponderance in depressive disorders (particularly major depression). We therefore argued that there may be a higher order common factor (and specifically a gender hormone-based one) that influenced the differential expression of both certain expressions of anxiety and depression at the time of puberty.

We (Parker & Brotchie, 2004) therefore overviewed candidate temperament styles, with neuroticism, as noted earlier, emerging as a clear candidate. Jorm (1987b) reported a meta-analysis of studies examining gender differences in neuroticism scores, and quantified that, while females had higher scores across all age groups, differences were more distinctive in young and middle-aged adults than in children and the very old. The curvilinear pattern for neuroticism scores (by gender) was very similar to that reported by Jorm (1987a) for depression. We then overviewed data indicating that neuroticism was (1) a strong risk factor for depression, and for first episodes of depression, (2) the strongest predictor of depression persistence in primary care, and (3) modifiable by social factors. In this context, what is the nature of 'neuroticism'? Again, in our review (Parker & Brotchie, 2004), we noted quite wide-ranging descriptions, including a neurotic character style, autonomic lability, a down-regulated HPA axis, brain activation response to negative stimuli (in neuroimaging studies) and 'stress responsiveness' (across sympathetic and parasympathetic autonomic system measures, and 'harm avoidance'. Consolidating these descriptions, a construct of 'emotional responsiveness' was clearly suggested.

We then overviewed hormonal changes at puberty, both in females and in males, examining for pubertal hormonal changes that lead to greater 'limbic system hyperactivation' (i.e. the diathesis factor) in women, so conferring greater responsivity to negative emotional stimuli, and leading to a greater likelihood of certain anxiety and depressive states. That review considered the possible contributions of oestrogen and progesterone, and their impact on several primary neurotransmitter systems (i.e. the locus ceruleus-norepinephrine system, the serotonin system, and the GABA-benzodiazepine receptor complex), and referenced studies demonstrating that brain sites associated with anxiety (e.g. limbic forebrain) have binding sites for gonadal steroids. We therefore argued that post-pubertal women are more likely to demonstrate limbic system hyperactivation in response to negative stressors as a consequence of gonadal hormone influences, with higher 'neuroticism' scores being a marker of the propensity to emotional responsiveness, and that such a diathesis generates the differences in prevalence rates of anxiety and depression.

Others have articulated a similar model. For example, Young and Korszun (1998) noted that 'Organisational differences between male and female brains are caused by exposure to gonadal steroids in the pre- and perinatal periods. The interaction of these organisational effects in females with cyclical steroid hormone changes after puberty, followed then by menopause and the loss of these same steroids, suggest that stress responsiveness and susceptibility to stress-related disorders could vary substantially over women's lifetimes'. They went on to state that 'it is possible. . .that the increased stress responsiveness of females, contributes to the increased prevalence of anxiety disorders and autonomic hyper-arousal in women compared to men.'

We suggested (Parker & Brotchie, 2004) that such a gender-based difference might, from an ethological perspective, have certain advantages. Such a behavioural pattern of vigilant defence would assist the individual's survival and the survival of those under their care. Such a propensity would be of distinct advantage to women (in their role as mothers) but a hindrance to the males engaged in requisite 'hunter

tribesman' independent activities, and where fearlessness would have group survival advantages.

Manifestations of depression

Here we expand on some material presented earlier in relation to any artefactual impact on measurement in community surveys.

A number of studies (e.g. Simpson, Nee, & Endicott, 1997) have examined for gender differences in depressive patterns, with most studies showing no distinctive differences or only the occasional difference. In the latter studies, reports have variably implicated women as more likely to experience hypersomnia, hyperphagia and weight gain, feelings of guilt and worthlessness, fatigue ability, tearfulness, tension and somatic pain.

In terms of coping repertoires in response to depression, the general finding is that women are more likely to internalize (e.g. go quiet, go to their bedroom, cry) and men are more likely to externalize (e.g. show anger, increase their alcohol intake). Such differences may reflect coping per se and/or the impact of antecedent 'comorbidities'). In relation to the last point, in a report from the STAR*D study, Marcus et al. (2005) quantified that women reported more anxiety and somatoform disorders, bulimia and atypical symptoms, while alcohol and drug abuse were more common in men.

