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Mini-review findings including depression and genes involved in women

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Abstract
Women subjected to depression is one of the most prevailing causes among psychiatric diseases. There is a relation between social support and depression in whose predisposing factors are genetic, psychological, biological, environmental, and hormonal [1]. Our main focus of this review is to understand the genes and factors contributing to depression in women. We used PubMed and google search and finally concluded based on 19 papers extending back to the last five years and human species using Mesh terms. Among women with recently diagnosed with cancer and depression, the women must be given the benefit for genetic counseling and must be directly evaluated for current research intervention to reduce risk factors in women.

Keywords: depression, women, genes

Introduction
Depression is the leading cause of disability worldwide, and its prevalence is 2 times higher in women than in men. There is, however, a lack of data on sex-specific pathophysiology [2]. General orientation to some of the major accomplishments of the field of depression research. we aim to contribute to the understanding of genes and depression factors in women by reviewing selected components of the scientific pieces of literature on humans examining how mothers' physical contact with her infants, genetics, history of anxiety and depression and early-life and recent-life experiences contribute to individual difference. These studies together indicate that multiple biological and environmental factors beyond female maternal state shape affective responses during the postpartum period, and probably do so in an interactive manner. Furthermore, the similar capacity of some of these factors to modulate anxiety and depression in mothers suggests cross-species conservation of mechanisms regulating postpartum affectivity [3]. The genetics involved with the relationships between genes/pathways associated and known drug targets is a promising tool for drug repurposing and identification of new pharmacological targets. Increase in power thanks to larger samples and methods integrating genetic data with gene expression, the integration of common variants and rare variants, are expected to advance our knowledge and assist in personalized psychiatry [4].

Methods
We searched papers published in English on review, depression, genes, and women using the Pubmed and google search. Our search identified 75 papers, which were reviewed. We also searched for referenced papers to identify further studies. This review was finally based on 19 papers extending back to the last five years and human species has Mesh terms. Although our primary focus is on depression in women and genes involved could help us understand the factors for depression.

Results
For this review, 19 papers extending back to the last five years and human species using Mesh terms. This review is based on current research on the benefits of understanding factors contributing to depression and genes involved in women.

Mothers' physical contact with her infants
Maternal depression complicates a large proportion of pregnancies. Current evidence shows numerous harmful effects on the offspring. Reviews, which include depression, concluded that stress has harmful effects on the offspring's outcomes neuro-cognitive development, temperament traits, and mental disorders [5].

In this review, suggests that different susceptibility to postpartum depression (PPD) among postpartum women may be explained by the presence or absence of genetic variants that confer increased risk. We review three categories of genes known to code for proteins associated with depression in the general population or proteins known to be affected by childbirth for their possible association with PPD, including genes related to central nervous system monoamine availability, pro-inflammatory cytokines, and brain neuropeptides [6].

This review was to investigate whether there is an association between exposure to maternal antidepressants during pregnancy and epigenetic changes in the newborn. Epigenetic mechanisms that are important for the regulation of gene expression and differentiation in the fetus and the newborn child. Symptoms of

maternal depression and antidepressant use affect up to 20 % of pregnant women and may lead to epigenetic changes with a life-long impact on child health. [7].

Genetics

The genetic etiology of reproductive affective disorders, including premenstrual dysphoric disorder (PMDD) and postpartum depression (PPD). The most commonly studied genes include SERT, COMT, MAOA, BDNF, and ESR1 and 2. Evidence is stronger for the genetic basis for PPD, with positive associations found in family studies and in several genes associated with major depression as well as genes involved in estrogen signaling but only when PPD onset is shortly after delivery [8].

Pathogenic mutations in breast cancer susceptibility genes BRCA1 and BRCA2 increase risks for breast, ovarian, fallopian tube, and peritoneal cancer in women also one of leading factors for depression; interventions reduce risk in mutation carriers. Among women without recently diagnosed BRCA1/2-related cancer, the benefits and harms of risk assessment, genetic counseling, and genetic testing to reduce cancer incidence and mortality have not been directly evaluated by current research [9].

