

The microbiome & the menopause - an editorial meander

The gut microbiome is affected by diet, age, the environment, metabolic status, infections, antibiotics and hormones. It has a collaborative function with the brain nexus and as such, will be explored in every aspect of the way humans feel. This may appear an intimidatingly broad raft of inter-relationships to consider but how we feel about health and ill-health does depend on our gut/brain reciprocity.

It is a field that will encroach on all stages of women's health and the new vocabulary the topic uses will need to be understood by us if we are to gauge the value of research that appears in the journals. As an example, let us consider an article entitled "Impact of the gut microbiome composition on social decision-making" by [Falkenstein et al](#) (*PNAS Nexus* 2024;3:pgae166).

Your editor was attracted to the publication as an entrée to possible effects of menopausal transition hormone variations on emotions and behaviour. However, it rapidly became clear that I had a steep learning curve ahead of me if I was to absorb the gist of the research presented.

The authors begin by explaining that the gut microbiome has an important role in socio-affective behaviour which they explore by experimentally adjusting volunteers' intake of synbiotics.

To follow the science I would have to grasp the vocabulary.

It turns out that **socio-affective behaviour** encompasses:

- Empathy: The ability to understand and share the feelings of others.
- Emotional Regulation: The processes by which individuals influence their own emotional experiences and expressions.
- Social Communication: The use of verbal and non-verbal cues to interact with others, including body language, facial expressions, and tone of voice.
- Prosocial Behaviour: Actions intended to benefit others, such as helping, sharing, and comforting.
- Social Cognition: The mental processes involved in perceiving, interpreting, and responding to social stimuli

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Synbiotics are a mixture of probiotics (beneficial gut bacteria) and prebiotics (non-digestible fibre that help these bacteria grow). Specifically, they are a combination of ingredients that work synergistically in one's digestive tract.

It transpires that people fed synbiotics do change their serum levels of tyrosine, a dopamine precursor, which in turn can affect social decision-making (which the investigators tested using altruistic game theory methods).

The study highlighted that participants with the most significant initial microbiome imbalances showed the greatest behavioural changes and tyrosine level reductions, which underscored the potential for diet and gut health to influence the way people view things.

Interestingly the participants were limited to men, which the authors explain as follows: "We chose only men for our study, particularly due to the hormonal factors in women that are significant in decision-making," ([Moulun Medscape 2024](#)). Is this sexist - or pragmatic?

Emotions & GIT responses

We are all aware that our emotions affect our GIT but this is tricky to research. Scientists have found a way around this problem by giving volunteers a pill to ingest that monitored pH, pressure, and temperature in their GI tract while they watched videos inducing emotions like disgust, fear, happiness, and sadness ([Porciello et al Neuroscience 2024 doi 10.7554/eLife.85567](#)).

The study found a significant correlation between stomach acidity and emotional perception. More acidic pH levels corresponded with increased feelings of disgust and fear, while less acidic levels were linked to happiness. Participants also reported gastric sensations, such as nausea, particularly during fearful and disgusting clips. Disgusting stimuli increased heart rate variability. This innovative use of ingestible pills highlights the stomach's role in emotional experiences and suggests new research pathways for understanding psychosomatic disorders.

Probiotics & bone health

In another piece of research, scientists tested the theory that giving women a probiotic in their early postmenopausal years could reduce age-dependent bone loss ([Gregori et al JAMA Netw Open 2024;7:e2415455](#)). In Sweden *Limosilactobacillus reuteri* treatment was assigned to more than 200 women who were followed up for two years after receiving either high-dose or low-dose *L. reuteri* or a placebo together with cholecalciferol.



The primary outcome—tibia volumetric bone density—along with secondary outcomes such as areal bone density of the lumbar spine and hip, and bone turnover markers, showed no favourable impact from the probiotic supplementation.

I am convinced that the composition and manipulation of the gut microbiome will feature as an important variable in menopause-related publications going forward, and we will have to decide what is evidence-based science, and what is hokum.

Menopause, Misogyny & Medicalisation

This title is a sound-bite from an article that discussed whether the menopause is becoming too publicised, or not. This followed a feature in an issue of *The Lancet* entitled *Menopause 2024*.

