

Depression and menopause: why antidepressants are not enough?

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Background: Women are more prone than men to depression, from puberty onwards, with a specific exposure across the menopausal transition, that contributes to a specific “window of vulnerability”. Gender differences, related to a different sexual hormones scenario and hormone’s secretion patterns across the lifespan, contribute to the specific women’s vulnerability to mood disorders up to depression in critical moments of their life-cycle. However, controversy still exists in considering the fluctuation/loss of estrogen, and, possibly, androgens, as a specific etiologic factor(s) contributing to depression in perimenopause and beyond.

Aims of the presentation are to review:

- 1) the role of sexual hormones in modulating neuroplasticity and improving neuronal repair mechanisms in the brain;
- 2) the different mechanisms, direct and indirect, through which sexual hormones may reduce the vulnerability to depression and improve mood;
- 3) the interaction between changes in menopausal hormone levels, mood disorders, associated neuropsychological comorbidities, including sleep disorders, and aging;
- 4) to evaluate the currently available therapeutic options of perimenopausal mood disorders:
 - a) treatment of light to moderate mood disorders with hormonal therapy;
 - b) treatment of major depression with antidepressant;
 - c) the synergic effect between hormonal therapy and antidepressants in treating menopausal depression, with earlier therapeutic response and optimized clinical outcomes.

Results: Depression across the menopause has a multifactorial etiology. Predictive factors include:

- previous depressive episodes such as premenstrual syndrome and/or post-partum depression;
- comorbidity with major menopausal symptoms, especially hot flashes, nocturnal sweating, insomnia;
- menopause not treated with hormonal replacement therapy;
- major existential stress;
- elevated Body Mass Index;
- low socioeconomic level and ethnicity.

Specifically, postmenopausal depression is more severe, has a more insidious course, is more resistant to conventional antidepressants in comparison with the premenopausal women and has better outcomes when antidepressant are combined with hormonal therapy.

Conclusion: the current evidence contributes to a re-reading of the relationship between menopause and depression. The combination of antidepressants with a well tailored hormone therapy seems to offer the best therapeutic potential in terms of efficacy, rapidity of improvement and consistency of remission in the follow-up.