Clinical features have been observed in common between migraine and epilepsy (such as episodic attacks, triggering factors, presence of aura, frequent familiarity), but only in recent years, researchers have really engaged in finding a common pathogenic mechanism. A genetic link between these two diseases is particularly evident in familial hemiplegic migraine: mutations of ATP1A2, SCN1A and CACNA1A genes, identified in this disease, have also been involved in different types of epilepsy and febrile seizures. A chronic lowering of 5-HT (serotonin) levels has been demonstrated both in migraineurs and in depressed patients; amitriptyline and venlafaxine are the most indicated drugs in the treatment of migraine with comorbid depression currently [10].

Estradiol increases tryptophan hydroxylase-2 and serotonin transporter expression and decreases the expression of serotonin 1A receptor and monoamine oxidase A and B through the interaction with its intracellular receptors. The understanding of molecular mechanisms of estradiol regulation on the protein expression that modulates serotonin neurotransmission will be helpful for the development of new and more effective treatment for women with depression [11].

Many of the genes for which mutations have been associated with primary ovarian insufficiency(POI), either isolated or syndromic cases, function within mitochondria, including MRPS22, POLG, TWNK, LARS2, HARS2, AARS2, CLPP, and LRPPRC. Collectively, these genes play roles in mitochondrial DNA replication, gene expression, and protein synthesis and degradation. Although mutations in these genes clearly implicate mitochondrial dysfunction in rare cases of POI, data are scant as to whether these genes in particular and mitochondrial dysfunction in general, contribute to most POI cases that lack a known etiology [12].

Childhood physical abuse (PA) and sexual abuse (SA) interact with monoamine oxidase A (MAOA) gene polymorphism to modify risk for mental disorders. In addition, PA and SA may alter gene activity through epigenetic mechanisms such as DNA methylation, thereby further modifying risk for disorders.

SA, not PA, was associated with hyper-methylation of the MAOA first exon relative to no-abuse, and the association was robust to adjustment for psychoactive medication, alcohol and drug dependence, and current substance use. SA and MAOA-u VNTR genotype, but not their interaction, was associated with MAOA methylation. SA associated with all measured mental disorders. Hyper-methylation of MAOA first exon mediated the association of SA with current depression, and both methylation levels and SA independently predicted lifetime depression. Much remains to be learned about the independent effects of SA and MAOA-u VNTR genotypes on methylation of the MAOA first exon [13].

The efficacy of the CRF_1 receptor antagonist GSK561679 in female post-traumatic stress disorder (PTSD) patients. While GSK561679 was not superior to placebo overall, it was associated with a significantly stronger symptom reduction in a subset of patients with probable CRF system hyperactivity, i.e., patients with child abuse and CRHR1 SNP rs110402 GG carriers. Here, we test whether blood-based DNA methylation levels within CRHR1 and other PTSD-relevant genes would be associated with treatment outcome, either overall or in the high CRF activity subgroup. These reviews support a possible role of CRHR1 methylation levels as an epigenetic marker to track response to CRF_1 antagonist treatment in biologically relevant subgroups. Moreover, pre-treatment NR3C1 methylation levels may serve as a potential marker to predict PTSD treatment outcome, independent of the type of therapy. However, to establish the clinical relevance of these markers, the findings require replication and validation in larger studies [14].

Carriers of pre-mutation are at risk of developing a spectrum of neurological, psychiatric and immunological disorders in adulthood. Fragile X-associated disease caused by a dynamic mutation (expansion of CGG repeats) can be divided into three disorders: FXS - Fragile X syndrome, FXPOI - Fragile X-associated primary ovarian insufficiency, FXTAS -Fragile X-associated tremor/ataxia syndrome, which can be present in few generations of one family. Immuno-mediated disorders are more common in pre-mutation carriers as compared to the control group, especially hypothyroidism and fibromyalgia. Although FMR1-associated conditions are not curable, timely diagnosis through genetic testing is important as it can lead to the implementation of treatment strategies and behavioral interventions considered to improve symptoms. Knowledge of expanded allele status for females helps them to make more informed reproductive decisions [15].

History of anxiety and depression

In women, changes in estrogen levels may increase the incidence and/or symptomatology of depression and affect the response to antidepressant treatments. Estrogen therapy in females may provide some mood benefits as a single treatment or might augment clinical response to antidepressants that inhibit serotonin reuptake [11].