Across the differing depressive sub-types, gender differences in manifestations are most evident in 'atypical depression'. In this condition (which is defined in DSM-IV (APA, 1994)), individuals are held to have a highly reactive (or responsive) mood, be more likely to experience hyperphagia and hypersomnia, be more likely to experience a sense of 'leaden paralysis' and have a personality style marked by 'sensitivity to rejection'. We have previously argued (Parker et al., 2002) that the personality style is the primary feature, and that the atypical features of hypersomnia and hyperphagia may more be homeostatic features rather than symptoms.

The homeostatic interpretation was argued on the basis that the hyperphagia is weighted to certain foods (such as carbohydrates and chocolate) which release endorphins (promoting 'feel good' sensations), and other gut and brain peptides, while the hypersomnia restores slow wave sleep during stress. Pursuing the nature of 'atypical depression', we undertook a study (Parker & Crawford, 2007) where some 3000 individuals who had experienced an episode of clinical depression, completed a web-based survey. When depressed, 54% reported food cravings with chocolate craving being far more distinctive in women (51%) than in men (31%). For those who craved chocolate, they were distinctly more likely to report that it made them feel less (1) anxious, (2) irritated, (3) stressed, suggesting in essence that there was settling of 'emotional dysregulation'. We then examined the personality profiles of those who reported chocolate craving when depressed. Importantly, there was no relationship to personality or temperament styles that emerged from a higher order introversion style. However, all personality styles that emerged from a higher order 'neuroticism' style were associated with reporting of chocolate craving when depressed, and again we implicated a personality style of 'limbic cortex hyperactivity' or 'emotional dysregulation' as both contributing to depression, the aforementioned homeostatic coping repertoire and to a consequential impact on the gender difference in depression prevalence.

Treatment differences

We have recently reviewed (Parker et al., in press) literature examining whether there are gender differences in response to differing psychotherapies for depression. We found no consistent trend for women or men to report greater responsiveness to differing psychotherapies or counselling in the literature. In our own web-based survey (Parker & Crawford, 2009), we did find that, while males did not report any antidepressant treatment modality as preferentially beneficial, women were more likely to rate two of the three nominated psychological therapies (i.e. CBT and counselling) as more effective. If a valid difference, this could suggest that women may be more likely to reflect their greater affiliative tendencies and capacity to form a treatment alliance more readily in therapy, as against men being more defensive and guarded.

However, even if valid, any such propensity might theoretically be modified by the gender of that therapist. In pursuing the latter possibility, we reported (Parker & Hyett, 2009) two studies. In the first study we merely analysed referral letters to the Black Dog Institute's depression clinic and quantified female practitioners as writing more detailed referral letters than male practitioners (i.e. 220 versus 88 words). In the second study we surveyed 500 individuals who had experienced an episode of clinical depression in the previous year and sought assistance from their general practitioner. In this study we quantified that female general practitioners were perceived as more caring then male general practitioners and more likely to refer the patient to a mental health professional. By contrast, male general practitioners were more likely to show poor eye contact, to cut off the patient, to be verbally distant and to suggest a solution before hearing the patient out. Further, they were more likely to prescribe a drug as monotherapy and their female patients were

less likely to wish to return to see them than to a female general practitioner. In essence, this study suggested that there were also gender differences in managing depression, and that women might be preferentially more sensitive to those factors than men.

Returning to differential treatment responses, there has been the suggestion (Kornstein et al., 2000) that women may be more likely to respond to selective serotonin reuptake inhibitors (SSRIs) than a tricyclic antidepressants, and with the converse phenomenon holding for men. The differential gender response to SSRI antidepressants was again suggested in an analysis from the STAR*D study (Young et al., 2009), but has not been confirmed in a number of other studies as reviewed by Thase et al. (2000), and would benefit from refined studies (see also Keers & Aitchison, 2010 this issue).

Conclusions

The gender difference in unipolar depression rates has been a relatively (but not absolutely) consistent finding for over three decades and led to a rich set of studies that have sought to contemplate determinants. This review seeks to suggest that the phenomenon is somewhat dependent on the type of depression, that the gender difference is not restricted to depression (being mirrored in data for 'neuroticism' and for some anxiety disorders), that quantified data can be influenced by a range of artefactual factors, and that even after conceding social factor contributions there would appear to be strong biological underpinnings. Further, the richness of studies across community surveys and homogeneous social groups argues for a diathesis stress model, and with a strong contribution from gonadal hormones contributing to the diathesis factor of 'emotional dysregulation' being over-represented in women (and emerging at puberty), and disposing women to a greater propensity to both anxiety and depression.

