BJPsych The British Journal of Psychiatry (2026)
228, 6, 567–568. doi: 10.1192/bjp.2026.10627

Commentary

The nexus between anxiety and depression

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Keywords
Anxiety or fear-related disorders; depressive disorders; general adult psychiatry; mental health services; epidemiology.

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Response

'There is no such thing as pure pleasure; some anxiety always goes with it.'

Ovid (43 BC–17 AD), Roman poet

The article by Gkitakou et al[1] in this issue finds a consistent rise in the 12-month prevalence of anxiety and mood disorders over a period of 12 years that cannot be fully explained by changes in levels of public awareness, risk factors or changes in practice. Instead, the authors point to a possible 'decline in public mental health' and a lack of timely intervention with appropriate strategies – including in particular preventative measures.

The finding that both mood and anxiety disorders have increased should come as no surprise, as clinical co-occurrence between the two is the rule rather than the exception, and the clinical detection, characterisation and treatment of anxiety and mood disorders remains a challenge.[2] Indeed, to our minds, this highlights the fact that the overlap between anxiety and depression and any putative connection warrants further in-depth research, and perhaps our current approach of categorising disorders as separate entities needs to be reconsidered.

Diagnostically, anxiety and depression often appear co-mixed, hence the term 'mixed anxiety and depression' and the clinical descriptions of depression as 'anxious depression' and 'agitated depression'. This clinical co-mingling of symptoms is also seen in depression measurement scales such as the Hamilton Depression Rating Scale, which even in the 17-item version dedicates 2 items specifically to anxiety – that is, psychic and somatic (items 10 and 11) – and also alludes to anxiety in item 9, which inquires about agitation.[3] Reciprocally, the Trait Anxiety Inventory includes items that capture depressive symptomatology (items 3 and 4).[4] This symptomatic entanglement is noteworthy given that, diagnostically, anxiety does not feature in either ICD-11 or DSM-5 diagnostic criteria for major depression or a depressive episode. Indeed, the emergence of anxiety in the context of depression, especially if it entails agitation, is more likely to be construed as a 'mixed mood state'. Further, anxiety may be conflated with irritability and described as an 'irritable mood' or simply as 'irritability'.

Such symptomatic and diagnostic co-mingling of anxiety and depression is reflected in the commonality of management strategies for both sets of symptoms, with psychological and pharmacological strategies being shared. For example, cognitive behavioural therapy is effective for depression and anxiety management,[5] with overlapping targets of restructuring negative cognitions and behaviour modification, and it is perhaps why it is the most effective among the psychological strategies; in real-world settings it has seen increasing uptake through digital technologies. Similarly, selective serotonin reuptake inhibitors (SSRIs), arguably the most successful 'antidepressant' class, which, despite being regarded as agents that specifically target depression, are equally, if not more effective, in managing anxiety. This suggests that there are important neurochemical and possibly neuropsychological and neural network commonalities between anxiety and depression.

Nevertheless, in terms of the true underlying nature of anxiety and depression, there are some fundamental differences. For instance, in most cases anxiety is a normal physiological process and a healthy emotional response, one that permits adaptation to one's environment and is in fact necessary for survival. Clinical depression, however, entailing social withdrawal, inanition, functional impairment and an increase in the risk of suicide, is clearly a pathological state, and is an illness state distinct from sadness or grief. Indeed, it is only at the extremes of anxiety that there is significant functional impairment to constitute a disorder, and so, while there is considerable overlap, the mechanisms that underpin anxiety and depression are no doubt different.

This separation is perhaps most evident when the two sets of symptoms are tracked longitudinally. Further, anxiety often precedes depression, such that states of mixed anxiety and depression almost always begin with anxiety symptoms appearing first. There are three possible reasons for this. First, it could be that anxiety is the leading facet, the prelude to depression, so to speak, while still being an inherent component of the underlying disorder. Alternatively, it may be that anxiety is a reaction to the onset and emergence of depressive symptoms. That is to say, an intuitively mediated response and an adjustment to the onset of an illness – a reaction that is often noted more broadly with other diseases and disorders. Instead, again, it may be that depression is a reaction to a failed anxiety response, where anxiety that is a normative response to a stressor has not managed to overcome the difficulty the person is facing, akin perhaps to a model of helplessness following on from having tried to address a stressor. These speculations are not new,[6] but their value has been forgotten to some extent, partly because of reification of anxiety disorders as separate and distinct entities.

Another phenomenon that has also been overlooked and overlaps with both mood disorders and anxiety is that of irritability, which shares attributes with anxiety as it is a normative experience and clinically manifests transdiagnostically. Our recent examinations of irritability have shown that, like anxiety, its co-occurrence alongside mood symptoms may be interpreted in a myriad of ways.[7,8] Indeed, very much like anxiety, irritability's role as a potential precursor to these macrophenomena indicates that it may be a component of the same core entity, alongside anxiety and mood symptoms. Alternatively, irritability may be more indicative of an epiphenomenon that occurs somewhat independent of mood symptoms.

Irrespective of these relational conjectures, approaching anxiety pragmatically in the same way as we have tried to approach irritability, namely by adopting a broad and transdiagnostic perspective, may reveal nuanced findings that account for important factors such as psychosocial impacts on the manifestation and interpretation of the symptoms.

https://doi.org/10.1192/bjp.2026.10627 Published online by Cambridge University Press

The observation of increased prevalence, as well as the argument put forward by Miriam Olivola et al[9] for earlier detection of anxiety disorders, has prompted our proposal to refocus on the nexus between anxiety and depression. The aim would be to better understand the connection between these two sets of phenomena at all levels, ranging from physiology and pathophysiology through to our emerging understanding of neural networks and cognitive models within the brain and mind, to help reconfigure our symptomatic profiling of the phenomena and their classification into disorders.

In our view, this understanding and re-envisioning of anxiety is critical because it is likely to shed light on its true ontology when it strays outside of its normal physiological and emotional functions, either because of severity or chronicity, or because of as yet poorly understood functions that it serves within systems that underpin other psychiatric disorders such as depression.

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First received 5 Mar 2026, final revision 5 Mar 2026, accepted 5 Mar 2026

Acknowledgements

We thank the Greek Young Matrons' Association (GYMA) for their ongoing support.

Author contributions

G.S.M. drafted the initial manuscript. G.S.M., E.B., G.S. and K.S. contributed to, edited and approved the final manuscript.

Funding

The authors received no financial support for the research, authorship and/or publication of this article.

Declaration of interest

G.S.M. has received grant or research support from the Wellcome Foundation in the UK, National Health and Medical Research Council, Australian Rotary Health, NSW Health, American Foundation for Suicide Prevention, Ramsay Research and Teaching Fund, Elsevier, AstraZeneca, Janssen-Cilag, Lundbeck, Otsuka and Servier; and has been a consultant for AstraZeneca, Janssen-Cilag, Lundbeck, Otsuka and Servier. He is the recipient of an investigator-initiated grant from Janssen-Cilag (PoET Study), joint grant funding from the University of Sydney and National Taiwan University (Ignition Grant) and grant funding from The North Foundation. He is Editor-in-Chief of the *British Journal of Psychiatry* and College Editor and did not take part in the review process of this article. K.S. and G.S. have received grant funding from the GYMA. E.B. has received joint grant funding from the University of Sydney and National Taiwan University (Ignition Grant), grant funding from The North Foundation and grant funding from the GYMA.

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https://doi.org/10.1192/bjp.2026.10627 Published online by Cambridge University Press