The edition contained a leader called “Time for a balanced conversation about menopause” ([Lancet](#) 2024;403:877) and states that “Historically, women have been poorly served by both the research community and by society” and asks for a less emphasis on framing the menopause transition as “a disease of oestrogen deficiency that can be eased only by replacing the missing hormones” thus over-medicalising a natural process ([Meredith Medscape](#) 2024). An editorial in *Climacteric* gave a balanced and sensible response to this article (Nappi R, Panay, N Davis *Climacteric* 2024)

In the UK at least, there has been a push for the establishment of “Menopause Hubs” where information from clinical associates can be disseminated, assistance can be obtained and support provided as it is unrealistic to rely solely on time-constrained General Practitioner consultations ([El-Awady Medscape](#) 2024). There needs to be a more open acceptance of discussions of menopausal physiology so women know what to expect, and society does not devalue age. Cultural narratives should celebrate life-cycles and health-care professionals should be able to combat “menopause myths” and virtual health providers (both real and electronic) can be a source of education.

Since more than one million of the world’s population go through the menopause each year, and Artificial Intelligence assisted chatbots are the source information for more and more people, they can have practical role in the demand for knowledge. Personal, face to face, dialogue is the best form of inter-action and for countering misconceptions. For human assistants the following list is proposed as a starting point ([Seegert Medscape](#) 2024):



- Acknowledge to patients that you may not have all the answers; be willing to do follow-up research and have additional conversations as needed.
- Have a list of proven, scientifically-based, safe therapies to suggest and discuss.
- Ask for more details if a patient chooses to use a treatment based on influencer recommendations; review potential risks and encourage a follow-up visit after several months to assess efficacy and counsel them to stop if they are not improving or are experiencing adverse side effects.
- Share evidence-based plain-language books and articles with patients.
- Develop a simple fact sheet on various symptoms and treatments or use one from a credible source like The Menopause Society.
- Recommend several vetted user-friendly websites for more information about a specific symptom or condition.
- Suggest several social media menopause influencers whose messages are consistent with best practices.
- Don't write off menopause as simply a normal phase of life; regardless of age, clinicians should appropriately treat symptoms.
- Recognize your limitations; refer to a menopause specialist in your network when appropriate.
- Take continuing medical education courses, fill in knowledge gaps with additional reading, or consider becoming a certified menopause specialist.

There is considerable evidence that most young people use technology platforms as their first port of call for medical matters. They turn to the Internet to provide information and guidance. It is not a big step to using programmes as a conduit to self-help. Work shows Internet-accessed Cognitive Behavioural Therapy can help with the alleviation of anxiety and depression ([Beniet et al JAMA Psychiatry 2023 doi 10.1001/jamapsychiatry.2023.1675](#)).

Is it fanciful to believe that as younger people mature, they may turn increasingly to screen-delivered means of therapy? Are we a generation away from menopause information and guidance being majorly derived from on-line sources?

Estrogen Therapy

This is a presentation of the place of estrogen therapy from the United States perspective.

([Bacon et al Medscape 2024](#)). The summary gives normal values for estrogen throughout the life cycle, which estrogens are produced from which organs, different

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types and doses of pharmaceutical products with their names, the current status of hormone therapy, and discusses controversies. It has useful references.

It was an unexpected gem of information which is recommended to all practicing clinicians, no matter where they live. Why not Ctrl - click <https://emedicine.medscape.com/article/276107-overview> and have a browse yourself?

Recurrent UTIs revisited

This topic has been addressed in previous *Menopause Matters* but another article has appeared that specifically looks at the diagnosis and management in older women. It may be useful in providing up-to-date antibiotic options for prescribers, or to give to patients guidance and support. It is highly recommended ([Huang et al](#) *JAMA Intern Med* 2024 doi 10.1001/jamainternmed.2024.1069).

Follow up of discrimination against Black women

Last month's *Menopause Matters* concluded with a piece about racial discrimination and ended saying that "discrimination is a significant factor in the experience of VMS, particularly in Black women" ([Reeves et al](#) *Menopause* 2024;31:484-93).

