

# 'Unheard and undertreated': Menopausal mental health (September editorial)

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In our March 2018 Special Issue on Chronic Conditions and the Menopause, the absence of papers on mental health was a glaring omission. Unable, at the time, to find authors to contribute on this fundamental topic, we had failed in our objective to provide a truly rounded and holistic overview of the issues at hand. Debilitating as vasomotor symptoms can be, they are, by a significant majority, somewhat expected. For the countless perimenopausal women questioning their sanity and memory, however, there is often a sense of bewilderment and incredulity; yet, their suffering is all too real. The average age of menopause in the Western world is 51. In the UK, the highest suicide rate in females is seen between the ages of 50 and 54.<sup>1</sup> While correlation does not, of course, equal causation, this statistic should make us sit up and take notice.

It is from the early 40s, during the perimenopausal years, that symptoms of premenstrual syndrome also tend to worsen, and those with premenstrual dysphoric disorder (PMDD) may find their condition increasingly difficult to manage. This should be of little surprise given that symptoms associated with premenstrual disorders are believed to be a result of an abnormal physiological response to normal hormonal changes. Around 15% of PMDD sufferers attempt to take their own lives.<sup>2</sup> We cannot afford to be complacent.

And, yet, somehow, the connection between reproductive hormones and mental health remains poorly understood and vastly under-researched. While schizophrenia has a typical onset in the early adult years, we see a second peak in females in the menopausal transition.<sup>3</sup> Women with bipolar disorder are known to have significantly more depression and mood elevation symptoms during the later perimenopausal years compared with those earlier in the transition or in later post-menopause.<sup>4</sup> We know that hormone replacement therapy (HRT) is of more benefit in menopausal mood disorders than anti-depressant therapy, but we don't yet fully comprehend why.

In this special issue, it is a privilege to include author Rose George's piece 'High bridges and low mood: the

unheard voices of menopause', giving us an articulate and much-needed glimpse into the 'powerful and damaging cognitive and emotional upheaval' of hormonal disruption. She writes that women are 'still unheard and undertreated', a theme that reverberates throughout this edition. In 'Managing the Psychological Sequelae of Premature Ovarian Insufficiency (POI)', psychotherapist Dani Singer states that POI is a 'life-altering and emotional diagnosis for 1–3% of young women' and implores us to break bad news with compassion and sensitivity. We are reminded of the importance to truly listening to our patients and that 'primary care practitioners can play a vital role in mobilising processes to help young women self-manage effectively'. Empowerment is key.

GP Mandy Leonhardt's review of the evidence in 'Low mood and perimenopause – Should General Practitioners prescribe hormone replacement therapy or antidepressants as first line therapy?' should be compulsory reading for all. Simultaneously thorough and succinct, Leonhardt further cements the case that perimenopausal depression is a subtype of reproductive depression explaining that this has 'important clinical implications' for its prevention and/or treatment. While the 2015 NICE guidelines recommend consideration of HRT and/or cognitive behavioural therapy (CBT) as first-line treatment for mood disorder arising in menopause, over half of GPs prescribe antidepressants ahead of estrogen. As a nation, it appears that clinicians are still in the grip of the Women's Health Initiative hangover.

Premenstrual disorders are prevalent throughout reproductive life, from menarche through to menopause, and, as such, we felt it important to include Emma Bannister's work on the potential role of inflammation in psychiatric upset. Her article provides a fascinating insight into the theories surrounding

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neuroinflammation and the GABAergic system, and echoes the research of consultant psychiatrist Edward Bullmore. In his book ‘The Inflamed Mind’, he questions whether our understanding of mental illness, and our current treatments, is inherently flawed. Professor Bullmore explains that the menopausal transition is associated with an increase in peripheral inflammation – along with ‘a high rate of depression and antidepressant drug use’.<sup>5</sup>

A 2018 paper published in *Frontiers in Aging Neuroscience*, ‘Inflammation: Bridging Age, Menopause and APOEε4 Genotype to Alzheimer’s Disease’, details menopause-related immune drivers and suggests that the activation of microglia and neuro-inflammatory mechanisms may be involved in at-risk aging females.<sup>6</sup> The authors note that estradiol treatment decreases pro-inflammatory cytokines and MMP-9 – an inflammatory marker associated with cancer, arthritis, COPD and cardiovascular disease. The role of HRT in dementia prevention has, thus far, been contentious, and this is further explored in Pertesi et al.’s ‘Menopause, cognition and dementia – a review’. It is suggested that there is a ‘complex interaction between menopausal stages, HRT and genetic status’, with the authors recommending that ‘future interventional studies take a more personalised approach towards HRT use in postmenopausal women, by taking into account genetic vulnerability in dementia’.

A randomised controlled trial, at the University of Illinois in Chicago on PMDD and mindfulness-based stress reduction (MBSR) – known to reduce stress processes in other populations – completed in spring 2019. The results will be published next year. Meanwhile, in this issue, GP Wendy Molefi-Youri asks ‘Is there a role for mindfulness-based interventions (here defined as MBCT and MBSR) in facilitating optimal psychological adjustment in the menopause?’

NICE (2015) recommends CBT as a treatment option for women who experience anxiety during the menopausal transition, and this may be of particular relevance for patients who cannot or choose not to take hormonal therapy.<sup>7</sup> Similarly, appreciating that HRT is not a universal panacea, Shahmohammadi et al.

examine ‘The efficacy of herbal medicines in anxiety and depression in peri- and post-menopausal women: A systematic review and meta-analysis’. There are hints of promise, particularly in the area of the gut microbiome and the metabolism of bioactive isoflavone compounds, but the need for higher quality data is manifest.

I am grateful to all who have contributed their time and energy to this edition of *Post Reproductive Health*. If the papers within can serve as a springboard for further discussion and engagement in this arena, we will have achieved our aim. We may be scratching at the surface yet, but we have opened up the conversation. This Special Issue on Menopause and the Brain has been a long time coming. I hope it has been worth the wait.

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