Bipolar and Menopause: Case Reports of Late Onset Bipolar Disorder Following Acute Withdrawal of Hormone Replacement Therapy

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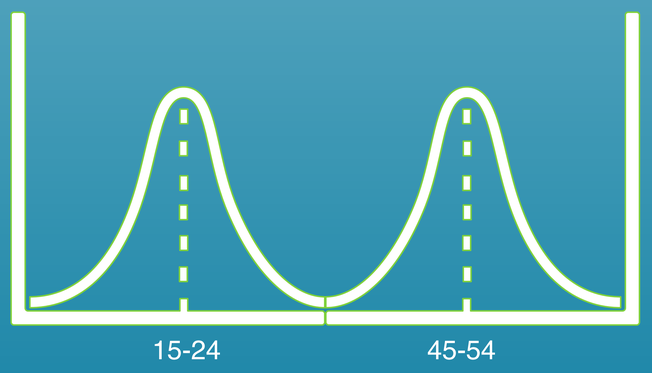
Background

The role of estrogen in bipolar disorder is not fully understood but evidence suggests that menopause may be associated with bipolar symptoms. Further work is needed to explore how menopause interacts with bipolar disorder over time (Perich, 2017). The relationship between bipolar disorder and menopause has been analyzed by few studies; an important but still debated topic is whether typical sex hormonal changes of menopause may be linked to development of bipolar disorder in middle-aged women (Aragno, 2022). Though the onset of menarche increases sex hormones and is linked to new onset bipolar I disorder, acute withdrawal of sex hormones leading to new onset bipolar I disorder is less understood. While traditional menopause may slowly reduce estrogen over time, those with total hysterectomies and receiving hormone replacement therapy (HRT) may give us more insight to the role estrogen plays in the conversion to bipolar disorder.

Bipolar I age of onset showing two peaks (Chen, 2017)



CASE 1

- **AGE 40** — Total hysterectomy with hormone replacement therapy(HRT) for 14 years
- **AGE 54** — Diagnosed with breast cancer and stopped HRT, cancer surgically removed with no signs of spreading.
- **WITHIN 2 MONTHS** — Started having depressive and hypomanic symptoms
- **WITHIN 6 MONTHS** — First episode of mania leading to multiple hospitalizations across 4 states

CASE 2

- **AGE 42** — Total hysterectomy with hormone replacement therapy(HRT) for 9 years
- **AGE 52** — Started becoming inconsistently compliant with HRT
- **WITHIN 5 MONTHS** — Started having bizarre behavior, hypomania and elevated anxiety
- **WITHIN 8 MONTHS** — First episode of mania leading to multiple hospitalizations

Discussion

According to Chen et al, menopausal transition usually begins in mid-to-late 40s and always lasts several years, most commonly 4-5 years. They go on to describe how estrogen multiple key factors in protecting the brain including a role in the production of brain-derived neurotrophic factor(BDNF) involved in intracellular signaling pathway found to be low in both depressed and manic patients. Acute decreased levels of estrogen impairs the production of BDNF, decreasing the protective effects and may further increase the risk of developing bipolar disorder. Chen et al goes on to describe how estrogen also plays an important role in the well-functioning and myelination of glial cells and induces the expression and release of growth factors by glial cells that promote neuronal survival. Loss of glial cells from decreased estrogen may exacerbate mood symptoms and diagnostic conversion to bipolar disorder.

Conclusion

Our cases support the theory that estrogen is protective to the brain and that acute withdrawal can be a primary trigger for converting to bipolar I.

References

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