Now an article has been published which examines a possible neurological explanation for this phenomenon using cerebral imaging ([Elbasheir et al](#) *JAMA Netw Open* 2024;7:e2416588). The study involving 90 Black women from the United States, correlated self-reported racial discrimination with increased functional connectivity in the brain, particularly in emotion processing networks involving deep brain regions, like the brainstem and midbrain. This heightened connectivity was linked to accelerated DNA methylation age, indicating a biological aging process.

The study's significance lies in uncovering how racial discrimination may induce neuroplastic changes and underscores the role of racial discrimination in exacerbating brain health disparities, potentially explaining the higher prevalence of mental health issues and cognitive disorders in Black individuals.

Biomarkers for Alzheimer's Disease

In another study, images of the brain using Magnetic Resonance Imaging were used as a biomarkers to predict future function. Specifically, researchers looked for MRI evidence of altered functional connectivity in individuals and correlated this with

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Alzheimer's Disease in later life. As part of the UK Biobank study they reviewed the MRI scans of 80 individuals who developed dementia up to nine years after imaging, compared with 1,000 matched controls ([Ereira et al Nat Mental Health 2024 doi 10.1038/s44220-024-00259-5](#)).

This is of huge importance given the long-term predictive nature of the findings. A screening test for Alzheimer's Disease would be a genuine "game-changer" and the progress in MRI technology is very promising. To quote an editorial comment about a breakthrough in the field:

"Magnetic resonance imaging (MRI) was invented more than 50 years ago and has continued to improve in resolution and image quality. These improvements are the result of ever more powerful magnets, which make for very heavy and noisy machines that require extensive shielding. These high-power MRI machines are also extremely expensive, which greatly limits patient access. By applying machine learning to the output of a lower-power MRI device, it has been possible to address these concerns ([Zhoa et al Science 2024 doi 10.1126/science.adm7168](#)). The lower-power machine was much cheaper to manufacture and operate, more comfortable and less noisy for patients, and the final images after computational processing were as clear and detailed as those obtained by the high-power devices currently used in the clinical setting".

(MM editor: The device uses one sixtieth the magnetic field strength of the standard MRI models common in hospitals today).

MM editor's comment. The use of imaging to explain function, is a concept that is growing in medical research. It is not new but its expansion in the field of neurology has become more advanced, more subtle but much more complicated.

As non-experts in the fields of physics and radiology, clinicians have to rely evermore trustingly on data that is beyond their understanding, and the use of vocabulary beyond their comprehension.

Take the summary above as an example:

We are asked to accept that emotions experienced by discrimination, engender changes in certain areas of the brain and that these changes are detectable using advanced imaging technology.

In the actual article the authors introduce their findings by saying they are measuring "greater resting-state functional connectivity (RSFC) between the locus coeruleus (LC) and precuneus" using functional Magnetic Resonance Imaging and "Significant indirect effects were observed for the association between racial discrimination frequency and DNA methylation age acceleration." Note this is in their abstract. It is not in the detail of their methodology. It is in their introduction



to the article in a non-specialist journal – JAMA Network Open – so presumably they, and the journal’s editors believe their readers will follow the language without resort to dictionaries.

Are the general medical journals becoming too technical?

It is inevitable that science creates its own living lexicon, but are the journals accepting language that is too esoteric? Reading the full article, there is a great deal of explanation for fellow experts to enjoy the detail, so it is not a question of space.

To me it is a question of “being in touch” with your readership.

I have two suggestions:

- *Once a year the editors of the general journals publish explanations of new phrases that commonly appear in the abstracts of the articles they publish. Additions could be sent to a panel of GPs who could say if they understand them – or not. This could be done on-line – to everyone’s advantage.*
- *Get ChatGPT to write a “common language” two-paragraph entrée. This is not dumbing-down – it’s educating.*

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Menopause Matters is a monthly review of matters menopausal that have recently appeared in the journals. These summaries and opinions do not necessarily reflect the views of the SA Menopause Society or the Australasian Menopause Society. Any clinical decisions made on the data presented are exclusively at the reader’s discretion. ChatGPT has been used to assist with the production of some of the summaries.

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