Women are not, of necessity, more likely to develop depression than men. There would appear to be a biological diathesis factor that predisposes women from puberty to be at greater risk but this diathesis is modified by socio-cultural factors.

Preliminary data indicating that women and men may differ in response to differing drug and non-drug therapies argue for more substantive studies to investigate this intriguing possibility and implications for managing the depressive disorders.

Future directions

There have been sufficient epidemiological studies considering and quantifying the impact of gender on depression rates. The topic would benefit from further explanation of the hypothesis that there may be a higher order impact (rather than being limited to depression per se) and the capacity of differing treatments to modify the higher order diathesis factor.

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References

American Psychiatric Association (1994). Diagnostic and statistical manual of mental disorders (DSM-IV) (4th ed). Washington, DC: American Psychiatric Association.

Angst, J., & Dobler-Mikola, A. (1984). The definition of depression. *Journal of Psychiatric Research*, *18*, 401–406.

Benazzi, F. (1999). Gender differences in bipolar II and unipolar depressed outpatients: A 557-case study. *Annals of Clinical Psychiatry*, *11*, 55–59.

Breslau, N., Schultz, L., & Peterson, E. (1995). Sex differences in depression: A role for preexisting anxiety. *Psychiatry Research*, *58*, 1–12.

Briscoe, M.E. (1982). Sex differences in psychological well-being. *Psychological Medicine Monograph*, *1*, 1–46.

Egeland, J.A., & Hostettet, A.M. (1983). Amish Study I. Affective disorders within the Amish, 1976–1980. *American Journal of Psychiatry*, *140*, 56–61.

Grant, K., Marsh, P., Syniar, G., Williams, M., Addlesperger, E., Kinzler, M.H. et al. (2002). Gender differences in rates of depression among undergraduates: measurement matters. *Journal of Adolescence*, *25*, 613–617.

Jenkins, R. (1985). Sex differences in minor psychiatric morbidity. *Psychological Medicine*, *7*, S1–53.

Jorm, A.F. (1987a). Sex and age differences in depression: A quantitative synthesis of published research. *Australian and New Zealand Journal of Psychiatry*, *21*, 46–53.

Jorm, A.F. (1987b). Sex differences in neuroticism: A quantitative synthesis of published research. *Australian and New Zealand Journal of Psychiatry*, *21*, 501–506.

Keers, R, & Aitchison, K. (2010). Gender differences in antidepressant response. *International Review of Psychiatry*, *22*(5), 485–500.

Kessing, L.V. (2004). Gender differences in the phenomenology of bipolar disorder. *Bipolar Disorders*, *6*, 421–425.

Kessing, L.V. (2005). Gender differences in patients presenting with a single depressive episode according to ICD-10. *Social Psychiatry and Psychiatric Epidemiology*, *40*, 197–201.

Kessler, R.C. (2000). Gender differences in major depression: Epidemiological findings. In E. Frank (Ed.), *Gender and its effects on psychopathology* (pp. 61–84). Washington DC: American Psychiatric Association.

Kessler, R.C., Berglund, P., Demler, O., Jin, R., Merikangus, K.R., & 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.

Kessler, R.C., McGonagle, K.A., Zhao, S., Nelson, C.B., Hughes, M., Eshleman, S. et al. (1994). Lifetime and 12-

month prevalence of DSM-III-R psychiatric disorders in the United States. *Archives of General Psychiatry*, *51*, 8–19.

Kornstein, S., Schatzberg, A.F., Thase, M.E., Yonkers, K.A., McCullough, J.P., Keitner, G.I. et al. (2000). Gender differences in treatment response to sertraline versus imipramine in chronic depression. *The American Journal of Psychiatry*, *157*, 1445–1452.

Leibenluft, E. (1999). *Gender Differences in Mood and Anxiety Disorders: From Bench to Bedside*. Washington DC: American Psychiatric Association.

Loewenthal, K., Goldblatt, V., Gorton, T., Lubitsch, G., Bicknell, H., Fellows, D. et al. (1995). Gender and depression in Anglo-Jewry. *Psychological Medicine*, *25*, 1051–1063.

Marcus, S.M., Young, E.A., Kerber, K.B., Kornstein, S., Farabaugh, A.H., Mitchell, J. et al. (2005). Gender differences in depression: Findings from the STAR*D Study. *Journal of Affective Disorders*, *87*, 141–150.

