Obsessive Compulsive Disorder
Risk Factors Behind OCD
Self-Study

Contributors
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There are several important risk factors behind general OCD and perinatal OCD, including genetic, hormonal, neuroendocrine and immunologic factors:

Genetic factors

Studies on genetic factors associated with perinatal OCD are limited. In general OCD, there does appear to be some heritability for OCD. Some genetic factors that are risk factors for general OCD that could be studied to see if these are risk factors for perinatal OCD include:

- **Neuronal and epithelial glutamate transporter gene (SC1A1)**

  Also known as EAAT3, located on chromosome 9p24; associated with glutamate transmission (gene codes for a glutamate transporter); no specific single nucleotide polymorphism has been found to be associated with OCD, however.

- **Chromosome 18**

  Two SNPs found in the large (Drosophila) homolog-associated protein 1 gene; possibly associated with a broad role of gene expression

- **PTPRD gene**

  Part of receptor protein tyrosine phosphatase family; helps with differentiation of glutamatergic synapse

- **Cadherin Clusters**

  CDH9 associated with general OCD

In terms of perinatal OCD and genetics, as noted above, there is not much data. There is data on genetic risk factors of postpartum depression, and these should be studied further to see if there are genetic risk factors included here that are also associated with perinatal OCD, especially when considering perinatal OCD is common with other disorders in the perinatal period (including depression):

- **Possible genome-wide linkage found in parts of chromosome 1 and 9**

- HMCN1 (hemicetin 1): on chromosome 1; largely in the hippocampus, involved with methyltransferase activity, when seen in rats, altered and there is a post-partum drop in estrogen; when there is HMCN1 polymorphism heterozygosity has been associated with symptoms of depression

- METTL13 (methyltransferase like 13): affects estrogen receptor-induced gene transcription due to involvement with methyltransferase activity

Other genes associated with postpartum depression

- SERT gene: short allele of the gene (S allele)- associated with mental health problems, depression

- COMT gene: Met/Met polymorphism led to low catechol-O-methyltransferase activity; low activity associated with this polymorphism had a positive association with immediate (6-8 weeks) post partum depression

- ESR1 gene: some small studies show some association

- OXTR gene: lower plasma levels of oxytocin are associated with postpartum depression

- MAOA gene: some studies show an association between a polymorphism of this gene and postpartum depression; two studies were positive only at 6 weeks postpartum but negative after this

Hormonal factors

There are several theories associated with hormonal factors associated with perinatal OCD. These theories include dysregulation or dysfunction of estrogen, progesterone, and oxytocin.

• **Estrogen and progesterone**

These may play a role, as they interact with serotonin. During pregnancy and the postpartum period, fluctuations in hormones occur rapidly. As these fluctuate, especially at the end of pregnancy, they could alter serotonergic transmission, reuptake and binding; data to support theory are scant.

• **Oxytocin**

Oxytocin is often elevated in pregnancy and the puerperium period. Patients with OCD without a personal or family history of a tic disorder were found to having higher levels of oxytocin in CSF. Some studies show links to oxytocin levels and severity of OCD. Oxytocin levels increase during pregnancy and this could contribute to symptoms of perinatal OCD as well.

Neuroendocrine factors

Neuroendocrine factors that are associated with general OCD include:

• **Corticotropin releasing hormone (CRH)**: OCD patients have been found to have higher levels of CRH in the CSF

• **ACTH**: when responding to CRH, blunts the effect of CRH in patients with OCD when comparing them to controls

• **Vasopressin**: elevated at baseline in patients with OCD

• **Cholecystokinin**: highest levels in the brain are in areas associated with anxiety; when a synthetic analog of cholecystokinin was given to patients with OCD (pentagastrin), this made people more anxious; however, statistical significance was not achieved in this study

When looking in the postpartum period and OCD:

• **Cortisol:** some previous studies have shown that there is more cortisol increase in women with postpartum OCD than healthy postpartum women when facing stress; also noted that women with postpartum OCD have higher afternoon cortisol levels than women postpartum who are healthy

• In previous fMRI studies, when looking at postpartum women with OCD, there is a heightened endocrine stress response when responding to stressful situations that involves the orbitofrontal cortex, the superior temporal gyrus, insula and the medial prefrontal cortex compared to healthy women during the postpartum period who had deactivation in these areas when responding to stress.

Immunology

Antibodies against prodynorphin (an endogenous opioid receptor) and decreased levels of beta-endorphins are seen in patients with general OCD, and there is evidence of increased inflammatory activity in general OCD.

For more information on how immune activity and autoimmune disorders are related to perinatal OCD, please see the self study section on autoimmune conditions associated with perinatal OCD.

Psychiatric Disorder

Psychiatric risk factors for the development of ppOCD include a personal history of depression, obsessive–compulsive personality disorder, avoidant personality disorder and the presence of OCD-related dysfunctional beliefs

OCD related disorders

There is not much data on OCD-related disorders and perinatal OCD. When seeing a patient with OCD or OCD symptoms, it is important to also ask about the following conditions, as symptoms of OCD are often co-morbid with the following disorders:

- Hoarding disorder
- Tic disorders
- Trichotillomania
- Body dysmorphic disorder
- Skin picking disorder

For each of these, the diagnosis is typically made in a similar way to non-perinatal patients; treatment is also usually the same (taking into account the increased risks if a woman is pregnant or breastfeeding).

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