Stress as a variable in depression research has led the program in many new directions, some of which I discuss briefly below. A opinion in understanding the role of stress and how it eventuates in depression is the central challenge in understanding the etiology of most forms of depression [16].

Suicidal behaviors are common in the general population and are

so a major public health problem. In order to improve suicide prevention and to reduce mortality by suicide, it appears essential to better identify suicide risk factors. Seasonality, circadian rhythms, and sleep abnormalities have been already associated with numerous psychiatric disorders. This review aimed to characterize the associations between seasonality, circadian rhythms, sleep and suicidal behaviors including suicide attempts and completed suicide

A suicide circadian distribution also exists depending on the suicidal behavior intensity and of the age. Numerous sleep disorders are also suicide risk factors and can be treated with Chrono therapeutics. Better identification of seasonality, circadian rhythms and sleep abnormalities in suicidal behaviors could allow better prevention in suicidal attempts and a reduction in death by suicide [17].

The neurotransmitter serotonin has a role in affective disorders such as depression and anxiety, as well as sleep, cognitive function, and appetite. The only difference between variants of the 5-HT transporter-linked promoter region (5-HTTLPR) has been investigated in relation to the behavioral effects of supplementation with the serotonin precursor amino acid l-tryptophan (TRP). The effects of 5-HTTLPR genotypes are usually compared between the alleles that are either high (L/L') or low (S/S') expressing of mRNA for the 5-HT transporter receptor. Yet, another key genetic variable is sex: in women, the S/S' genotype predicts sensitivity to improved mood and reduced cortisol by TRP supplementation, during stressful challenges, whereas the L/L' genotype protects against stress-induced mood deterioration [18].

Premature ovarian insufficiency (POI) is defined by the presence of primary or secondary amenorrhea, for at least 4 months, before the age of 40 years associated with follicle-stimulating hormone levels in menopausal range, exciding 40 UI/L. An important genetic component exists, supported by both a frequent recurring familiar event (20-30%) and the association with other different genetic disorders, in particular, the X chromosome defects and the implication of some different genes with significant functions in ovarian development. Moreover, it should be considered the associate comorbidities of POI such as bone loss, cardiovascular disease, and endocrine disease [19].

Early-life and recent-life experiences

The "Cumulative Psychological Stress and Cardiovascular Disease Risk (CVD) in Middle-Aged and Older Women" study is embedded within the landmark Women's Health Study (WHS) follow-up cohort and seeks to evaluate the individual and joint effects of stressors (cumulative stress) on incident CVD risk, including myocardial infarction, stroke, coronary revascularization, and CVD death [20].

For most of the women, the diagnosis of Premature ovarian insufficiency (POI) is unexpected because there are no obvious signs or symptoms that precede the cessation of periods with a normal menstrual history, age of menarche and fertility prior to the onset of menopause. The diagnosis of POI has a deleterious psychological impact on the emotional sphere of the women affected: anger, depression, anxiety, and sadness are common and the fact that the diagnosis coincides with infertility needs psychological support [19].

Females have unique and additional risk factors for neurological disorders. Among classical estrogen receptors, estrogen receptor beta (ERβ) has been suggested as a therapeutic target. However, little is known about the role of ERβ in the female brain. Six electronic databases were searched for articles evaluating the role of ERβ in the female brain and the influence of age and menopause on ERβ function. To establish potential therapeutic and preventive strategies targeting ERβ, future studies should be conducted in humans to further our understanding of the importance of ERβ in women's mental and cognitive health [21].

Particularly in recent years, there has been an enormous focus on maternal depression occurring prenatally or postnatal, suspected to be especially disruptive of healthy development in the infant. Longitudinal studies, conducted mostly in high-income countries, reported higher levels of emotional, behavioral, and social difficulties in children of prenatally depressed women and women with postnatal depression [22].

Conclusions

According to this review study, the implications of women with recently diagnosed cancer and depression must be given the benefit for genetic counseling on factors such as having no support from relatives and family, knowledge of genetic testing is important as it can lead to the implementation of treatment strategies and behavioral interventions considered to improve symptoms, expanded allele status for females helps them to make more informed reproductive decisions. However, understanding genes involved in depression to establish clinical relevance, the findings require replication and validation in larger studies which can be directly evaluated for current research to reduce risk factors in women.

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Conflicts of interest

There are no conflicts of interest

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