Oakley Browne, M.A., Wells, J.E., Scott, K.M., & McGee, M.A. (2006). Lifetime prevalence and projected lifetime risk of DSM-IV disorders in Te Rau Hinengaro: The New Zealand Mental Health Survey. *Australian and New Zealand Journal of Psychiatry*, *40*, 865–874.

Parker, G., & Crawford, J. (2007). Chocolate craving when depressed: A personality marker. *British Journal of Psychiatry*, *191*, 351–352.

Parker, G., & Crawford, J. (2009). Personality and self-reported treatment effectiveness in depression. *Australian and New Zealand Journal of Psychiatry*, *43*, 518–525.

Parker, G., Crawford, J., & Blanch, B. (2010). Does gender influence response to differing psychotherapies by those with unipolar depression? *Journal of Affective Disorders* (in press).

Parker, G., & Hadzi-Pavlovic, D. (2001). Is any female preponderance in depression secondary to a primary female preponderance in anxiety disorders? *Acta Psychiatrica Scandinavica*, *103*, 252–256.

Parker, G., & Hadzi-Pavlovic, D. (2004). Is the female preponderance in major depression secondary to a gender difference in specific anxiety disorders? *Psychological Medicine*, *34*, 461–470.

Parker, G., & Hyett, M. (2009). Management of depression by general practitioners: Impact of physician gender. *Australian and New Zealand Journal of Psychiatry*, *43*, 355–359.

Parker, G., Roy, K., Mitchell, P., Wilhelm, K., Mahli, G., & Hadzi-Pavlovic, D. (2002). Atypical depression: A reappraisal. *The American Journal of Psychiatry*, *159*, 1470–1479.

Parker, G.B., & Brotchie, H.L. (2004). From diathesis to dimorphism: The biology of gender differences in depression. *The Journal of Nervous and Mental Disease*, *193*, 210–216.

Simpson, H.B., Nee, J.C., & Endicott, J. (1997). First-episode major depression: Few sex differences in course. *Archives of General Psychiatry*, *54*, 633–639.

Stevenson, B., & Wolfers, J. (2009). The paradox of declining female happiness. *American Economic Journal: Economic Policy*, *2*, 190–225.

Tennant, C., Bebbington, P., & Hurry, J. (1982). Female vulnerability to neurosis: The influence of social roles. *Australian and New Zealand Journal of Psychiatry*, *16*, 135–140.

Thase, M.E., Frank, E., Korstein, S., & Yonkers, K.A. (2000). Gender differences in response to treatments of depression. In E. Frank (Ed.), *Gender and its effects on Psychopathology* (pp. 103–129). Washington, DC: American Psychiatric Press.

Weissman, M.M., & Klerman, G.L. (1977). Sex differences and the epidemiology of depression. *Archives of General Psychiatry*, *34*, 98–111.

Weissman, M.M., Bland, R.C., Canino, G.J., Faravelli, C., Greenwald, S., Hwu, H.-G. et al. (1996). Cross-national epidemiology of major depression and bipolar disorder. *Journal of the American Medical Association*, *276*, 293–299.

Wilhelm, K., & Parker, G. (1989). Is sex necessarily a risk factor to depression? *Psychological Medicine*, *19*, 401–413.

Wilhelm, K., & Parker, G. (1994). Sex differences in lifetime depression rates: Fact or artefact? *Psychological Medicine*, *24*, 97–111.

Wilhelm, K., Parker, G., & Asghari, A. (1998). Sex differences in the experience of depressed mood state over fifteen years. *Social Psychiatry and Psychiatric Epidemiology*, *33*, 16–20.

Wilhelm, K., Parker, G., & Hadzi-Pavlovic, D. (1997). Fifteen years on: evolving ideas in researching sex differences in depression. *Psychological Medicine*, *27*, 875–883.

Wilhelm, K., Parker, G., Geerligs, L., & Wedgwood, L. (2008). Women and depression: A 30-year learning curve. *Australian and New Zealand Journal of Psychiatry*, *42*, 3–12.

Young, E.A., & Korszun, A. (1998). Psychoneuroendocrinology of depression. Hypothalamic-pituitary-gonadal axis. *Psychiatric Clinics of North America*, *21*, 309–323.

Young, E.A., Kornstein, S.G., Marcus, S.M., Harvey, A.T., Warden, D., Wisniewski, S.R. et al. (2009). Sex differences in response to citalopram: A STAR*D report. *Journal of Psychiatric Research*, *4*, 503–511.